2. The results obtained with potassium iodide have been compared with those obtained by other investigators with other reagents and found to be in general agreement in regard to the primary compounds. The secondary halides appear to be less reactive in the reaction in question than in the majority of cases hitherto examined.

3. The rates of the reaction of five widely different halides with potassium, lithium and sodium iodides have been measured. The rate of the reaction of a given halide is the same with all three inorganic iodides. This points to the reaction being between the iodide ion and the organic chloride.

4. Additional evidence is presented that the velocity coefficient may be calculated from the usual bimolecular equation and is independent of the concentration of the reactants in the range of concentrations employed.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE RELATION BETWEEN THE STRUCTURE OF ORGANIC HALIDES AND THE SPEEDS OF THEIR REACTION WITH INORGANIC IODIDES. III. THE INFLUENCE OF UNSATURATED GROUPS

BY J. B. CONANT, W. R. KIRNER AND R. E. HUSSEY

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It is a well-known fact that a halogen atom in the alpha position to many unsaturated groups is extraordinarily reactive. The so-called negative groups such as the carbonyl, carbethoxy and phenyl manifest the property of activating halogen atoms and it is the purpose of this paper to attempt to evaluate this influence. Our method of comparing the reactivity of halogen atoms in organic compounds consists in measuring the rate of the reaction, $RX + MeI \longrightarrow RI + MeX$, absolute acetone being employed as the solvent and potassium iodide as the inorganic iodide; sodium or lithium iodides might be employed equally well, as the rate of a given reaction is essentially *the same with all three substances,*[1] the reaction probably being between the organic halide and the iodide ion. The reaction velocity corresponds to that of a simple bimolecular reaction and a comparison of the reaction velocity coefficients calculated on this basis is an index of the relative reactivities of the substances examined.

The average values of the reaction velocity coefficients are given in Table I for substances of the type ACH_2Cl where A is an unsaturated group; the experimental details are given in the latter part of this paper. With the aid of the equation, $\log k_{50}/\log k_{+t} = A\left(\frac{1}{273+t} - \frac{1}{323}\right)$ we have

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[1] (a) Conant and Hussey, THIS JOURNAL, **47,** 476 (1925). (b) Conant and Kirner, *ibid.*, **46,** 232 (1924).

calculated the value of k_{50} for all those substances which were so reactive that they had to be measured at lower temperatures, using the average value of 4000 for A; numbers so calculated are enclosed in parentheses in the table. It is evident from an inspection of the values of A actually found, as well as a consideration of the data presented in the second paper of this series (Ref. 1) that A is constant within the limits of our experimental error and that 4000 is a convenient average value.[2] The relative reactivities given in the last column are compared with that of butyl chloride which is taken as unity; the relative reactivities of the substances marked with a letter *a* are different from those given in our first paper which were calculated on the erroneous assumption that A = 4850 for carbonyl compounds. These earlier values are now discarded and those given in Table I substituted; none of the other figures for the reactivity at 50° were affected by this error and therefore all are correct as first printed. The change in the relative reactivities of these five substances does not affect any of the conclusions of the first communication.

Table I

Summary of Results

Compound	k_{10}	k_0	k_{10}	k_{20}	k_{25}	k_{30}	k_{50}	A	Relative reactivity at 50° R	log R
$^a C_6H_5COCH_2Cl$	5.91^b	22.4^c	...	...	...	...	(4190)	4200	$105{,}000^a$	5.02
CH_3COCH_2Cl	..	7.62	28.3	...	...	...	(1428)	4300	35,700	4.55
$CNCH_2Cl$	..	...	2.24	7.08	...	...	(123)	4100	3,070	3.49
$^a C_2H_5OOCCH_2Cl$	..	...	...	...	6.37^c	10.5^b	(68.9)	3900	$1{,}720^a$	3.24
CH_3OCH_2Cl	..	0.196	0.61^d	...	...	...	(36.7)	..	918	2.96
$^a C_6H_5COCl$	..	$0.16^{c,d}$	...	...	...	...	(28)	..	700^a	2.85
CH_3COOCH_2Cl	...	...	...	0.586	0.984	...	(10.8)	4000	270	2.43
$^a C_6H_5COCH_2CH_2CH_2Cl$	..	...	...	...	0.848^c	...	(9.27)	..	230^a	2.36
$C_6H_5CH_2Cl$	..	...	...	...	0.786^b	1.31^c	7.89^b	4000	197	2.30
NH_2COCH_2Cl	..	...	...	...	0.360	0.603	3.95	4000	99	2.00
$CH_2{=}CH{-}CH_2Cl$	..	...	...	...	0.288	...	(3.16)	..	79	1.90
$^a C_2H_5OOCCl$	..	...	...	...	$.0954^c$	...	(1.05)	..	26^a	1.42
$CH_3(CH_2)_2CH_2Cl$	..	...	...	...	...	...	0.402^b	..	1	0
$(C_6H_5)_3CCl$	..	8.18^d	...	...	...	...	(1520)	..	38,000	4.58
$(C_2H_5OOC)_2CHCl$	..	12.9^d	24.0^d	...	...	...	(2420)	..	60,200	4.78

[a] To replace the previous value. [b] From the second paper of this series. [c] From first paper of this series. [d] Approximate only.

