965. *Energy–Entropy Relations in Acylations. Part I. Effects of Structure and of Polar Substituents.*

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The parameters of the Arrhenius equation, $k = Ae^{-E/RT}$, have been determined for various series of bimolecular second-order acylations

$$YY'C_6H_3{\cdot}NHZ + R{\cdot}COX \longrightarrow YY'C_6H_3{\cdot}NZ{\cdot}COR + HX$$

in benzene solution.

Both mono- and di-substituted anilines and one *N*-substituted derivative were used. Various acylating agents in both the aromatic and the aliphatic series were investigated, X being Cl, Br, or $CH_3{\cdot}CO_2$. Changes in Y, Y′ for reactions with any one acylating agent operate almost entirely through the activation energy, the frequency factor remaining approximately constant. Substituent effects are independent of the acylating species.

Substituents close to the reaction centre, whether in the acid chloride or in the aniline, affect *E* and log *A* in a complex manner. These energy–entropy relations are discussed in terms of the linear relation between *E* and log *A* which has been observed in many other series. A generally coherent picture can be formed if steric hindrance affecting the geometry of the transition state is assumed to give a correlated variation of *E* and log *A*, while upon this variation may be superimposed a polar effect which influences *E* alone.

A USEFUL means of studying the influence of substituents on reactivity is based upon the Arrhenius equation $k = Ae^{-E/RT}$, where *k*, *E*, and *A* are the rate constant, activation energy, and frequency factor respectively. One of the most important effects of a substituent group in a reacting molecule is to modify the activation energy. When a variable substituent is separated from the reaction centre by a benzene ring there are two classes of behaviour according to whether *A* remains constant or increases functionally with *E*.[1] The first type is the more characteristic and is exemplified in the benzoylation of anilines,[2] the alkaline hydrolysis of benzoic esters in 85% alcohol [3] or in 56% aqueous acetone,[4,5] and in the reaction between methyl iodide and dimethylanilines.[6] The second type is exemplified in the reduction of nitrobenzenes by titanous chloride [7] and in the alcoholysis of substituted benzoyl chlorides.[8] When the substituent group is in close proximity to the reaction centre steric effects complicate the picture and simultaneous variations in *E* and *A* occur. This has been shown in 15 esterification reactions,[9] in the alcoholysis of acid anhydrides,[10] and in the reaction between alkyl halides and tertiary amines.[11]

The energy–entropy relationship and its implications have been discussed by Leffler [12] and Blackadder and Hinshelwood.[13] The present investigation was designed to yield further information about the conditions determining the occurrence of the one or the other of the main types of behaviour.

In the reaction between an acid halide or an acid anhydride and an amine, the amine is

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[1] Laidler, Timm, and Hinshelwood, *J.*, 1938, 848.
[2] Williams and Hinshelwood, *J.*, 1934, 1079.
[3] Ingold and Nathan, *J.*, 1936, 222.
[4] Tommila and Hinshelwood, *J.*, 1938, 1801.
[5] Tommila, *Ann. Acad. Sci. Fenn.*, 1941, *A*, **57**, No. 13.
[6] Laidler, *J.*, 1938, 1786.
[7] Newton, Stubbs, and Hinshelwood, *J.*, 1953, 3384.
[8] Branch and Nixon, *J. Amer. Chem. Soc.*, 1935, **58**, 2499.
[9] Legard and Hinshelwood, *J.*, 1935, 587.
[10] Kosakikallio, *Ann. Acad. Sci. Fenn.*, 1954, *A*, II, 57.
[11] Winkler and Hinshelwood, *J.*, 1935, 1147.
[12] Leffler, *J. Org. Chem.*, 1955, **20**, 1202.
[13] Blackadder and Hinshelwood, *J.*, 1958, 2728.

nucleophilic and the acylating species is electrophilic. Available data refer chiefly to the reaction between substituted benzoyl chlorides and substituted anilines [2] in benzene [14] and nitrobenzene.[15] Substituents change the rate by influencing E, leaving the frequency factor approximately constant. The reactivity runs parallel with the positivity of the carbonyl-carbon atom and the negativity of the nitrogen atom. Previous investigations were confined to the effect of substitution in the benzene ring. The present work is designed to study the following: (1) structural variations within the acid chloride on the acylation of a given aniline in benzene solution; (2) change in X in the acylation of substituted anilines by R·COX, also in benzene solution; (3) *N*-substitution in the amine; and (4) changing the solvent composition in the acylation of some substituted anilines in benzene–nitrobenzene and benzene–phenyl cyanide mixtures (following paper).

