

KINETIC STUDIES IN ESTER HYDROLYSIS

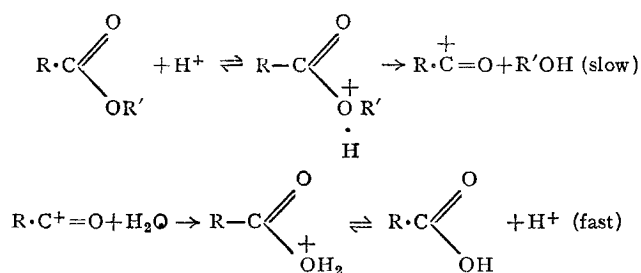
Part I. The Hydrolysis of Halogeno-aliphatic Esters

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THOUGH the hydrolysis of esters has been the subject of study for nearly half a century since de Hemptinne's first paper,⁷ it is only recently that a systematic study has been made. The accepted mechanism for both acid and alkaline hydrolysis is that due to Lowry¹³ involving a common intermediate complex. For acid hydrolysis, three alternative courses are possible, but, by the use of isotopic oxygen, Ingold, Day and Datta³ have shown that the best scheme is as follows :—



With the advent of the electronic theory, it is natural to use it in the interpretation of group influences on hydrolytic reactions as well. The susceptibility to polar influences has been well demonstrated by Kindler working with benzoic esters¹² and the more systematic and thorough studies of Ingold and Nathan,¹⁰ Evans, Gordon and Watson⁵ and Hinshelwood and co-workers.⁹ It has further been noticed that in the case of meta and para substituents, the PZ values of the Arrhenius' equation remains the same while E changes with structure. Now, the activation energy may be considered to involve a repulsion term and a bond energy term in which the latter is influenced by the polar characteristics of the substituent group. Evans and Jenkins⁶ were able to obtain for the hydrolysis of benzoic esters a relation of the form

$$E = E_B + E_X/\epsilon_{20}$$

where E is the activation energy, E_B the bond energy and E_X/ϵ_{20} is the repulsion energy.

Most of the work generally described deals with aromatic esters while the aliphatic series seems to be comparatively neglected. It is well known that the behaviour of halogens is anomalous in the aromatic series among themselves, though they fall in the right position as regards the group as a whole. Further, it is usual to assume, since saturated carbon atoms are involved, that the influence of the halogens arises only from the transmission of the inductive effect. The present communication deals with a preliminary investigation of a few halogeno-aliphatic esters, a systematic study of which may be expected to clarify the position.

The choice of Dioxan-water as solvent needs some explanation. Usually the reaction has been studied in alcohol-water and acetone-water systems. The range of working temperature available precluded the use of acetone for any fair degree of accuracy and at the same time it was considered desirable to avoid a solvent taking part in the reverse reaction. At the same time, for comparison of results, a solvent of about the same dielectric constant and viscosity had to be chosen. The influence of the solvent is considered in greater detail in the next part. All the reactions described herein have been carried out in 60% dioxan (by weight) and the results are tabulated below (Tables I, II, III and IV).

TABLE I
Ethyl Esters of Alkyl-substituted Acids

Acid	Temperature in °C.	Time for % reaction in minutes				$k_1 \times 10^5$	E (from graph)	PZ
		5	10	20	40			
Acetic	35	69	138	285	636	13.09	16,930	1.47
	42	37	75	150	342	24.41		
	50	22	42	84	178	43.01		
	60	9	18	36	75	100.2		
Propionic	35	78	162.5	345	780	10.63	15,960	0.24
	42	45	87.5	187.5	425	19.93		
	50	25	50	102.5	220	36.13		
	60	12.5	25	51	110	68.75		
<i>n</i> -Butyric	35	190	380	740	1600	4.93	15,510	0.065
	42	85	175	365	830	10.03		
	50	45	95	190	380	19.36		
	60	20	40	90	200	41.69		

TABLE II
Ethyl Esters of Chloro Acids

Acid	Temperature in °C.	Time for % reaction in minutes				$k_1 \times 10^5$	E (from graph)	PZ
		5	10	20	40			
Chloroacetic ..	35	102	202	420	864	8.686	16,640	0.61
	42	60	120	240	522	15.05		
	50	24	54	121	263	31.51		
	60	12	24	54	128	75.27		
α -Chloropropionic ..	35	234	468	1044	2502	3.763	15,060	0.20
	42	108	244	522	1170	7.169		
	50	80	162	288	630	12.04		
	60	43	72	145	324	25.09		
β -Chloropropionic	35	300	660	1590	4380	2.441	16,070	0.065
	42	180	360	900	2460	4.516		
	50	108	225	480	1200	7.785		
	60	50	100	210	570	17.37		