Figures in parentheses were calculated using 4000 for value of A.

The reactivities of two substances of the type A_2CHCl and A_3CCl are given at the end of Table I. Many more substances of these types must be investigated before any definite conclusions can be drawn but it is evident that the influence of several unsaturated groups is greater than the sum and less than the product of the single groups. Thus a comparison of chloromalonic ester with chloro-ethyl acetate shows that while the reactivity of the former is six times that of the latter, it is only about 0.01

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[2] Besides the data present in this and the second paper we have determined A for phenyl, amyl and hexyl chlorides and three chloro-esters; the average value was 3900.

of what it would be if the influence of the carbethoxy groups increased geometrically. Similarly, the reactivity of triphenyl-chloromethane is only about 0.005 of the value calculated from the cube of the influence of the phenyl group in benzyl chloride. The general decrease in reactivity of secondary and tertiary alkyl halides as compared with the primary, apparently manifests itself with these unsaturated groups in about the same degree as with the saturated alkyl compounds (Ref. 1).

Results of Previous Investigators

Since very few measurements have been made with the more reactive organic halides, our results can be compared in only a few instances with those of previous workers. Leaving aside for the moment studies of substituted benzyl halides, the only quantitative data comparable to those presented in Table I are to be found in the work of Slator[3] and in that of H. T. Clarke,[4] although a few isolated measurements of Conrad and Brückner,[5] Preston and Jones,[6] and Thomas[7] should also be mentioned. Slator measured the rate of the reaction between organic halides and sodium thiosulfate in water and mixtures of alcohol and water; Clarke determined the speed of the reaction with pyridine in absolute alcohol solution. Since Slator worked with chlorides, bromides and iodides and in some cases in water and others in alcohol and water, his results are difficult to reduce to a common basis for comparison. However, by assuming that the activating influence of a group is independent of the nature of the halogen atom, one can apply the ratio of reactivities of iodide, to bromide, to chloride found for α-halogen esters, to other compounds and thus calculate reactivities for a complete series of iodides. We have calculated such a series of values from Slator's results, taking the ratio of chloride to iodide as 1:100 found for the esters. The ratio 1:40 was found for the methyl halides; if this were used somewhat lower reactivities would be obtained. Clarke's values were obtained by comparison of the rates of reaction of a series of bromides at one temperature and therefore are directly comparable with one another.

In Table II are collected the relative reactivities of a series of six halides as measured by our method, by Slator (calculated as explained above) and by Clarke; the *n*-propyl compound is taken as the standard but since we have found that *n*-propyl and *n*-butyl chlorides have the same reactivity within the limits of experimental error, all the values are on essentially the same basis. Slator's results place the six groups in exactly the same order as that given in Table I, and except for the ketonic compounds the numerical discrepancy is not great. Clarke's values, however, are not so

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[3] Slator, *J. Chem. Soc.*, **85**, 1286 (1904); **87**, 481 (1905); **95**, 93 (1909).

[4] Clarke, *ibid.*, **97**, 416 (1910); **99**, 1927 (1911); **101**, 1788 (1912); **103**, 1689 (1913).

[5] Conrad and Brückner, *Z. physik. Chem.*, **4**, 631 (1889).

[6] Preston and Jones, *J. Chem. Soc.*, **101**, 1930 (1912).

[7] Thomas, *ibid.*, **103**, 594 (1913).

TABLE II

COMPARISON OF RESULTS OF SEVERAL INVESTIGATORS

	Relative reactivities		
Compound	Organic chlorides with KI in acetone (Table I)	Organic iodides with $Na_2S_2O_3$ in water-alcohol (Slator)	Organic bromides with C_5H_5N in alcohol (Clarke)
n-C_3H_7X	1	1	1
CH_2CH—CH_2X	79	170	70
$C_6H_5CH_2X$	197	300[a]	286
$C_2H_5OOCCH_2X$	1720	1200[b]	56
CH_3COCH_2X	35,700	9200[a]	(208)[c]
$C_6H_5COCH_2X$	105,000	10,500[a]	406

[a] Calculated on the assumption that $k_{\text{iodide}}:k_{\text{chloride}} = 100:1$.