EXPERIMENTAL

Materials.—Commercial products were purified by crystallisation to constant m. p. or by distillation in all-glass apparatus to constant b. p. The purity of the acid halides corresponded to 99·5—98·8%.

Solvent.—" AnalaR " benzene was used throughout. For reactions involving acid bromides it was dried for several days over phosphoric oxide and redistilled from fresh phosphoric oxide in all-glass apparatus previously baked and cooled in a current of dry air.

Technique.—*Acid halides.* The reaction between an acid halide and aniline takes place quantitatively according to the equations

$$C_6H_5{\cdot}NH_2 + R{\cdot}COX \longrightarrow C_6H_5{\cdot}NH{\cdot}COR + HX$$
$$C_6H_5{\cdot}NH_2 + HX \longrightarrow C_6H_5{\cdot}NH_2,HX$$

The completely insoluble amine hydrohalide was filtered off and dissolved in water: the halogen was then estimated by Volhard's method. The experimental details have already been described.[16, 2] All the reagents were mixed at the temperature of the experiment. The concentrations in most of the experiments were: acid halide M/200, and aniline M/100. In the reactions of chloroacetyl chlorides M/400 and M/200 were used, and for a few slow reactions M/50 and M/100. Changes in concentration do not affect the values of the rate constants.[2, 14]

TABLE 1. *Velocity constants (k in l. mole^{-1} sec.$^{-1}$) at 25° for the reaction of acetyl bromide and* p-*nitroaniline.*

" AnalaR " benzene			Specially dried benzene		
Time (min.)	Change (%)	10^2k	Time (min.)	Change (%)	10^2k
4	36·0	23·37	7	33·5	11·98
9	46·0	15·78	12·1	45·0	11·27
15	57·0	14·72	18	56·0	11·79
22	62·0	12·36	25	63·0	11·35
30	67·0	11·28	35	70·5	11·38
40	72·5	10·98		Average value	11·55

TABLE 2. *Velocity constants (k in l. mole^{-1} sec.$^{-1}$) at 25° for reactions of acetic anhydride.*

Aniline			3-Chloro-4-methylaniline		
Time (min.)	Change (%)	10^2k	Time (min.)	Change (%)	10^2k
30	15·0	1·961	22	16·0	1·443
45	21·0	1·969	30	20·5	1·432
65	27·5	1·945	45	27·5	1·405
90	34·0	1·908	65	36·0	1·442
120	38·0	1·703	(100	45	1·368)
150	40·0	1·481		Average value	1·431
	Extrapolated value	2·075			

[14] Stubbs and Hinshelwood, *J.*, 1949, 71.
[15] Bose and Hinshelwood, *J.*, 1958, 4085.
[16] Grant and Hinshelwood, *J.*, 1933, 1351.

The course of the reaction is expressed by the formula

$$k = \frac{1}{2 \times 60t}\left\{\frac{1}{100 - x} - \frac{1}{100}\right\}\frac{100}{a}$$

where t is the time in minutes, x the percentage change, and k the velocity constant (l. mole^{-1} sec.$^{-1}$), a is the initial concentration of the acid halide, and b that of the amine in mole l.$^{-1}$; $a = b/2$.

Crotonoylation. All the acid halides gave good constants within the limits of experimental error except crotonoyl chloride with which they fell as the reaction proceeded. To overcome this difficulty the second-order constants were plotted against the % reaction and extrapolated to zero change. The activation energy determined at 5 temperatures for zero reaction was found to be very nearly the same as that calculated for 10, 20, and 30% reaction.

