[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE RELATION BETWEEN THE STRUCTURE OF ORGANIC HALIDES AND THE SPEED OF THEIR REACTION WITH INORGANIC IODIDES. I. THE PROBLEM OF ALTERNATING POLARITY IN CHAIN COMPOUNDS

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Introduction

This is the first of a series of papers dealing with the ease of replacement of halogen atoms in various types of organic halides. The object of the investigation is to compare the reactivities of the halogen atoms in as great a variety of organic halides as possible by measuring the speed of a certain metathetical reaction which will proceed normally with all the halides employed. Results so obtained are only relative but are, at least, strictly comparable with one another; whether or not they are comparable with similar results obtained by studying other reactions of alkyl halides remains to be seen. This question forms the basis of another investigation, and this aspect of the work will be discussed in a later paper. A comparison of our results with those of previous investigators in this field will be reserved, therefore, for this later article.

In deciding on a particular reaction to be employed in comparing the reactivities of organic halides, it seemed important to find one that would give the same type of product with a large variety of halogen compounds. Furthermore, the reaction should be as far as possible free from side reactions and other complicating possibilities. The difficulty of using amines,[1] alcoholates,[2] phenolates[3] or any alkaline reagent in alcoholic or aqueous solution[4] is seen by considering the possibility of comparing such a series of compounds as ACH_2Cl, ACH_2CH_2Cl, $ACH_2CH_2CH_2Cl$, where A is a strongly negative group such as carboxyl or benzoyl. Obviously, with any reagent which can cause the elimination of hydrochloric acid the results obtained with this series of compounds would be meaningless. The group A not only affects the reactivity of the chlorine atom, but also the activity of the hydrogen in the α position; unsaturated and cyclic compounds are thus easily formed. We particularly desired to study a series of compounds, such as that just mentioned, in order to discover whether or not the "alternating polarity," predicted by various electronic theories of valence, would manifest itself by alternations in the reactivity

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[1] Menschutkin, *Z. physik. Chem.*, **6**, 41 (1890). Clarke, *J. Chem. Soc.*, **103**, 1689 (1913). Moore, *ibid.*, **101**, 2459 (1912). Hawkins, *ibid.*, **121**, 1170 (1922).

[2] Conrad and Brückner, *Z. physik. Chem.*, **7**, 274 (1891). Haywood, *J. Chem. Soc.*, **121**, 1904 (1922). Acree, *ibid.*, **105**, 2582 (1914).

[3] Segaller, *ibid.*, **105**, 106 (1914). Cox, *ibid.*, **117**, 493 (1920).

[4] Senter, *ibid.*, **109**, 681 (1916); Madsen, *ibid.*, **103**, 965 (1913).

of the halogen atom. To find a suitable reagent for such a comparison was thus of prime importance.

The reaction between an organic chloride or bromide and potassium or sodium iodide in absolute acetone is almost ideal for the purposes we had in mind: RX + KI ⟶ RI + KX. Finkelstein[5] has shown that this simple metathesis occurs fairly rapidly with a variety of halides, and in most cases the product is the corresponding iodide. The reaction, of course, has its limits, and in the case of the dihalides, for example, generally yields an unsaturated or cyclic compound; the simple aryl halides do not react. A number of earlier investigators have used aqueous or alcoholic solutions of the alkali iodides for preparing a great number of organic iodides. Spindler,[6] a number of years ago, made a quantitative study of the reaction at 75° between the crystalline hydrate of calcium iodide and organic halides. For various reasons his results were only approximate, but he did show the marked difference between certain types of organic halides, such as allyl chloride and chloro-acetic ester on the one hand, and chlorobenzene on the other.

The use of aqueous or alcoholic solutions of the inorganic iodide is out of the question for our present purposes, because of the fact that hydrogen iodide, which is formed to some extent in these solvents, causes a partial reduction of the organic iodide, thus: $RI + HI \longrightarrow RH + I_2$. By using very pure acetone, this complication and any danger of hydrolysis or alcoholysis can be avoided. The reaction can even be carried out with such a reactive substance as ω-chloro-acetophenone without any iodine being liberated. In the method which we employed for following the course of the reaction, the organic halide and an acetone solution of potassium iodide were mixed and allowed to stand at a definite temperature for a certain period of time. The mixture was then rapidly introduced into cold, dil. hydrochloric acid and the amount of inorganic iodide determined by titration with iodate solution as described in the experimental portion of this paper. In some cases it was found advisable to extract the solution with chloroform to remove the organic material before the titration was performed. This procedure also enabled us to determine whether or not appreciable hydrolysis of the organic iodide had occurred in the cold aqueous acid, by comparing the results of parallel experiments in which the mixture was allowed to stand for different intervals of time before the extraction. The only substance we have so far investigated which is hydrolyzed sufficiently rapidly to vitiate the results is benzoyl iodide; the method cannot be applied, therefore, to benzoyl chloride and in all probability will fail with all acid chlorides.

Since potassium chloride is completely insoluble in acetone, it crystal-

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

[6] Spindler, *Ann.*, **231,** 257 (1885).

lizes from the reaction mixture during the course of the reaction. In order to see whether or not this solid might occlude potassium iodide and thus cause our results to be in error, several experiments were conducted with relatively large amounts of benzyl chloride. The potassium chloride was filtered off on a suction filter, washed twice with absolute acetone, and tested for iodide. It was found to be practically free from any iodide. Further evidence that the separation of the solid potassium chloride does not interfere was obtained by continually agitating the reaction tubes in several experiments. There was no difference within our experimental error between the results thus obtained and those obtained with stationary tubes.