[b] Calcd. from the value of k in water *assuming* an increase in k, with change of solvent, parallel to increase for CH_3I.

[c] From ratio of chloro-acetone to chloro-acetophenone.

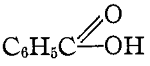
NOTE: Thomas (Ref. 7) finds that benzyl bromide is 4 to 7 times more reactive than allyl bromide in addition reactions with amines. Preston and Jones in a similar reaction find allyl iodide 300 to 360 times as reactive as *n*-propyl iodide. Conrad and Brückner (Ref. 5), using sodium alcoholate, give the ratio of benzyl:allyl:propyl as about 120:60:1.

closely in agreement with our measurements, although with two exceptions the groups fall in the same order in a scale of increasing influence. The discrepancies are, perhaps, not surprising when one considers that the reaction of an organic halide with potassium iodide and thiosulfate are both metathetical reactions with an inorganic ion, while the reaction with pyridine is an addition reaction; it is probable, for example, that spatial considerations play a more important part in such an addition reaction than in double decompositions involving inorganic salts.

We have chosen the reaction with potassium iodide for quantitative study, because in absolute acetone the reaction proceeds smoothly with a wide variety of halides and in each case yields the corresponding iodide. The only other reactions which are known to occur with this reagent or, indeed, seem possible are the union of two molecules with liberation of iodine ($2RX + 2KI \longrightarrow R{-}R + 2KX + I_2$), reduction, if hydrogen iodide is present and complete decomposition of the organic iodide first formed. In each of these abnormal reactions iodine is liberated and therefore in those experiments in which our tubes were colorless, we feel certain we were dealing with a simple metathetical reaction free from side reactions. Even in the cases in which some iodine is liberated our results are still significant since all of the reactions mentioned above probably proceed through the formation of an organic iodide as the first product. Since our procedure measures the amount of inorganic iodide which has disappeared from the reaction mixture, the subsequent fate of the organic iodide does not affect our results unless the side reaction also removes inorganic iodide from the solution. This it does if reduction takes place, but even this complication can be corrected for by determining the amount of iodine liberated. Such a correction has been applied to the results obtained with all substances which liberated any iodine except chloromalonic ester and triphenylchloromethane[8] where the side reaction is known to involve the formation of an ethane derivative and liberation of iodine. The correction is not large in any case and the values for the relative reactivity are nearly the same whether the correction is applied or not.

Perhaps some of the differences between our results and those of the two earlier investigators may be due to the possibility that the reactions they employed did not always give the same product with each halide. For example, while Slator in most cases isolated the compounds formed in his reaction and showed them to be sodium salts of thiosulfonic acids, he postpones consideration of the products formed with chloro-acetone and chloro-acetophenone and as far as we have been able to discover has never published anything further concerning them. If some other product is formed with these compounds the numerical discrepancy between his results and ours might be explained since the reaction between α-halogen ketones and inorganic iodides has long been known to proceed normally and yield the iodoketones.[9] Similarly, Clarke's results may possibly have been affected in certain instances by the formation of some substance other that the pyridinium halide.

The Activating Power of Unsaturated Groups

It was pointed out in our first paper that the reactivity of the halogen atom in a series of compounds of the type ACH_2Cl, was more or less proportional to the activity of the α-hydrogen atom in a similar series of the type ACH_3. In other words, what has often been called "the negativity" of the group A determines the activity of both the α-hydrogen and α-halogen atoms. If A is an activating or negative group, it is well known that with increase in the activating influence of this group (or its "negativity"), ANH_2 becomes a weaker base, AOH a stronger acid and the α-hydrogen atom in ACH_3 more reactive; we wish to call attention particularly to the fact that the halogen atom in ACH_2X *also increases in reactivity;* thus from Table I, RCO— > CN— > C_6H_5 > alkyl. This increase in reactivity of compounds of the type ACH_2Cl which parallels the increased dissociation of AOH appears to be just the reverse of what would be predicted from a consideration of polarity. Thus, while it might be argued that  $C_6H_5C\overset{O}{\diagup\!\!\!\diagup}$—OH was a stronger acid than C_6H_5OH because the benzoyl group drew the electrons of the oxygen atom toward it in a greater degree than the phenyl group, thus rendering the

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[8] Finkelstein, *Ber.*, **43**, 1528 (1910).