Acid bromides. Whereas the reactions of the acid chlorides and anhydrides were unaffected by very small quantities of water,[2,17] acetyl bromide was found to be highly sensitive to hydrolysis by the traces present in the " AnalaR " benzene. It was thus necessary to carry out all manipulations with an apparatus in which samples could be withdrawn without introducing moist air, transfer of benzene or solution from one vessel to another being effected by the application of pressure through a guard tube. All apparatus was dried, baked, and cooled in a stream of dry air before use. The constants obtained at 25° for both " AnalaR " and dried benzene are given in Table 1 and the constancy in the latter is obvious.

Acetic anhydride. In the reaction between aniline and acetic anhydride, the acetic acid liberated does not give a precipitate with the amine and the experimental technique had to be modified. The reaction was followed by shaking samples at known intervals with an excess of a benzene solution of hydrogen chloride whereby free aniline was completely precipitated as hydrochloride which was estimated as before.

As the reaction goes to an equilibrium, the initial value only of the forward velocity constant was determined from the ordinary second-order formula up to about 35% reaction. The constants so obtained were averaged or extrapolated to zero time, as illustrated in Table 2.

There being no precipitation of salt, equal concentrations of anilines and acetic anhydride, M/100 or M/50, were used, and the second-order constants were calculated from the formula

$$k = \frac{1}{60t}\left\{\frac{1}{100 - x} - \frac{1}{100}\right\}\frac{100}{a}$$

N-*Substituted anilines.* The use of these presented unexpected difficulty owing to the solubility of the hydrochlorides. The only satisfactory pair of reactants which could be found were *p*-nitro-*N*-methylaniline and benzoyl bromide. In this reaction the precipitate of the hydrobromide was not formed until about 46% of the reaction was over. After that, however, the reaction went on as usual and gave good bimolecular constants. The tubes were shaken frequently to prevent supersaturation.

Temperature.—Activation energies were calculated by the method of least squares from rate constants at 4 or 5 temperatures. Between 13° and 60° electrically regulated thermostats constant to within ±0·05° were used. Experiments at 5·1° were carried out in a Dewar vessel which contained melting benzene (±0·2°). All thermometers were checked against N.P.L. standards. The rate constants are not corrected for thermal expansion of the solvent.

RESULTS

Tables 3—7 contain the principal experimental data for all the compounds studied, k and A being expressed in l. mole^{-1} sec.$^{-1}$. The values of E for benzoyl chloride have been taken from the results of Stubbs and Hinshelwood.[14]

The results may be summarized as follows:

(1) For a given acylating agent and a series of substituted anilines differences in rate are due only to changes in E, the entropy of activation remaining approximately constant. This confirms and extends the conclusions reached by earler workers.[2,14] Fig. 1 shows the plots of log k at 25° against E for the acylation of anilines with the various acylating species. The lines are of slope $-2{\cdot}303\boldsymbol{R}T$.

[17] Kosakikallio, *Acta Chem. Scand.*, 1959, **55**, 1725.

(2) The order of reactivity of the acylating species is $CH_3{\cdot}COBr > CH_3{\cdot}COCl > (CH_3{\cdot}CO)_2O$, and $CH_3{\cdot}COX > C_6H_5{\cdot}COX$.

(3) The change (ΔE) in E due to any given substituent in the aniline is approximately constant and independent of the acylating agent. Table 8 contains the values of ΔE caused by some of the substituents in the aniline for the reaction with various acylating agents. E for the reactions of aniline with $C_6H_5{\cdot}COBr$, $CH_3{\cdot}COCl$, and $CH_3{\cdot}COBr$ was calculated by the method of Bose and Hinshelwood.[15]

(4) When the structure of the acid chloride is changed, log A varies in a complex manner but there is a general tendency for it to follow E.

(5) When X in R·COX is changed from Cl to Br there is a lowering of E but an actual increase in log A.

(6) The value of E is partly governed by the strength of the C–X bond in the acylating agent, as is made clear when X is changed from Cl to Br.

(7) *N*-Methylation of the aniline lowers both E and log A in an approximately proportional way.