This separation of a precipitate enables one to follow the course of the reaction roughly by estimating the amount of solid potassium chloride formed. By the aid of this procedure we were able to obtain some approximate measurements for the speed of reaction of benzoyl chloride.

The tubes were examined for iodine color in each experiment and were uniformly found to be colorless or very faintly yellow. The possibility of reduction during the reaction is thus eliminated as a source of error.

The organic chloride and potassium iodide were taken in such quantities that the ratio of organic substance to iodide was 5 to 1. Several experiments with benzyl chloride in different dilutions showed that the reaction velocity was influenced by change of concentration of the factors in accord with a bimolecular equation; Table I gives these results. The reaction velocity constant (k) was, therefore, calculated according to the well-known bimolecular formula.[7]

TABLE I

EFFECT OF DILUTION ON THE SPEED OF THE REACTION BETWEEN BENZYL CHLORIDE AND POTASSIUM IODIDE AT 25°

The amount of benzyl chloride reacted at definite times is given below for two experiments; in (A) 0.001 mole of benzyl chloride and 0.0002 mole of potassium iodide were dissolved in 5 cc. of acetone; in (B) the same amounts of material were dissolved in 10 cc. of acetone.

	Hours	%	*Hours*	%	*Hours*	%	*Hours*	%
(A)	0.5	15.41	1.0	27.52	2.0	46.20	3.0	57.50
(B)	1.0	18.21	2.0	32.35	4.0	52.55	6.0	62.00

Discussion of Results

In order to obtain significant values it was necessary to measure the speed of the reaction at a temperature at which the reaction would proceed at a measurable but not excessive rate. With the most reactive halides the measurements were made at 0°, with certain others at 25°, while for the less reactive substances 50° or 60° was employed. The

[7] We have not attempted an exhaustive study of the underlying mechanism of this reaction from the kinetic standpoint. Potassium iodide is probably dissociated to a considerable extent in acetone and the actual reaction may be $RX + I' \longrightarrow RI + X'$, which might be influenced by the concentration in several ways.

TABLE II

SUMMARY OF RESULTS

Compound	k_0	k_{25}	k_{40}	k_{50}	k_{60}	A	Relative reactivities 25°	50°	60°
$CH_3(CH_2)_2CH_2Cl$	...	(0.00219)	..	0.0415	0.119	4920	(1)	1	1
$CH_3(CH_2)_3CH_2Cl$	...	.....	..	....	.128	....	....	....	1.07
$C_6H_5CH_2Cl$	...	0.774	..	(8.07)	..	(3920)	(354)	(195)	...
$C_6H_5CH_2CH_2Cl$	...	.....	..	0.0466	.108	3920	....	1.12	0.907
$C_6H_5CH_2CH_2CH_2Cl$	...	.....	..	.0713	.160	3770	....	1.72	1.35
$C_6H_5CH_2(CH_2)_2CH_2Cl$	...	.....	..	.0617	.135	3660	....	1.49	1.13
$C_6H_5CH_2(CH_2)_3CH_2Cl$	...	.....	..	(.0590)	.129	(3660)	....	(1.42)	1.08
$C_6H_5CH_2(CH_2)_4CH_2Cl$	...	.....	..	(.0607)	.133	(3660)	....	(1.46)	1.12
$C_6H_5CH_2(CH_2)_5CH_2Cl$	...	.....	..	(.0580)	.127	(3660)	....	(1.40)	1.07
C_2H_5OOCCl	...	0.0954	..	(1.74)	..	(4850)	(43.7)	(42.0)	..
$C_2H_5OOCCH_2Cl$	...	6.37	..	(116)	..	(4850)	(2920)	(2800)	..
$C_2H_5OOCCH_2CH_2Cl$	...	.....	..	0.0667	..	....	....	1.61	..
$C_2H_5OOCCH_2CH_2CH_2Cl$	...	.....	..	.0686	..	....	....	1.65	..
$C_2H_5OOCCH_2(CH_2)_2CH_2Cl$	...	.....	..	.0562	..	....	....	1.35	..
$C_6H_5COCH_2Cl$	22.4	.....	..	12600.	..	(4850)	....	(302000)	..
$C_6H_5COCH_2CH_2Cl$	...	.....	1.19	3.60	..	4850	....	86.7	..
$C_6H_5COCH_2CH_2CH_2Cl$	...	0.848	..	(15.4)	..	(4850)	(389)	(372)	..
C_6H_5COCl	0.16[a]	(4.95)[a]	..	(90)[a]	..	(4850)[a]	....	(2220)[a]	..

[a] Approximate only.

temperature coefficient was determined in a number of cases by making measurements at two different temperatures. In order to make all the results comparable the results were calculated to 50° according to the following formula,

$$\log \frac{k_{50^\circ}}{k_{t^\circ}} = \mathrm{A}\left(\frac{1}{273 + t^\circ} - \frac{1}{323}\right)$$

Three series of compounds were investigated. The first consisted of three substances containing the benzoyl group, $C_6H_5COCH_2Cl$, $C_6H_5COCH_2CH_2Cl$ and $C_6H_5COCH_2CH_2CH_2Cl$; the second was composed of the following esters, $ClCOOC_2H_5$, $ClCH_2COOC_2H_5$, $ClCH_2CH_2COOC_2H_5$, $ClCH_2CH_2CH_2COOC_2H_5$ and $ClCH_2CH_2CH_2CH_2COOC_2H_5$; the third series had the general formula $C_6H_5(CH_2)_nCl$ starting with benzyl chloride and ending with η-phenylheptyl chloride. The preparation of these compounds is discussed in the experimental portion of this paper.