TABLE III
Ethyl Esters of Bromo Acids

Acid	Temperature in °C.	Time for % reaction in minutes				$k_1 \times 10^5$	E (from graph)	PZ
		5	10	20	40			
Bromoacetic ..	35	72	165	378	888	10.39	15,780	0.16
	42	48	105	240	571	15.85		
	50	27	54	114	270	32.26		
	60	12	24	54	126	69.49		
α -Bromopropionic ..	35	390	825	1800	4260	2.030	16,830	0.20
	42	240	465	945	2040	3.844		
	50	90	225	480	1050	7.749		
	60	60	114	225	504	16.43		
β -Bromopropionic ..	35	390	900	2280	5400	1.737	18,690	3.40
	42	210	510	1140	2640	3.346		
	50	90	210	540	1320	8.370		
	60	48	100	225	570	17.37		

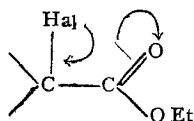
TABLE IV
Ethyl Esters of Iodo Acids

Acid	Temperature in °C.	Time for % reaction in minutes				$k_1 \times 10^5$	E (from graph)	PZ
		5	10	20	40			
Iodoacetic ..	35	180	350	654	..	5.408	14,230	0.007
	42	102	243	483	960	7.460		
	50	57	120	246	510	14.80		
	60	24	57	111	228	32.26		
α -Iodopropionic ..	35	1230	2280	4560	10,080	0.8065	17,260	0.16
	42	480	1020	2070	4230	1.135		
	50	300	600	1200	2490	3.011		
	60	120	276	510	1020	6.949		
β -Iodopropionic ..	35	510	990	2250	5310	1.69	16,320	0.068
	42	300	690	1290	2850	2.779		
	50	150	315	645	1380	5.645		
	60	75	156	303	630	11.89		

It will be noticed that the alkyl substituents do not affect the magnitude of the rate constant to any considerable degree but the drop in the value from ethylpropionate to ethyl butyrate is pronounced, while that from ethylacetate to propionate is slight. This change is traceable to two factors: first, the influence of the group on the formation of the transition state complex and secondly the steric factor. Alkyl groups (class + I) facilitate polarisation of the C=O bond, thereby stabilizing the complex. Further it is known from other studies that the ethyl group is a better electron-donor than the methyl. Consequently, there is a slowing down in the reaction as one ascends the homologous series, the rate tending to a more or less constant value higher up the series. This increase in stability of the activated complex is combined with a corresponding ease of formation of the complex as well. A diminishing energy of activation from ethyl acetate to ethylpropionate bears out this conclusion. The value of E also presumably tends to a constant value in line with other properties of the aliphatic acids (*e.g.*, ionisation constant) which are influenced by polar characteristics of substituents.

The influence of the halogens is of a more complex nature. Such halogen derivatives belong to the class - I + T, the inductive and tautomeric

effects varying with the halogen. As is well known, the $-I$ effect is in the order $Cl < Br < I$. One may therefore expect that reactivity towards electrophilic reagents will diminish as one changes from the chloro to the iodo-compound. The trend in the rate constant for ester hydrolysis (*vide* Tables II, III and IV) clearly brings this out. The behaviour of ethyl bromoacetate at lower temperatures is somewhat anomalous. The slowest reaction among esters studied is the hydrolysis of ethyl α -iodopropionate. Now, Pauling and others have shown that the C-halogen bond possesses a certain amount of double bonded character¹⁴ arising from resonance and this gives rise to a "conjugated system" in the α -halogeno esters.



The iodine atom is the most polarisable and one may expect from *a priori* considerations that this resonance effect will be most pronounced in α -iodopropionic ester.

Taking the halogens as a whole, the $-I$ effect diminishes the ease of formation of the activated complex while the $+T$ acts in the opposite direction. The resultant of these two opposing tendencies must account for the observed values of activation energy and rate constant. In the case of the halogeno acetates the value of E progressively decreases from the chloro to the iodo-derivative (the mono-halogeno compounds alone are considered here). On the other hand, in the case of α -halogeno propionates the position is reversed. α -Chloropropionate exhibits the lowest energy of activation while the iodo-compound shows the highest. One has to take into account, not merely, the halogen but also the alkyl group, with the result that group influences are more complex. Probably, the electron donating alkyl group attached to the same carbon atom as the halogen suppresses wholly or in part the $+T$ effect. The net result is a decrease in the ease of formation and the stability of the transition state, a slowing down of the reaction as a whole and a reversal of the relative order of the halogens. Ethyl iodopropionate is found to give the highest value for E .