TABLE 3. *Base*: m-*nitroaniline.*

Acid chloride	10^2k_{20}	E	log A	$k/k_{CH_3\cdot COCl}$	$E - E_{CH_3\cdot COCl}$
Acetyl	1·231	7700	3·816	1	0
Propionyl	0·945	7750	3·736	0·768	—
Butyryl	0·683	7650	3·521	0·555	—
Hexanoyl	0·687	8000	3·784	0·564	—
Lauroyl	0·761	7850	3·716	0·618	—
Crotonoyl	0·480	9250	4·567	0·390	+1550
Phenylacetyl	2·079	8800	4,860	1·690	+1000
Isobutyryl	0·378	10,400	5·309	0·307	+2700
Chloroacetyl	41·64	6500	4·445	33·83	−1200
Trichloroacetyl	27·69	5700	3·682	22·50	−2000
Benzoyl	0·0324 *	10,550	4,378	0·026	+2850

* Calc. from the Arrhenius equation.

TABLE 4. *Acylating agent*: *benzoyl bromide.*

Amine	10^2k_{25}	E	log A	$Q = (E - E_{C_6H_5\cdot COCl})$
m-Nitroaniline	3·632	9050	5·128	−1600
p-Nitroaniline	0·571	10,000	5·088	−2030
o-Nitroaniline	0·045	11,650	5·161	−1950
o-Chloroaniline	6·979	8600	5·132	−1980
2,4-Dichloroaniline	1·480	9200	5·045	−2340
4-Chloro-3-nitroaniline	1·042	9650	5·112	−1930
3-Methoxy-5-nitroaniline	4·843	8800	5·144	−1970
		Average	5·115 ± 0·0025 *	−1970 ± 90
4-Nitro-*N*-methylaniline	1·221	8400	4·226	

* The limits given are not estimates of experimental error, but indicate the variations among the values for the various compounds given in the Table.

TABLE 5. *Acylating agent*: *acetyl chloride.*

Amine	10^2k_{25}	E	log A	$Q = (E - E_{C_6H_5\cdot COCl})$
m-Nitroaniline	1·481 *	7700	3·816	−2850
p-Nitroaniline	0·153	9250	3·974	−2780
m-Chloroaniline	12·08	6650	3·883	−2620
4-Chloro-3-nitroaniline	0·537	8600	4·034	−2970
		Average	3·926 ± 0·055	−2800 ± 85

* Calc. from Arrhenius equation.

TABLE 6. *Acylating agent*: *acetyl bromide.*

Amine	10^2k_{25}	E	log A	$Q = (E - E_{C_6H_5\cdot COCl})$
p-Nitroaniline	11·55	8050	4·975	−4000
o-Nitroaniline	2·048	9100	4·981	−4500
2,5-Dichloroaniline	11·770	7850	4·824	−4600
4-Methyl-2-nitroaniline	9·055	8200	4·958	−4600
		Average	4·931 ± 0·042	−4425 ± 165

TABLE 7. *Acylating agent: acetic anhydride.*

Amine	10^2k_{25}	E	log A	$Q = (E - E_{C_6H_5 \cdot COCl})$
Aniline	2·075	10,450	5·976	+2850
m-Chloroaniline	0·1965	12,200	6·243	+2930
3-Chloro-4-methylaniline	1·431	11,100	6·300	+2740
α-Naphthylamine	0·336	11,550	5·976	+2850
		Average	6·124 ± 0·095	+2840 ± 45

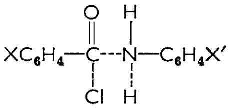
TABLE 8. *ΔE due to some substituents in aniline.*

Substituent	$C_6H_5 \cdot COCl$	$C_6H_5 \cdot COBr$	$CH_3 \cdot COCl$	$CH_3 \cdot COBr$	$(CH_3CO)_2O$
H	0	0	0	0	0
m-NO_2	3040	3350	2940	—	—
p-NO_2	4430	4300	4400	4800	
o-NO_2	6000	5950	—	5850	
o-Cl	2980	2900			
m-Cl	1670	—	1800	—	1750
(α-Naphthylamine)	1170				1100