[9] *Ber.*, **32**, 532 (1899).

oxygen more negative and the hydrogen more positive, the same line of argument would lead to the conclusion that the chlorine atom in C_6H_5-$COCH_2Cl$ was more *positive* than in benzyl chloride; yet it is 500 times more reactive in a reaction in which the chlorine is *eliminated as a negative ion* and *is replaced by a negative ion.* Similar considerations apply to nearly all the compounds listed in Table I. It seems evident that no adequate interpretation of the facts presented in this paper can be stated solely in terms of polarity.

Instead of considering these unsaturated groups (and the methoxy group) as negative groups (or positive groups, depending on definition) which change the polarity of the adjacent, oxygen, nitrogen or carbon atom, we prefer to look upon them as groups which in some manner make more mobile the linkages of the adjacent atom; we therefore prefer the terms activating group and activating power to terms involving the concept of polarity. The facts seem to indicate clearly that these groups can thus "labilize" the union between the adjacent atom and other atoms, which may then either dissociate as positive ions or be rapidly eliminated from the molecule as negative ions, depending on the nature of the compound. These groups (A) can thus render the atom C in compounds of the type ABC *either* more positive or negative, depending on B and C; indeed there is some qualitative evidence that these activating groups can influence the halogen atom in compounds of the type ACH_2X so that it is very reactive in *both* a positive and a negative sense; thus α-chloroketones are extraordinarily reactive towards potassium iodide and thiosulfate and they are also easily reduced by hydrogen iodide—the first a reaction of a "negative" halogen atom, the second of a "positive" atom.

The Influence of Activating Groups at a Distance

In the above discussion we have considered only the effect of a group on the halogen atom attached to the immediately adjacent carbon atom. Quite another problem is that of the manner in which the influence of such a group is transmitted through a chain of carbon atoms; in the first paper of this series we considered this problem and presented measurements of the relative reactivity towards potassium iodide of three series of compounds of the type ACH_2Cl, ACH_2CH_2Cl, etc. In the series in which A = C_6H_5 and $COOC_2H_5$, the influence of the activating group did not extend to any significant extent beyond the α-carbon atom, but when the activating group was benzoyl, the reactivity of the first three members was in the order 104,000:80:230, all much more active than the alkyl halides and the influence being less with the β than with the γ compound.

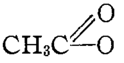
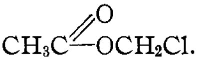
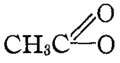
These facts show the complexity of this problem and that it is not safe to generalize one way or the other as to the reactivity of halogen atoms in the β, γ, δ, etc., positions with respect to unsaturated groups. It should be noted that even in the case of the benzoyl compound there was no alternation in reactivity such as would be predicted by a theory of alternating polarity or from Flurscheim's hypothesis of alternate strong and weak valences. That is, the second member of the benzoyl series is less active than the first or third, but is still some 80 times more reactive than the simple alkyl halides; a benzoyl group in the beta position has not diminished in any way the reactivity of the chlorine atom; its influence in increasing it is merely less than that of the same group in the alpha- or gamma position. The only fact among those presented in our first paper which seems consistent with a theory of alternating polarity or valence strength is the lack of reactivity of chlorobenzene as compared with benzyl chloride and the alkyl chlorides. But even with the compounds of the type ACl (which might be considered the real first members of the series we have been considering) there is no uniformity in regard to whether they are more or less active than compounds without unsaturated groups. Thus C_6H_5-OOCCl and C_6H_5COCl have reactive chlorine atoms whereas C_6H_5Cl and probably $CH_2{=}CHCl$ have not, although in every case the statement is true that the compound ACH_2Cl is more reactive than the compound ACl.

TABLE III

SERIES OF CHLORO-ALKYL ESTERS

Compound	k_{20}	k_{25}	k_{30}	k_{50}	k_{60}	Relative reactivity at 50° A	R
CH_3COOCH_2Cl	0.586	0.984	...	(10.79)	....	4000	270
$CH_3COOCH_2CH_2Cl$	...	...	...	0.0179	0.0454	4300	0.45
$CH_3COOCH_2CH_2CH_2Cl$	...	.144	0.242	(1.58)	....	4100	39.5

Values in parenthesis calculated using A = 4000.

We have now measured three members of a series in which the group  $CH_3C{\genfrac{}{}{0pt}{}{/\!\!/O}{-O}}$ has proved to have an activating influence in the compound  $CH_3C{\genfrac{}{}{0pt}{}{/\!\!/O}{-OCH_2Cl}}$. The tabulation (Table III) shows that now for the first time we have found the type of alternating reactivity which would apparently be expected from certain theories of valence. It is to be noted, however, that while the  $CH_3C{\genfrac{}{}{0pt}{}{/\!\!/O}{-O}}$ group in the beta position definitely makes the chlorine atom less reactive than in the simple alkyl chlorides, the depressing influence is not very large, though the third member shows a considerably enhanced reactivity. It is unfortunate that the fourth members of this series and the benzoyl series are still lacking; we hope to obtain and measure these compounds at some later time.