Table II summarizes the results of the individual measurements which are given in detail in the second part of this paper. The first five columns give the average values of the velocity constant of the reaction at the temperatures indicated; the numbers enclosed in parentheses were calculated from the results at another temperature by means of the equation given above and the value of A was recorded in the sixth column. This value of A was calculated from the results obtained at two different temperatures except for those values given in parentheses which were assumed on the basis of the similarity of the compound in question to one whose temperature coefficient had been determined.

For purposes of comparison the velocity constant of *n*-butyl chloride has been taken as unity at each temperature (25°, 50° and 60°) and the relative reactivities of all the other chlorides are expressed in terms of this standard. These relative reactivities are given in the last three columns of Table II. It is evident that since the temperature coefficient of the velocity constant varies considerably with the nature of the halide (compare butyl, phenylethyl and β-benzoylethyl chlorides) the relative reactivities will not be the same at all temperatures. This is a serious difficulty in connection with a study of slight changes in reactivity caused by slight change of structure. For the present purposes, however, this complication is of little consequence since we are primarily concerned with relatively large differences. Furthermore, our most significant comparison, which is the basis of this discussion, has been made at 50° and in all but five cases the measurements were made at this temperature or at 60° and any error introduced by the variations in the temperature coefficient is consequently small.

In Fig. 1, the common logarithms of the relative reactivities at 50° are plotted vertically and the increment of CH_2 groups horizontally. The logarithmic scale has been used merely to enable us to include all the substances in a convenient figure. An examination of this diagram brings out some interesting relationships. Considering, first of all, compounds of the type ACH_2Cl where A is the activating group, it is apparent that the groups in descending order of influence are: $C_6H_5CO > COOC_2H_5 > C_6H_5$; this is the same order in which these groups influence the mobility of an α hydrogen atom and the usual order of what has often been called their "negativity." An accurate measure of the reactivity of the corresponding compounds ACl is only available in one case, $A = COOC_2H_5$, in which it is considerably lower than that of the compound ACH_2Cl; chlorobenzene will not react with potassium iodide (nor will even trinitrochlorobenzene in boiling acetone for several days) so that in the case of the phenyl group the same increase of reactivity with an introduction of one CH_2 is very striking. In spite of the great reactivity of benzoyl chloride towards substances containing an hydroxyl group we are inclined to believe (on the basis of very crude experiments) that the speed of its reaction with potassium iodide is less than that of chloro-acetophenone. As a tentative generalization based on the three series so far studied it would seem that the halogen atom in compounds of the type ACH_2Cl is considerably more reactive than in compounds of the type ACl where A is a "negative" group. If the measurements with benzoyl chloride are significant the "activating influence" of the groups in the compound ACl is $C_6H_5CO > COOC_2H_5 > C_6H_5$, the same order as that for compounds of the type ACH_2Cl.

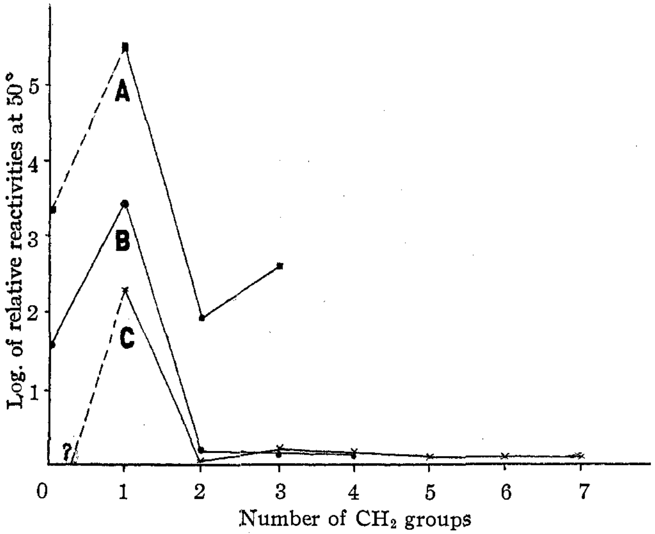

Fig. 1.—Relative reactivities compared to butyl chloride at 50°. of compounds $A(CH_2)_nCl$. Curve A = benzoyl series; Curve B = carbethoxy series; Curve C = phenyl series

In each of the three series there is a very great decrease in reactivity of the chlorine atom when we pass from ACH_2Cl to ACH_2CH_2Cl. In the two series in which phenyl and carbethoxy, respectively, are the activating groups this fall is practically to the level of the normal aliphatic chlorides (butyl and amyl); the second member of the benzoyl series, however, is some 80 times more reactive than butyl chloride, although the decrease in reactivity compared to $C_6H_5COCH_2Cl$ is parallel to that in the ester series.