DISCUSSION

General.—The effect of a substituent in the benzene ring, whether of the acid chloride or of the amine, is exerted almost entirely on the activation energy. Electron-repelling substituents in the acid chloride increase E and lower the rate, while electron-attracting substituents decrease E, the effect being reversed when the substituents are in the amine. The direction of the influence is consistent with the assumption that variation of the repulsion between the reactants is here the principal factor determining the changes in activation energy.[1]

The transition state can be represented as follows:



$$XC_6H_4\!-\!\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle Cl}{\vdots}}{C}}\cdots\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{\vdots}}{N}}\!-\!C_6H_4X'$$

The constancy of the entropy of activation when X and X′ are varied is perhaps not surprising since the strongly polar reaction centre remains the same and the substituents are remote from it.[18,19] On the other hand, when the acylating agent is varied, quite complex changes occur in both E and log A. Similarly complex changes occur if the solvent changes.

When variations are made in the structure of a reactant, so that the pattern of the transition state is seriously changed, there is often a general tendency for log A to show a linear increase with E. The present group of results can be reduced to better order if the variations in E are assumed to occur from two causes: first, polar effects, which from the analogy of the benzene-ring substituents are taken to involve no corresponding changes in log A, and, secondly, structural effects which may be termed steric in the broadest sense and involve a linear correlation [20] of E and log A.

In the study made by Blackadder and Hinshelwood,[13] the commonest slope found for the linear correlations of E and log A when they occur was about 0·6. In Fig. 2, accordingly, log A is plotted against $E - E_{CH_3 \cdot COCl}$ and a line of slope 0·6 is drawn through the point corresponding to the reaction with acetyl chloride. This line divides the acylating species into two groups. We shall now be in a position to test the idea that reasons other than steric ones, and usually connected with polarity or bond strength, determine whether the value of E is greater or smaller than that corresponding to the line.

Substitution Effects in the Anilines.—The experimental results for a series of anilines

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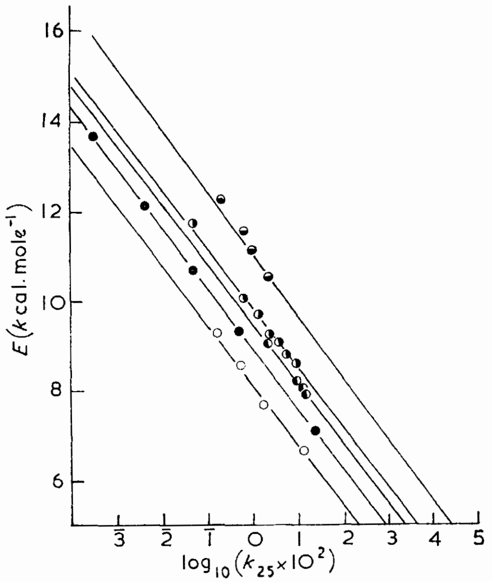
[18] Hinshelwood, *J.*, 1935, 1112.

[19] Wynne-Jones and Eyring, *J. Chem. Phys.*, 1935, **3**, 492.

[20] Cf. (for equilibria) Laidler, *Trans. Faraday Soc.*, 1959, **55**, 1725.

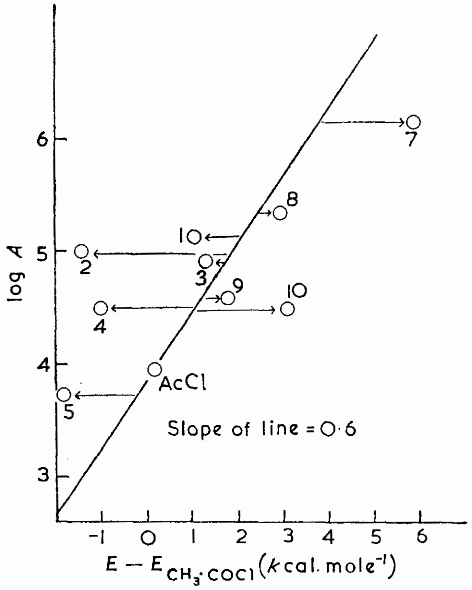
with each acylating agent (Tables 4—7) are consistent with the view that the repulsion energy is the principal governing factor. Log A is constant for each acylating species and changes in rate are entirely due to changes in E (Fig. 1). The influence of different substituents is approximately constant (Table 8) and is independent of the acylating agent.