The Substituted Benzyl Chlorides

Like the problem of the influence of distant groups in straight-chain compounds, the behavior of substituted benzyl chlorides seems to be very complicated and generalizations for a wide variety of reagents are almost impossible. We have measured only a few substances of this type and present these incomplete results in Table IV without attempt at a detailed discussion of their possible significance.

The reactivity of the *p*-nitro- and 2,4-dinitrobenzyl chlorides corresponds to the enhanced acidity of the corresponding phenols but the behavior of the chloro and bromo compounds is entirely anomalous. Both the *ortho* and *para* isomers of the chloro- and bromobenzyl chlorides appear to be extraordinarily reactive towards potassium iodide, and yet the corresponding amines and phenols differ only slightly from phenol and aniline as regards the acid and basic dissociation constants. Furthermore, other investigators who have worked with these compounds have found no such great reactivity.[10] We are at a loss to explain these results; the suspicion that the nuclear halogen atom might be directly involved seems to be disposed of by an experiment with the bromo compound in which no test for bromide ion was obtained after the reaction had run to completion.

The recent investigations of Franzen,[11] Olivier[12] and Lapworth[13] should be consulted by those interested in this problem. Franzen, using sodium ethylate, and Olivier, studying the direct alcoholysis of the compounds, have arrived at conclusions which are in many cases conflicting. Olivier finds the three nitro derivatives much less reactive than benzyl chloride.

TABLE IV

SUBSTITUTED BENZYL CHLORIDES

Compound	k_{10}	k_0	k_{25}	k_{30}	k_{60}	A	R
$C_6H_5CH_2Cl$	..	..	0.786[a]	1.31[a]	7.89[a]	4000	197
o-$NO_2C_6H_4CH_2Cl$	..	..	6.64	..	(72.6)	..	1800
m-$NO_2C_6H_4CH_2Cl$	..	..	2.87	..	(31.4)	..	780
p-$NO_2C_6H_4CH_2Cl$	..	..	5.03	..	(55.1)	..	1370
2,4$(NO_2)_2C_6H_3CH_2Cl$	..	11.0	..	..	(2040)	..	50,800
o-$ClC_6H_4CH_2Cl$	..	..	2.68[a]	4.38[a]	(28.7)	3800	718
p-$ClC_6H_4CH_2Cl$	..	..	2.02	3.37	(22.1)	4000	553
o-$BrC_6H_4CH_2Cl$	4.31	16.5	..	..	(3092)	4200	77,300
p-$BrC_6H_4CH_2Cl$	2.92	10.3	..	..	(1925)	3900	48,100

The values in parentheses were calculated using the value of A of 4000.

[a] From the second paper of this series.

Slator,[3] however, found that while the *o*-nitro compound was almost identical with benzyl chloride, the *para* and *meta* compounds were 1.8 and 1.5 times as reactive as the unsubstituted compounds. While the influence

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[10] Franzen [(a) *J. prakt. Chem.*, **209**, 333 (1920)] finds for the bromo compounds m > H > O. Olivier [(b) *Rec. trav. chim.*, **41**, 646 (1922)] finds *p*-bromo 0.2 as compared to benzyl chloride.

[11] Franzen, *J. prakt. Chem.*, **205**, 61 (1918); Ref. 10 a.

[12] Olivier, *Rec. trav. chim.*, **41**, 301 (1922); **42**, 516 (1923).

[13] Lapworth, *J. Chem. Soc.*, **113**, 937 (1918).

of the nitro group is here less than in our reaction, the results are more nearly in accord with ours than with those of Olivier. Indeed, it should be noted that if these substances had been included in Table II, Slator's results and our own values would have placed the *meta* and *para* compounds in exactly the same positions, with respect to each other and the other substances listed.

We wish to acknowledge our indebtedness to the Elizabeth Thompson Science Fund for a grant in aid of this investigation.