The behavior of the chlorine atom in the compounds $A(CH_2)_3Cl$ and the higher homologs is most interesting. In the benzoyl series there is a fourfold increase in reactivity of the halogen in $C_6H_5COCH_2CH_2CH_2Cl$ as compared with that in $C_6H_5COCH_2CH_2Cl$; information concerning the higher homologs, unfortunately, is still lacking. The series of esters behaves quite differently; there is no appreciable difference in the reactivity of the compounds with two and three CH_2 groups and the next member shows only a small and insignificant decrease of reactivity. This great divergence between the benzoyl and ester series can hardly be attributed to the difference in activating power of the groups (as measured by the most active member) because the much less active phenyl compounds show a slight but definite increase in reactivity on increasing the number of CH_2 groups from two to three. Until more information is available it is profitless to speculate on the reasons for the lack of uniformity in the three series. We are now starting an investigation of several series of compounds with such activating groups as CH_3CO. Consequently,

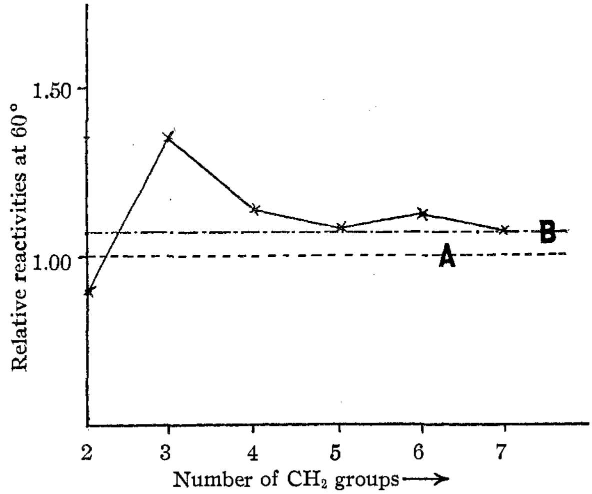

Fig. 2.—Relative reactivities at 60° of phenylethyl chloride and higher homologs. A = butyl chloride; B = amyl chloride

we will defer any detailed consideration of the bearing of our results on certain electronic and other valence theories until more data are at hand. However, from the results now available it seems certain that it is unsafe to assume that in an homologous series of the type $A(CH_2)_nCl$ there will be any marked alternations in the reactivity of the halogen atom even if the group A is of such a nature as to greatly affect the reactivity of the chlorine in the compound ACH_2Cl.

The data for the compounds $C_6H_5CH_2CH_2Cl$ to $C_6H_5(CH_2)_6CH_2Cl$ are plotted on an arithmetical scale in Fig. 2 in order to show the slight variations more clearly than in Fig. 1. The relative reactivities at 60° (referred to butyl chloride at the same temperature) were chosen for this diagram rather than those at 50° since measurements of all these substances were made at the former temperature. The slight differences between phenylethyl, phenylpropyl and phenylbutyl chlorides have already been discussed. The values for the last four compounds of the series are the same within the probable experimental error (5%) and are not significantly different from the values of *n*-butyl and *n*-amyl chlorides. If the influence of a phenyl group extends to more than the first three carbon atoms of an attached chain, this influence is too small to be measured by our methods.

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Experimental Part

1. The Preparation of the Organic Halides. A. The Chloroketones

The second member of this series was made by the following reaction according to the method of Hale,[8] $CH_2ClCH_2COCl + C_6H_5 \xrightarrow{AlCl_3} CH_2ClCH_2COC_6H_5$, the necessary β-chloropropionic acid being prepared from ethylene cyanohydrin by heating it with concd. hydrochloric acid in a sealed tube.[9] The γ-chlorobutyrophenone was synthesized by the following reactions, the experimental details of which will appear in another paper. We are indebted to Mr. J. B. Segur for the preparation of this compound.

$$CH_2ClCH_2CH_2CN + C_6H_5MgBr \longrightarrow CH_2ClCH_2CH_2C(C_6H_5) = NMgBr + H_2O \longrightarrow CH_2ClCH_2CH_2COC_6H_5$$

Chloro-acetophenone.—A high grade commercial product was purified by recrystallization from petroleum ether. It was pure white and melted at 57°.

β-Chloropropiophenone.—Ten g. of β-chloropropionic acid was treated with 9 g. of phosphorus trichloride. After the first vigorous reaction was complete the mixture was heated on a steam-bath for 1 hour. To the β-chloropropionyl chloride thus formed, 100 cc. of dry benzene was added and the mixture filtered to remove phosphorous acid. It was then gradually poured onto 15 g. of finely ground, anhydrous aluminum chloride;

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[8] Hale, This Journal, **41**, 845 (1919).

[9] Jacobs and Heidelberger, *ibid.*, 39, 1465 (1917).

copious amounts of hydrogen chloride were immediately evolved. The reaction was completed by heating at 80° for 1 hour. The product was decomposed by treating with ice, and the benzene layer washed with water, dried and evaporated under diminished pressure. The residue solidified to a mass of white crystals; yield, 10 g. or 65%. After one crystallization from petroleum ether the β-chloropropiophenone melted at 47–48°; repeated recrystallizations from petroleum ether or dil. alcohol failed to raise the melting point above 49–50°, although the previous investigators of this substance give 57–58° as the melting point. We believe that the high melting point previously reported is in error since our product was repeatedly crystallized (it was obtained in crystals over an inch long by slow crystallization from petroleum ether), the melting point was determined with a standardized thermometer and the analysis was satisfactory.

Analysis. Calc. for C_9H_9OCl: Cl, 21.04. Found: 21.21.

γ-Chlorobutyrophenone.—The preparation of this substance will be described in detail in another paper. It was carefully purified by crystallization from a dilute anhydrous petroleum ether solution at —20°; m. p., 19–20°.

Analysis. Calc. for $C_{10}H_{11}OCl$: Cl, 19.4. Found: 19.4.