FIG. 1. *The lines are of slope* $-2{\cdot}303\boldsymbol{R}T$.



○ *Acetyl chloride;* ● *benzoyl chloride;* ◐ *acetyl bromide;* ◑ *benzoyl bromide;* ◒ *acetic anhydride.*

FIG. 2. *Slope of line* = 0·6.



1, $C_6H_5{\cdot}COBr$; 2, $CH_3{\cdot}COBr$; 3, $Ph{\cdot}CH_2{\cdot}COCl$; 4, $Cl{\cdot}CH_2{\cdot}COCl$; 5, $Cl_3C{\cdot}COCl$; 7, $(CH_3{\cdot}CO)_2O$; 8, iso-$C_3H_7{\cdot}COCl$; 9, crotonoyl chloride; 10, $C_6H_5{\cdot}COCl$.

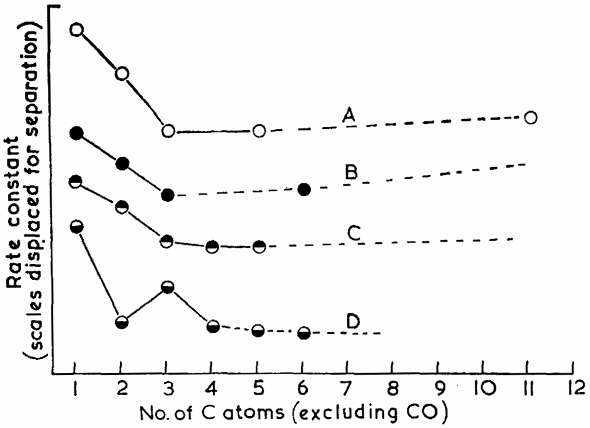


FIG. 3. *A, Acylation; B, esterification; C, acid-hydrolysis; D, dissociation constant.*

The values of ΔE for a series of anilines calculated for the various acylating agents with reference to any one agent as a standard are independent of the aniline used (Tables 4—7, last column). This additivity of ΔE and Δ log A makes it possible to use the values of E obtained for one series of acylations to calculate E for any other acylation reaction provided that the reaction of at least one aniline in the second series has been measured.

The values of E calculated as above for the acylation of aniline with $CH_3{\cdot}COBr$,

C_6H_5·COBr, and CH_3·COCl are in good agreement with those calculated for the same reactions by the method of Bose and Hinshelwood.[15] These results are given in Table 9.

TABLE 9. *Values of* E *for the reaction of aniline and* R·COX *calculated by different methods.*

Acylating species	*E* by the method of Bose and Hinshelwood	$E = 7600 - Q$
Benzoyl chloride	7600 *	—
Benzoyl bromide	5700	5630
Acetyl chloride	4850	4800
Acetyl bromide	3250	3175
Acetic anhydride	10,450 *	10,440

* Experimental values.

Structural Variations within the Acid Chloride.—Acetyl chloride is taken as the reference standard and a temperature 20° has been selected for comparison of the rates. The relevant data are contained in Table 3.

For the series of straight-chain compounds *E* is approximately constant, 7790 ± 45 cal. The rate sequence for the first three members is:

$$CH_3\cdot COCl > CH_3\cdot CH_2\cdot COCl > CH_3\cdot [CH_2]_2\cdot COCl$$

in the ratios 1 : 0·76 : 0·55. Further lengthening of the chain has no effect. The results closely parallel those for similar reactions involving the carbonyl carbon atom.[21–24] Fig. 3 shows the dependence on chain length of the rate of this reaction together with that for ester hydrolysis and formation and also that of the dissociation constant of the acid.

Alkyl groups repel electrons [25] and a slight progressive increase in *E* is expected from acetyl to propionyl.[26] The differences between these acid chlorides are, however, so small as to be within experimental error. Thus it is inappropriate to discuss them in detail. If propionyl chloride had the same value for log *A* as acetyl chloride, *E* would have to be 7850 cal., which is barely outside the error. For similar reactions Smith [27] and his co-worker [28] conclude that the rate difference is entirely due to steric effects, whereas Evans and his co-workers [29,30] conclude that it is due to inductive effects.