Experimental Part

Materials Employed.—The preparation of pure potassium iodide and acetone has already been described. The chloro- and bromobenzyl chlorides, chloromethyl ether, chloro-acetone, β-chloro-ethyl acetate and triphenylchloromethane were available on the market in a state of high purity and were further purified by fractional distillation, except in the case of the triphenylchloromethane which was recrystallized from acetyl chloride and dried in a vacuum. The other organic chlorides were prepared in this Laboratory by the usual procedures given in the literature, which require no special comment; in the case of liquids whose only criteria of purity were boiling points, total halogen analyses were also made. The boiling point or melting point of the compounds employed are given in the tabulation of the experimental results. We are indebted to Mr. A. C. Glennie for the preparation of the three isomeric nitrobenzyl chlorides, the dinitrobenzyl chloride and the measurements of the reactivity of the latter substance. Since the dinitrobenzyl iodide has never been described in the literature, Mr. Glennie prepared this substance by the action of potassium iodide in acetone; it melted at 69.5–70° and by analysis was found to contain 41.22% of iodine as compared with that calculated, 41.21%.

Procedure and Results.—The method of measuring the rate of the reaction with potassium iodide was exactly the same as that described in the first and second papers of this series. In the following compilation (Table V) only the time in hours, percentage reacted and the value of k are given: k was calculated from the usual bimolecular equation which in all the following experiments takes the form $k = \frac{1}{4bt} \log \frac{5-z}{5(1-z)}$, where t is in hours, z is the fraction of the inorganic iodide reacted and b the concentration of the inorganic iodide (moles per liter) which was in every case 0.04. Since each tube contained 0.001 mole of the organic halide and 5 cc. of acetone in which was dissolved 0.0002 mole of potassium iodide, the concentration of reactants was in each case, potassium iodide 0.04 M, organic chloride 0.2 M. Those cases in which iodine was liberated either during the reaction or after breaking the tube in hydrochloric acid are noted below and the values for the percentage reacted in every case except two have been corrected for this liberation of iodine as outlined in the first paper; the results with chloromalonic ester and triphenylchloromethane

Table V

Results

Reaction between Chloromethyl Ether (B. p., 59–60°) and Potassium Iodide

A small amount of iodine was liberated during the reaction; correction applied.

At 0°

Time, hours	20	2.5	3.0	3.5	4.0	
Corr. % reacted (100 z)	17.78	20.14	22.89	26.33	27.55	
k	0.219	0.198	0.185	0.192	0.184	Av., 0.196

Chloro-acetone (B. p., 118.8–119.4°) and Potassium Iodide

The iodine liberated when the tubes were broken in acid was determined and a correction applied

At 10°			At 0°		
Time Hours	Percentage reacted (corr.)	k	Time Hours	Percentage reacted (corr.)	k
0.05	50.40	31.90	0.166	41.68	7.33
.0666	58.03	30.66	.200	50.96	8.22
.0833	60.57	26.50	.250	55.00	7.40
.10	63.90	24.01	.333	65.54	7.54
	Av.	28.3		Av.,	7.62

Chloro-acetonitrile (B. p., 123.5–124.5°) and Potassium Iodide

At 20°			At 10°		
Time Hours	Percentage reacted	k	Time Hours	Percentage reacted	k
0.10	26.36	6.85	0.166	15.76	2.27
.20	46.20	7.09	.50	39.40	2.27
.30	59.78	7.09	.75	51.10	2.20
.40	70.65	7.20	1.0	61.14	2.21
	Av.	7.08		Av.,	2.24

Chloro-acetamide (M. p., 116°) and Potassium Iodide

At 30°			At 25°		
0.5	12.92	0.608	0.5	7.88	0.360
1.0	23.49	.596	1.0	14.95	.358
2.0	41.43	.608	2.0	27.70	.362
4.0	64.11	.600	4.0	46.74	.360
	Av.	.603		Av.,	0.360

Chloromethyl Acetate[a] (B. p., 113–115°) and Potassium Iodide

Very little iodine was liberated in the acid; correction applied

At 25°			At 20°		
	(Corr.)			(Corr.)	
0.25	10.02	0.925	0.333	8.72	0.580
0.50	21.90	1.09	0.5	12.93	.607
1.0	36.34	1.02	1.0	23.22	.587
2.0	57.92	1.00	2.25	43.01	.570
	Av.	.984		Av.,	.586

TABLE V (*Continued*)

β-CHLORO-ETHYL ACETATE (B. P., 144–145°) AND POTASSIUM IODIDE

At 60°			At 50°		
Time Hours	Percentage reacted	*k*	Time Hours	Percentage reacted	*k*
3	5.97	0.0450	24	17.58	0.0178
6	12.23	.0466	32	22.80	.0179
16	27.99	.0459	48	32.14	.0181
24	37.50	.0443	72	42.86	.0177
	Av.	.0454		Av.,	.0179

CHLOROPROPYL ACETATE (B. P., 168–169°)[b] AND POTASSIUM IODIDE

Little iodine was liberated in acid solution; correction applied.