B. The Phenyl Alkyl Chlorides

The synthesis of an extended series of alcohols of the general formula $C_6H_5(CH_2)_nCH_2OH$ and the corresponding halides has been accomplished by von Braun.[10] In our synthesis of phenylpropyl, phenylbutyl, phenylamyl, phenylhexyl and phenylheptyl alcohols we have preferred to use a general method rather than to employ the various methods used by von Braun and other investigators in preparing each compound. This general method is merely an extension of the reaction used by Grignard[11] in preparing phenylethyl alcohol; it is illustrated by the following reactions.

$$C_2H_5MgBr + ClCH_2CH_2CH_2OH \longrightarrow ClCH_2CH_2CH_2OMgBr + C_2H_6$$
$$RMgX + ClCH_2CH_2CH_2OMgBr \longrightarrow RCH_2CH_2CH_2OMgBr + MgClX$$
$$RCH_2CH_2CH_2OMgBr + HCl \longrightarrow RCH_2CH_2CH_2OH + MgClBr$$

In the preparation of ω-phenylpropyl alcohol, ethylene chlorohydrin was used in place of trimethylene chlorohydrin; the Grignard reagent in this case was prepared from benzyl chloride. Starting with benzyl chloride and trimethylene chlorohydrin, phenylbutyl alcohol was prepared; phenylethylmagnesium bromide in a similar reaction yielded phenylamyl alcohol. For the preparation of the last two members of the series, the ω-phenylpropyl and ω-phenylbutyl alcohols (prepared as above) were converted into the bromides from which the corresponding Grignard reagent was made.

The use of ethylmagnesium bromide to remove the active hydrogen of the hydroxyl group is of great advantage, as Grignard showed, both because one molecule of a more expensive halide is saved and because there is less contamination of the final product with the high-boiling hydrocarbon which is always an unfortunate by-product of the reaction between magnesium and the phenylalkyl halides. In fact the formation of these

[10] von Braun, (a) *Ber.*, **43**, 2841 (1910); (b) **44**, 2871 (1911).

[11] Grignard, *Ann. chim.*, [8] **10**, 23 (1907).

hydrocarbons is the one disadvantage of this method of synthesis. These substances (such as dibenzyl) are in many cases very difficult to separate by distillation from the final product. In two instances (with phenylpropyl and phenylbutyl alcohol) the hydrocarbon was removed by converting the alcohol into the half ester of phthalic acid and dissolving this in alkaline solution; the alcohol obtained by hydrolysis of this ester was pure. The chlorides were prepared from the alcohols by heating the latter in a sealed tube with aqueous hydrochloric acid. The final product boiled over a narrow range in every case but one; a halogen analysis served as a check of the purity of each compound. η-Phenylheptyl chloride was not obtained pure because of the difficulties mentioned and the small amount of material available; the impurity present (a hydrocarbon) was of such a nature, however, that it did not interfere with the reaction with potassium iodide, and the measurements with this impure compound are probably not greatly in error.

Benzyl Chloride.—A good grade of commercial product was allowed to stand over anhydrous calcium chloride for several weeks and was then filtered and distilled under diminished pressure with the use of a fractionating column; b. p., 57–58° (8 mm.).

β-Phenylethyl Chloride.—The corresponding alcohol was converted into the chloride by heating with[12] fuming hydrochloric acid in a sealed tube at 140° for 4 to 5 hours. After the chloride was separated and dried in the usual way it was shaken with concd. sulfuric acid to remove unchanged alcohol. It was then washed with water, dried over calcium chloride and repeatedly distilled under diminished pressure through a fractionating column. The final fraction collected boiled at 68.5–69° (4 mm.); yield, 57%.

Analysis. Calc. for C_8H_9Cl: Cl, 25.2. Found: 25.5.

Phenylpropyl Chloride.—Since the method of Grignard[11] for the preparation of phenylpropyl alcohol from ethylene chlorohydrin, ethylmagnesium bromide and benzylmagnesium bromide is typical of the procedure we employed for all the homologs of benzyl alcohol, the following brief description is perhaps not out of place.

Ethylmagnesium bromide, prepared from 12.2 g. of magnesium and 55 g. of ethyl bromide in the usual way, was treated with 42 g. of ethylene chlorohydrin dissolved in an equal volume of dry ether. The addition was carried out slowly since a vigorous evolution of ethane took place; loss of ether was prevented by having the flask equipped with a return condenser, the chlorohydrin being added through a separatory funnel. The mixture was finally heated for 30 minutes on a steam-bath and was occasionally shaken. Benzylmagnesium chloride prepared from 24 g. of magnesium, and 126 g. of benzyl chloride in 100 cc. of dry ether was slowly allowed to siphon into the reaction mixture. The siphon was started by applying air pressure to the flask containing the benzylmagnesium chloride; the rate of flow was regulated by a wide-bore stopcock which formed part of the siphon. As the Grignard reagent entered the flask a slight reaction took place which caused the ether to boil and slowly drop back into the flask from the end of the attached return condenser. The flask was shaken from time to time. After all the benzylmagnesium chloride had been added the ether was distilled off through a stopcock attached to a suitable condenser, the flask being warmed in a water-bath. After a considerable amount of the ether had distilled a reaction began to take place

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[12] *Ber.*, **45**, 1268 (1912).

which was attended by considerable foaming. To prevent the contents of the flask from frothing over into the condenser, the stopcock was closed from time to time, the ether vapors being condensed by the return condenser and returned to the flask; the ether which thus refluxed back into the flask served to break the foam and moderate the reaction. All the ether was finally removed by heating the flask to 90–95°; a porous gray mass remained. This was broken up and added to a mixture of ice and hydrochloric acid. An oily layer formed which was dissolved in ether, dried over sodium sulfate and after the ether had been evaporated, distilled under diminished pressure. The fraction which boiled at 80–100° at 8 mm., weighed 43.6 g., a yield of 64%. Considerable dibenzyl was obtained from a higher fraction.