The β -halogenopropionates are of a different type. An intervening saturated carbon atom, which might considerably diminish even the inductive effect, makes the influence of the tautomeric effect on the carbethoxy group negligible. The CH_2 Hal. group appears essentially as an electron acceptor and the reaction becomes slow. The trend of E values shows a slight increase from the chloro to the iodo-compound.

Our attention so far has been directed to the relation between one of the Arrhenius parameters, E , and the substituent. It is now necessary to consider the other parameter. Plotting $\log_{10} k$ against E (Fig. 1) it will be noticed

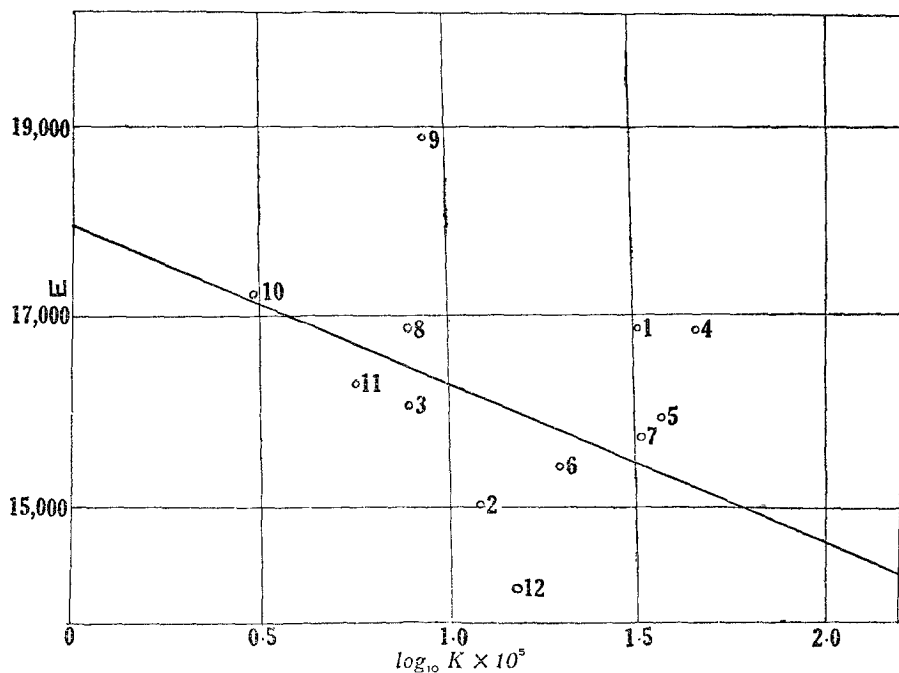


FIG. 1

KEY TO NUMBERS

- | | |
|-------------------------------------|------------------------------------|
| 1. Ethyl acetate | 7. Ethyl bromacetate |
| 2. Ethyl propionate | 8. Ethyl α -bromopropionate |
| 3. Ethyl butyrate | 9. Ethyl β -bromopropionate |
| 4. Ethyl chloracetate | 10. Ethyl iodopropionate |
| 5. Ethyl α -chloropropionate | 11. Ethyl α -iodopropionate |
| 6. Ethyl β -chloropropionate | 12. Ethyl β -iodopropionate |

that very few points lie along the slope $-2.303 RT$. Most of the points are distributed at random. This is a clear indication that the aliphatic esters studied differ on this important aspect from the aromatic compounds. The PZ values are obviously different. Now, this factor is primarily dependent on the mean molecular diameter of the interacting molecules and on the orientation of the molecule. While an increase in size increases the frequency of molecular collisions, in the present instances, this very factor appears to lead to ineffective collisions not involving the carboxy group. Consequently, the iodo-compound has the smallest value for this probability factor.

This same result can also be shown in another way. Hinshelwood⁸ has shown that if the constant χ in the equation

$$k = \chi e^{-E/RT}.$$

were the same for all reactions, there is a linear relationship between the energy of activation and the temperature at which the reaction attains a given rate. An examination of the present series gives a random distribution of points when the E-T curve is plotted for a speed such that the reaction is half completed in one hour using the concentrations used (Table V and Fig. 2).