At 30°			At 25°		
	(Corr.)			(Corr.)	
1.0	10.20	0.234	2.45	15.07	0.147
2.0	19.83	.244	3.00	17.97	.146
3.25	29.80	.243	7.00	35.50	.141
5.00	41.90	.248		Av.,	.144
	Av.	.242			

ALLYL CHLORIDE (B. P., 44.6–45.2°) AND POTASSIUM IODIDE

At 25°

Time, hours	1.00	2.10	3.50	6.30	7.50	
Percentage reacted	12.32	22.90	36.63	54.35	61.00	
k	0.288	0.278	0.294	0.288	0.294	Av., 0.288

TRIPHENYL-CHLOROMETHANE AND POTASSIUM IODIDE

Iodine was liberated during the reaction; the solution was extracted before titration but no correction applied. The results are considered only preliminary.

At 0°			
Time, hrs.	0.0833	Percentage reacted 31.1	*k* 9.95
	.1667	37.4	6.39
		Av.,	8.18

CHLOROMALONIC ESTER (B. P., 140–143°, 30 MM.) AND POTASSIUM IODIDE

Iodine was liberated in the reaction; the acid solution was extracted with chloroform before titration but the titrations were not corrected.

The results are considered only preliminary.

Time, hours	0.05	0.10	0.166	0.25	
Pecentage reacted	30.6	45.0	56.2	64.5	
k	16.4	13.7	11.8	9.8	Av., 12.9

o-NITROBENZYL CHLORIDE (M. P., 49–50°) AND POTASSIUM IODIDE

At 25°

Time, hours	0.125	0.25	0.50	
Percentage reacted	31.4	51.8	73.8	
k	6.79	6.73	6.41	Av., 6.64

m-NITROBENZYL CHLORIDE (M. P., 45–46°) AND POTASSIUM IODIDE

At 25°

Time, hours	0.125	0.25	0.50	0.75	
Percentage reacted	15.42	27.93	46.52	58.65	
k	2.90	2.94	2.87	2.76	Av., 2.87

TABLE V (*Concluded*)

p-NITROBENZYL CHLORIDE (M. P., 71–72°) AND POTASSIUM IODIDE

At 25°

Time, hours	0.125	0.25	0.583	
Percentage reacted	24.83	43.23	69.00	
k	5.14	5.18	4.76	Av. 5.03

o-BROMOBENZYL CHLORIDE (B. P., 110–111°, 15 MM.) AND POTASSIUM IODIDE

At 0°			At −10°		
Time Hours	Percentage reacted	*k*	Time Hours	Percentage reacted	*k*
0.0666	41.30	17.94	0.25	35.80	4.05
.0833	46.75	17.65	.333	49.72	4.63
.10	47.79	15.01	.416	55.40	4.49
.1017	52.82	17.03	.50	58.20	4.06
	Av.	16.53		Av.	4.31

p-BROMOBENZYL CHLORIDE (B. P., 110–111°, 9 MM.) AND POTASSIUM IODIDE

At 0°			At −10°		
0.10	36.20	10.09	0.30	34.05	3.16
.133	41.72	9.28	.40	38.86	2.78
.166	55.62	11.09	.50	47.02	2.92
.20	60.06	10.70	.666	55.40	2.80
	Av.	10.29		Av.	2.92

p-CHLOROBENZYL CHLORIDE (B. P., 106.5–107.5°, 23 MM.) AND POTASSIUM IODIDE

At 30°			At 25°		
0.166	23.08	3.48	0.50	35.67	2.01
.25	31.06	3.33	.75	48.38	2.00
.50	51.45	3.33	1.0	57.67	2.02
.666	61.54	3.51	1.5	72.21	2.02
	Av.	3.37		Av.	2.01

[a] Prepared by the chlorination in sunlight of methyl acetate [Henry, *Ber.*, **6**, 740 (1873)].

[b] Prepared from acetyl chloride and trimethylene-chlorohydrin.

are uncorrected for the reasons given in the first part of this paper. Unless otherwise stated, satisfactory results could be obtained in the titration with potassium iodate without removing the organic material by extraction with chloroform. With a few substances it was found that more consistent results could be obtained by removing the organic material by an extraction with chloroform;[14] these instances are noted in Table V.

Because of the difficulty attendant on the liberation of considerable amounts of iodine in the experiments with chloromalonic ester and chloromethyl ether, a few experiments were carried out in which the amount of reaction was estimated by the precipitate of potassium chloride. This method was employed in our first paper with benzoyl chloride. These very

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[14] See Ref. 1 b, p. 247.