The crude phenylpropyl alcohol thus obtained presumably contained some dibenzyl as evidenced by the wide range of its boiling point. In one experiment it was purified by conversion into the half ester of phthalic acid by heating it with phthalic anhydride for 16 hours at 110–120°. The half ester was dissolved in sodium carbonate and the organic impurities (such as dibenzyl) removed with ether. On acidification, the pure phthalic acid ester was obtained. It was saponified by heating with aqueous sodium hydroxide at 100° for 2 hours; the product was extracted with ether, dried and distilled in the usual manner. From 13.6 g. of crude alcohol 8 g. of pure alcohol was obtained which boiled at 105–107° (7 mm.).

The pure alcohol was converted into the chloride by heating it with concd. hydrochloric acid (saturated with hydrogen chloride at 0°) at 100° for 8 hours. The chloride thus prepared boiled at 85–87° (9 mm.); 8 g. of alcohol yielded 7 g. of chloride, a 77% yield. The purity was checked by analysis.

Analysis. Calc. for $C_9H_{11}Cl$: Cl, 22.94. Found: 23.24.

It is probably unnecessary to purify the alcohol by the phthalic anhydride process, since in another experiment the chloride was prepared directly from the crude alcohol and was found to boil within 3° and give a satisfactory analysis. The dibenzyl which was dissolved in the crude alcohol separated during the treatment with hydrochloric acid and was filtered off.

δ-Phenylbutyl Chloride.[13]—Forty-nine g. of trimethylene chlorohydrin was treated with ethylmagnesium bromide and benzylmagnesium chloride in the manner described for the preparation of phenylpropyl alcohol. The yield of crude phenylbutyl alcohol was 37 g. or 50% of the calculated yield. It boiled at 105–114° (4 mm.); an analysis for carbon and hydrogen corresponded to the presence of 3–4% of dibenzyl. It was purified through the phthalic anhydride process and yielded a pure product boiling at 117–119° (4 mm.). This was converted into the chloride in the manner described above. The phenylbutyl chloride thus obtained boiled at 100–101° (6 mm.); yield, 74%.

Analysis. Calc. for $C_{10}H_{13}Cl$: Cl, 21.0. Found: 21.2.

A sample of chloride made directly from the crude alcohol boiled over a range of 2° and was apparently pure as shown by a satisfactory analysis for chlorine.

ε-Phenylamyl Chloride.—Phenylethyl bromide was prepared[14] from phenylethyl alcohol and hydrobromic acid. It was converted into the corresponding Grignard reagent[15] according to the procedure outlined by Gilman.[16] The reagent was then added to the product formed by the action of ethylmagnesium bromide on trimethylene chlorohydrin, and the resulting phenylamyl alcohol was obtained by the procedure previously outlined for the lower homologs. A 36% yield of alcohol boiling at 135–136° (5–6

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[13] Ref. 10a, p. 2846.

[14] Ref. 10b, p. 2872.

[15] Norris, THIS JOURNAL, **38,** 1071 (1916).

[16] Gilman, *ibid.*, **45,** 159 (1923).

mm.) was obtained. It was converted into the chloride by heating it with concd. hydrochloric acid in a sealed tube. The phenylamyl chloride thus prepared boiled at 111–112° (5–6 mm.) and was pure, as shown by the following analysis.

Analysis. Calc. for $C_{11}H_{15}Cl$: Cl, 19.42. Found: 19.32.

ζ-Phenylhexyl Chloride.—Phenylpropyl bromide was prepared[17] from phenylpropyl alcohol by the use of aqueous hydrobromic acid. The Grignard reagent prepared from it was allowed to interact with the product obtained from trimethylene chlorohydrin and ethylmagnesium bromide. The procedure was exactly the same as that outlined for the other compounds. Phenylhexyl alcohol boiling at 140–141° (3 mm.) was obtained in a 33% yield. It was converted into the chloride in the usual way and gave a product which boiled at 115–116° (4 mm.); yield, 88%. The analytical results given below indicate that the phenylhexyl chloride thus prepared contained about 2% of impurity. Since this was presumably a hydrocarbon and would not interfere seriously with our measurements, the compound was not further purified.

Analyses. Calc. for $C_{12}H_{17}Cl$: Cl, 18.0. Found: 17.6, 17.6.

Phenylheptyl Chloride.[18]—The method of preparing this substance was identical with that used for the hexyl chloride except that phenylbutyl bromide was used in place of phenylpropyl bromide. The alcohol which was obtained boiled at 142–145° (7 mm.); yield, 21%. The chloride obtained in the usual manner boiled over a wide range (120–140° (3 mm.)) and was about 88% pure, as indicated by the following analysis.

Analysis. Calc. for $C_{13}H_{19}Cl$: Cl, 16.8. Found: 14.9.

Owing to the difficulties of preparing this substance no attempt was made to obtain it in a pure condition; the amount taken for each measurement was corrected for 12% of inert impurity.

C. The Chloro Esters

The β-chloropropionic acid and γ-chlorobutyric acid necessary for the preparation of the corresponding esters were prepared by heating ethylene cyanohydrin and trimethylene cyanohydrin, respectively, in a sealed tube with hydrochloric acid. The δ-chlorovaleric acid was synthesized according to the following scheme by the malonic ester synthesis.

$$C_6H_5OCH_2CH_2CH_2Br + Na[CH(COOC_2H_5)_2] \longrightarrow C_6H_5OCH_2CH_2CH_2CH(COOC_2H_5)_2$$

$$\longrightarrow C_6H_5OCH_2CH_2CH_2CH(COOH)_2 \longrightarrow C_6H_5OCH_2CH_2CH_2CH_2COOH \xrightarrow{+\,HCl} Cl\text{-}CH_2CH_2CH_2CH_2COOH.$$

Ethyl Chlorocarbonate.—A high grade commercial material which boiled at 93–94° was employed.