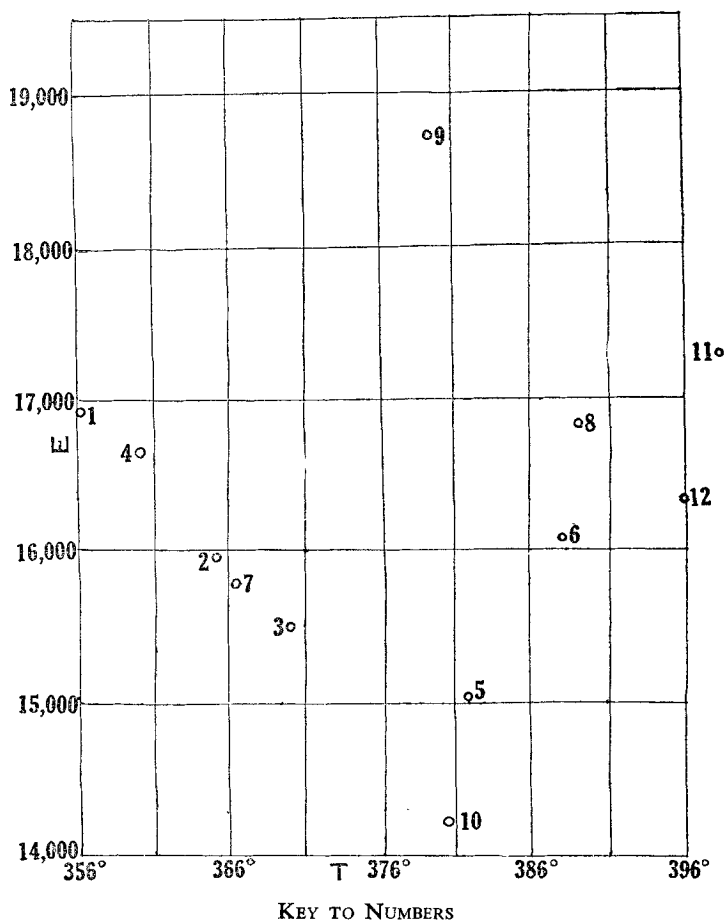


FIG. 2

E—Energy of activation in calories.

T—Temperature in degrees absolute for equal velocity of reaction.

TABLE V

Hydrolysis of ethyl ester of acid	Temperature of equal velocity in ° absolute	Energy of activation
Acetic	355·8	16,930
Propionic	364·9	15,960
<i>n</i> -Butyric	369·0	15,510
Chloroacetic	360·0	16,640
α -Chloropropionic	381·7	15,060
β -Chloropropionic	387·9	16,070
Bromoacetic	366·5	15,780
α -Bromopropionic	387·9	16,830
β -Bromopropionic	379·5	18,690
Iodoacetic	380·0	14,230
α -Iodopropionic	398·0	17,260
β -Iodopropionic	396·0	16,320

Any quantitative deductions on this aspect may be attempted only after a further study of a larger number of substituted aliphatic esters.

Experimental

Dioxan (Kodak) was purified by the method of Eigenberger⁴ and the fraction, b.p., 104° C. and m.p. 11·8° C., was used. Exactly decinormal solutions of hydrochloric acid were prepared using purified dioxan diluted with 40% by weight of water.

Ethyl esters of acetic, propionic, *n*-butyric, monochloroacetic, monobromoacetic, α -bromopropionic and β -iodopropionic acids (Kahlbaum) were used, after purification by the usual processes, fresh samples being used for each set of experiments. Ethyl- β -chloropropionate was of Schucardt's manufacture.

Ethyliodoacetate was prepared by a modification of Kekule's method.¹¹ 35 Grams of ethylchloroacetate was refluxed with 50 grams of sodium iodide (molar proportions) in dry acetone solution for 3 hours. After filtering of the sodium chloride, the solvent was distilled off. From the residue, the fraction boiling between 178° and 180° was taken, washed with sodium carbonate and water, dried over anhydrous sodium sulphate and fractionated. Yield 40 g. pure ester b.p. 179–80°.

Ethyl- α -chloropropionate was prepared by the method of Walker.¹⁵ Care is needed in controlling the initial violent reaction of lactic acid with phosphorous pentachloride, but warming is needed in the later stages to complete the reaction. The pure ester boiled at 47°/20 mm.

Ethyl- α -iodopropionate was obtained by the method of Bodroux and Taboury,¹ b.p. 78°·5/28 mm.

Ethyl- β -bromopropionate was prepared by the method described in *Organic Syntheses*,² b.p. 65°/15 mm.

The reactions were carried out in an electrical thermostat between 35 and 60° C., the accuracy of control being ± 0.02 . Air-tight, glass stoppered bottles of resistance glass were used as containers for the reaction mixture, 200 c.c. of the acid solvent was allowed to attain the temperature of the thermostat, calculated amounts of the ester for a decimolar solution added and the change with time measured acidimetrically. N/40 Baryta was used for the estimations involving unsubstituted compounds and ammonia of the same strength for the halogenated esters. The catalytic action of the acid products of hydrolysis was negligible (see also Hinshelwood *et al.*). The loss of esters by volatilisation was also inappreciable.

Summary

The kinetics of acid hydrolysis of some aliphatic esters have been studied at four different temperatures in 60% dioxan. The effect of the halogen on the parameters of the Arrhenius equation have been discussed from the standpoint of the electronic theory of organic reactions.

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