TABLE VI

REACTION BETWEEN 2,4-DINITROBENZYL CHLORIDE AND POTASSIUM IODIDE

Concn. of organic chloride, 0.125 *M;* of KI, 0.025 *M;* *k* calculated from the usual equation in which *b* = 0.025.

At 0°					
Time Hours	Percentage reacted	*k*	Time Hours	Percentage reacted	*k*
0.108	30.01	11.8	0.451	69.13	9.9
.226	45.10	9.7	.504	80.10	12.4
.290	60.01	11.8	.637	83.44	11.0
.318	58.43	10.3			
.424	69.98	10.8	.683	86.46	11.5
				Av.	11.0

rough determinations are included here merely to show the accuracy of this very rapid method. A comparison of the average value for *k* with the values given in Table V (at a 10° lower temperature) demonstrates that the method gives results of the right order of magnitude.

TABLE VII

DETERMINATION OF RATE BY ESTIMATION OF PRECIPITATED POTASSIUM CHLORIDE

CHLOROMETHYL ETHER AND POTASSIUM IODIDE			CHLOROMALONIC ESTER AND POTASSIUM IODIDE		
At 10°			At 10°		
Time Hours	Estimated percentage reacted	*k*	Time Hours	Estimated percentage reacted	*k*
1.0	25	0.63	0.05	48	30.0
1.5	32	.58	.0666	52	16.6
2.0	40	.58	.0833	60	25.5
2.5	50	.64	.10	64	24.0
	Av.	.61		Av.	24.0

Summary

1. The rates of reaction with potassium iodide of a number of organic chlorides containing unsaturated groups have been measured. The results have been compared with those of previous workers and have been found to be in fair agreement with the relative rates measured with sodium thiosulfate but very different from the values obtained with pyridine.

2. The relative reactivity toward potassium iodide of compounds of the type ACH_2Cl where A is an activating group has been found to be roughly proportional to the acidity of the corresponding AOH compound, the activity of the alpha hydrogen atom in ACH_3 and inversely as the basicity of the ANH_2 compound. It is pointed out that this activating influence of unsaturated groups is not consistent with certain theories concerning the varying polarity of the halogen atoms.

3. A series of chloro esters has been measured in which a definite (though slight) alternation in reactivity is evident.

4. A few substituted benzyl chlorides have been measured. The results are not in accord with those obtained by other investigators with other reagents. The reactivities of the mononitro and dinitro compounds are in agreement with the other methods of evaluating the activating power of the substituted phenyl group but the reactivities of the chloro and bromo compounds are anomalous; these substances show a surprisingly great reactivity.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, COLUMBIA UNIVERSITY, No. 463]

THE "IRREGULAR SERIES" IN THE PRECIPITATION OF ALBUMIN[1]

BY ARTHUR W. THOMAS AND EARL R. NORRIS

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The "Irregular Series" or "Tolerance Zone" observed in the precipitation of albumin by salts of the heavier metals is accepted as a colloid-chemical phenomenon. Our knowledge concerning the precipitation of albumin by heavy metal metals and the dissolution of the coagulum upon addition of excess of the heavy metal salt is nearly a century old.[2] It has also been recorded[3] that an excess of ferric chloride causes dissolution of the precipitate first formed.

The first zone of precipitation (obtained with very dilute heavy metal solutions) has been ascribed by Bechhold[4] and by Pauli[5,6] to the formation of an insoluble complex between the albumin and the metallic oxide formed by hydrolysis of the salt. The zone of no precipitation or "Tolerance Zone" (obtained with increasing concentration of heavy metal salt) according to Bechhold[7] "results from ionization." Pauli[6] attributes it to the formation of soluble basic metallic compounds of albumin, while the second zone of coagulation is attributed by him to the salting out of the protein by the high concentration of heavy metal salt.

The existence of one soluble and two insoluble heavy metal compounds

[1] Abstract of the dissertation submitted by Earl R. Norris to the Faculty of Pure Science, Columbia University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] For a review of the literature dating from 1831 see Harnack, *Z. physiol. Chem.*, **5**, 198 (1881), and O. Cohnheim, "Chemie der Eiweisskörper," F. Vieweg and Sohn, Braunschweig, **1911**.

[3] Sigfried, *Z. physiol. Chem.*, **21**, 360 (1895).

[4] Bechhold, *Z. physik. Chem.*, **48**, 385 (1904).

[5] Pauli, *Beitr. Chem. Physiol. Pathol.*, **6**, 233 (1905).

[6] Pauli and Flecker, *Biochem. Z.*, **41**, 461 (1912).

[7] Bechhold-Bullowa, "Colloids in Biology and Medicine," D. Van Nostrand Co., New York City, **1919**, p. 157.