Since a saturated carbon chain is not a good conductor for inductive effects,[22] the rate decrease from propionyl to n-butyryl chloride is probably steric. n-Butyryl chloride can form a ring-structure similar to that proposed for n-butyric acid by various workers [26,27,29,31] and the frequency factor could be lowered by steric hindrance of a purely geometric kind. Further lengthening of the chain would have little effect.

In the acid chlorides generally a complex interplay of inductive, steric, and mesomeric effects is discernible.

(1) Electrophilic substituents such as Cl and C_6H_5 in acetyl chloride increase the rate as expected,[25] and the electron-repelling methyl group decreases it.

(2) The proximity of the substituent to the reaction centre in the aliphatic acid chlorides complicates the picture of steric effects. Changes in *E* govern the rate except in phenylacetyl chloride, but there is a general tendency for log *A* to follow *E*, except in the case of chloroacetyl chloride.

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[21] Smith and Reichardt, *J. Amer. Chem. Soc.*, 1941, **63**, 605.
[22] Fairclough and Hinshelwood, *J.*, 1939, 593.
[23] Smith and Steele, *J. Amer. Chem. Soc.*, 1941, **63**, 3466.
[24] Willems and Bruylents, *Bull. Soc. chim. belges*, 1951, **60**, 191.
[25] Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Sons, London, 1953, p. 70.
[26] Dippy, *J.*, 1938, 1222.
[27] Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 254.
[28] Smith and Levenson, *J. Amer. Chem. Soc.*, 1939, **61**, 1172.
[29] Evans, Gordon, and Watson, *J.*, 1938, 1439.
[30] Evans and Gordon, *J.*, 1938, 1434.
[31] Magee, Ri, and Eyring, *J. Chem. Phys.*, 1941, **9**, 419.

(3) Steric hindrance appears to depend essentially upon a high value of E, as has been pointed out for acid esterification.[9]

The results show:

(*a*) A considerable increase in E and log A from acetyl to isobutyryl chloride, the reaction rate decreasing in the expected order

$$CH_3{\cdot}COCl > CH_3{\cdot}CH_2{\cdot}COCl > (CH_3)_2CH{\cdot}COCl$$

in the ratios 1 : 0·76 : 0·31; (*b*) a decrease in E but an increase in log A from acetyl to chloroacetyl chloride, the rate being several times faster with the latter; (*c*) an increase in both E and log A from acetyl to phenylacetyl chloride, the rate being slightly faster with the latter; (*d*) a decrease in E and log A from chloro- to trichloroacetyl chloride; (*e*) an increase in E and log A with crotonyl and benzoyl chloride, the rates being lower than with acetyl chloride, and the benzoyl compound having the lowest rate among the acid chlorides studied.

The effect in (*a*) seems to be due to the combined operation of electronic and steric effects, the latter being more important,[32,33] the corresponding points lying close to the line in Fig. 2. In (*b*) and (*c*) the electron-attracting Cl and C_6H_5 substituents in acetyl chloride lower E, causing an increase in rate. Because of their size they seem also to exert steric hindrance, causing a rise in the values of both E and log A. The polar and steric effects act in opposite directions.[34] In Fig. 2 the points corresponding to these compounds are to the left of the line, indicating that E is lower than the purely steric effect would demand. Phenylacetyl chloride can form a ring structure as proposed by Smith [27] for phenylacetic acid, and this factor may cause the big rise in E and log A. As regards (*d*), trichloroacetyl chloride is the one example where there is no increase in log A for a reaction in which steric hindrance is expected. Both E and log A are lowered. E decreases from chloro- to trichloro-acetyl chloride in accordance with the expectations based on the electronic theory. Similar results have been obtained for the hydrolysis of chloroethyl esters.[35]