Ethyl Chloro-acetate.—A commercial product was distilled through a fractionating column, the fraction boiling at 142.2–142.8° being collected.

Ethyl β-Chloropropionate.—The esterification of β-chloropropionic acid was carried out by saturating an absolute alcohol solution of the compound with hydrogen chloride. The product was isolated and purified in the usual manner; it was fractionally distilled thrice at atmospheric pressure. The final fraction was collected between 160° and 162°; all but a small amount of it[19] boiled constantly at 161°. The yield was 59%.

Ethyl γ-Chlorobutyrate.—This substance was prepared according to Henry's method[20] by converting trimethylene chlorohydrin into the cyanohydrin, heating

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[17] Ref. 10b, p. 2876.

[18] Ref. 10b, p. 2880.

[19] *Bull. soc. chim.*, [3] 9, 416 (1893).

[20] Henry, *ibid.*, **45**, 341 (1886).

this in a sealed tube with hydrochloric acid and then esterifying the resulting γ-chlorobutyric acid in the usual manner. The γ-chlorobutyric acid, which we prepared in this way, melted at 10.4°, the point recorded by Henry. A later investigator[21] claims that Henry's acid was impure and the melting point of the pure acid is 16°. As the chief impurity that would be present is undoubtedly the butyro lactone which is converted into γ-chlorobutyric acid during esterification we did not attempt to purify the acid further. The ester was distilled through a fractionating column under diminished pressure; b. p., 64–66° (10 mm.).

Ethyl δ-Chlorovalerate.—The phenoxyvaleric acid was prepared essentially according to Funk's[22] directions from γ-bromopropylphenyl ether and malonic ester. A 64.6% yield of phenoxypropyl malonic ester was obtained in the first step; the saponification of the ester was quantitative and the yield of phenoxyvaleric acid from the malonic acid was 96%. A somewhat improved method of preparing and purifying the chlorovaleric ester was developed since Funk reports a very low yield by his method.

Fifteen g. of δ-phenoxyvaleric acid was placed in a sealed tube with 150 cc. of c. p. concd. hydrochloric acid and the mixture allowed to stand overnight. On the next morning the tube was placed in a furnace and heated for 5 hours at 180°. When the tube was cooled and opened, two layers were present which smelled strongly of phenol. The mixture was diluted, three-fourths neutralized with solid sodium bicarbonate and extracted 5 times with ether, the combined ethereal layers being dried over calcium chloride.

The ether was distilled, the residue dissolved in absolute ethyl alcohol and esterified by saturating the solution with dry hydrogen chloride and allowing it to stand overnight. The mixture was poured into water, nearly neutralized with solid sodium bicarbonate and extracted five times with ether, and the ethereal layer dried over calcium chloride. After the ether was distilled the residue was fractionated in a vacuum.

The boiling point of phenol is 182.6° (760 mm.), and δ-chlorovaleric ester boils at 205–206° (760 mm.), so it was expected that the separation by vacuum fractional distillation would be difficult, if at all possible. After carefully fractionating the mixture five times under diminished pressure it was found that the first fraction was nearly pure phenol, for it crystallized on cooling. However, the higher fractions all contained considerable amounts of phenol as indicated by the addition of bromine water to an extremely dilute solution of the ester-phenol mixture. After the fifth fractionation the last fraction was analyzed by the Carius method and shown to be only about 83% pure chlorovaleric ester.

After various methods of purification had been tried, the following was found to give excellent results. Preliminary tests showed that the halogen was not rapidly hydrolyzed from the ester by 10% sodium hydroxide solution, while this solution would rapidly and completely remove the phenol. It was found that when the chloro ester was shaken with this alkaline solution at a low temperature and then rapidly extracted from the alkali a pure ester was obtained, and that practically no hydrolysis took place. The last fact was established by acidifying a portion of the alkaline solution and treating it with silver nitrate solution. Practically no precipitate of silver chloride was formed and hence practically no ionic chlorine was present which would have come from the hydrolysis of the chlorine of the ester.

The actual procedure used was as follows. The higher fractions remaining from the fifth fractionation were placed in a 100cc. separatory funnel; 50 cc. of 10% sodium hydroxide solution was cooled to —5° and then added to the ester in the separatory funnel and the mixture shaken very vigorously for $1^1/_2$ minutes. Then 30 cc. of ether was

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[21] *Ann.*, **319**, 360 (1901).

[22] Funk, *Ber.*, **26**, 2568 (1893). Mellor, *J. Chem. Soc.*, **79**, 132 (1901).

added, the whole shaken for 30 seconds and the aqueous layer separated; the aqueous layer was then extracted twice more with 30cc. portions of ether, the first being shaken for 30 seconds and the second for 15 seconds and all operations were carried on as rapidly as possible. The combined ethereal layers were then dried over anhydrous sodium sulfate.

The ether was removed by means of a water pump and the residue fractionally distilled through a fractionating column at 10mm. pressure. The third fraction, weighing 6.3 g., contained the bulk of the material; it distilled at 80–83° (8 mm.), the distillation being continued to dryness. The boiling point of the product was 83° (8 mm.); Funk gives the boiling point as 205–206° at ordinary pressure.