In Fig. 2 the points corresponding to benzoyl and crotonoyl chloride occur to the right of the line. These molecules possess double bonds conjugated with the C=O group. The rates are low because of a high value of E and in spite of a high log A value. For benzoyl chloride it has been argued that both the inductive effect of the phenyl group and the influence of substitution are outweighed by resonance between the carbonyl and phenyl groups.[36,37] The resonance between the C=O group and the conjugated double bond [38] may be responsible for the high value of E in crotonoyl chloride. Stabilization of the carbonyl groups involved in conjugation with an aromatic radical or a double bond is shown in the reduced Raman frequencies of carbonyl groups in benzoyl and crotonoyl chlorides as compared with those of acetyl and phenylacetyl chloride.[39,40]

Variation of X *in* R·COX.—The results in Tables 4—7 show that the rates follow the sequence R·COBr > R·COCl > $(R{\cdot}CO)_2O$, the acid bromides reacting faster in virtue both of a lower E and a higher log A. The anhydride reacts slowly because of a very high E, and in spite of a high log A.

In Fig. 2 the bromides lie to the left of the line, acetic anhydride to the right. In the acid bromides steric and structural effects might be assumed to raise both E and log A in the usual way, but E must then be supposed to be simultaneously lowered by an

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[32] Hughes, *Trans. Faraday Soc.*, 1941, **37**, 620.
[33] Dostrowsky, Hughes, and Ingold, *J.*, 1946, 173.
[34] Emery and Gold, *J.*, 1950, 1455.
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independent effect. The rate sequence R·COBr > R·COCl corresponds to that observed for similar reactions.[41–43] The non-steric lowering of E suggests that the strength of the bond between X and the carbon atom here plays an important part in determining the energy of the transition state.

TABLE 10. *Factors contributing to change in E.*

Criterion	Acid bromide	Acid chloride	Acid anhydride
(1) Positivity of the carbon atom	+	0	++
(2) C–X bond strength	− − −	0	+++
(3) Size of X	+	0	++
(4) Resonance in X	0	0	+
Total	—	0	8+

When the base is kept constant and X is changed, the repulsion between the reactants depends upon the positivity of the carbonyl carbon atom. In general, the order of reactivity of the acid derivatives to be expected from the inductive effects of the hetero-atoms is R·COCl > R·COBr > $(R·CO)_2O$. But as far as the influence of the C–X bond is concerned, we should expect the order of reactivity in terms of their bond dissociation energies to be R·COBr > R·COCl > $(R·CO)_2O$. The space requirements of the group X must also be considered in that a bigger group may impede the approach of the base and so cause E to rise.[9] This contribution to E should be in the order anhydride > bromide > chloride.

Further, the acylating agents contain the C=O group and, like the parent acids, they are mesomeric. This effect is negligible in the acid halides but is important in anhydrides,[47] where it may make an additional contribution to E. This is seen by the reduced Raman frequencies of the CO group in acetic anhydride.[44]

A schematic assessment of the contributions to the change in E for the various acylating agents is shown in Table 10. The acid chloride is taken as the standard.

Of these factors, the most important one seems to be the relative strength of the C–X bond, so that E is low for the acid bromides. In the acid anhydride all the factors are additive and the value of E is very high. In the change in rate from benzoyl chloride to bromide, E accounts for 85% of the increase. It is rather less important with the acetyl compounds where it contributes only 44% of the increase. This difference may be connected with the difference in bond dissociation energies of the C–X bond in R·CO–X. The difference is about 1·8 kcal. $mole^{-1}$ greater for the benzoyl halides than for the acetyl derivatives.[45,46]

N-*Substituted Anilines.*—The methyl group is a source of electrons,[25] and its purely electronic effect on E alone is shown, in the benzoylation of anilines, when it is substituted in the benzene ring.[2] When, however, it is in close proximity to the reaction centre, it also exerts the kind of effect which is reflected in correlated changes in E and log A, as observed in the reaction of acetyl and isobutyryl chlorides with *m*-nitroaniline. A similar effect is noticed in the acylation of *p*-nitro-*N*-methylaniline with benzoyl bromide. The methyl group causes a decrease of both E and log A and the net result is a slight increase in rate. The plot of log A against E for the two reactions gives a line of slope of about 0·56, a value in the range commonly found for other reactions where compensation between E and log A exists.[13]

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