This fraction gave no test for phenol with bromine water. Analysis proved that the product was pure δ-chlorovaleric ester; yield, 7.8 g., or 61.5%. Some of the crude material was used up in making the preliminary tests, so that the real percentage yield probably approached 75%.

Analysis. Calc. for $C_7H_{13}O_2Cl$: Cl, 21.54. Found: 21.57.

n-**Butyl Chloride.**—A commercial material was fractionally distilled. The product boiled at 78–79°.

n-**Amyl Chloride.**—A high grade *n*-amyl alcohol was converted into the chloride by heating it in a sealed tube with hydrogen chloride; b. p., 107–108°.

Reagents Employed

Acetone.—It is essential that the acetone be free from impurities which would cause the formation of hydrogen iodide, or which would liberate iodine from the inorganic iodide. U. S. P. acetone was heated under a return condenser with calcium oxide (or solid sodium hydroxide) and solid potassium permanganate; it was then fractionally distilled with a Glinsky still-head, and the portion which boiled at 56.5° to 57.0° was collected in a receiver protected from moisture. Such material did not color anhydrous copper sulfate in 30 minutes, and would retain for 30 minutes the faint pink color caused by a trace of potassium permanganate. When kept in the dark it did not liberate any perceptible amount of iodine when potassium iodide was dissolved in it.

Potassium Iodide.—A highest purity commercial material was recrystallized twice from distilled water. It was dried in an oven at 110° for two hours and cooled in a desiccator before being dissolved in the acetone. The solution in acetone must be kept in the dark and when so kept is very stable.

Procedure

Thick-walled glass tubes 15cm. long and 15 mm. in diameter or thick test-tubes of the same dimensions were used as the reaction vessels. A definite volume (5 cc.) of a standard solution of potassium iodide in acetone was introduced into each tube, and then a thin-walled bulb-tube containing the organic halide was inserted. The tube was kept in a vertical position to prevent the mixing of the reactants and sealed off in a blast lamp. The amount of organic halide in the inner tube was regulated by introducing a definite weight of the pure material (liquid or solid) into each tube. Essentially the same amount of organic halide and the same volume of potassium iodide-acetone solution was used in each experiment of a series.

The tubes were placed in a vertical position in a thermostat at the desired temperature for half an hour. The reaction was started by vigorously shaking the tube; the inner bulb-tube was thus broken, and the reactants intimately mixed. At the end of a given period of time a tube was withdrawn from the thermostat, and the contents quickly introduced into a mixture of ice and hydrochloric acid. This was accomplished by holding the tube directly over a wide-mouth bottle containing the ice mixture and applying a hot glass rod to a scratch previously made about halfway up the tube. The bottom half thus dropped directly into the ice; the rest of the tube was then introduced into the bottle, which was stoppered and shaken. This sudden dilution of the reaction mixture with cold aqueous acid effectively checks the reaction, and the amount of potassium iodide still unreacted can then be determined by titration with potassium iodate.

The equation for the reaction used in the titration of the iodide is, $2KI + KIO_3 + 6HCl \longrightarrow 3KCl + 3ICl + 3H_2O$. This method of determining iodide ion in the presence of chloride ion was developed by Andrews.[23] We have varied his procedure somewhat in order to find the most suitable conditions for obtaining a sharp end-point. It is necessary to keep the solution cold, and to have a large excess of hydrochloric acid present in order to prevent hydrolysis of the iodine monochloride. A small amount (5 cc.) of chloroform serves as the indicator; it becomes colored with iodine at the start of the titration, and the end-point is reached when this color is just discharged. The titration requires 8 to 10 minutes, and the following conditions were found to give the most satisfactory results. The reaction tube is broken (as described above) into a 250cc. glass-stoppered, wide-mouth bottle containing 20 cc. of concd. hydrochloric acid, 5 cc. of chloroform, and 20 g. of ice. The potassium iodate solution (0.00301 *N*) is then added from a buret until the yellow color which first appears begins to lighten. A further quantity (30 g.) of ice is added, the bottle stoppered and shaken for 20 seconds. The addition of the potassium iodate is continued with frequent shakings until the end-point is reached as shown by the water-white color of the chloroform layer. A series of preliminary experiments on the titration of small amounts of potassium iodide enabled us to establish these optimum conditions for the titration, and showed that the method was sufficiently accurate for the present purpose. It was found that 0.006 to 0.03 g. of potassium iodide could be determined with an accuracy of ±4% (about 0.3 cc. of 0.003 *N* potassium iodate solution). The error is greatest with the smallest quantity of iodide as the end-point is less sharp.

The value thus obtained for the amount of potassium iodide in a given volume of acetone was also checked by evaporating 5 cc. of the solution to dryness and weighing the solid potassium iodide left. The agreement was excellent between the values thus obtained, and those calculated from the titration with standard iodate solution.

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[23] Andrews, This Journal, **25,** 756 (1903).

The solution of potassium iodide in acetone becomes more concentrated on standing due to evaporation. It was, therefore, necessary to determine its concentration before each set of tubes was filled. This was done by pipetting the known volume (5 cc.) into ice and hydrochloric acid, and titrating in the usual way with potassium iodate. This "blank" determination gave the value for the amount of iodide used in each run.

The method as described above was found entirely satisfactory for determining the speed of the reaction in the case of the majority of chlorides investigated. In the case of certain compounds to be considered in a later paper, it did not give entirely satisfactory results. The difficulty was found to lie in the fact that in the presence of the organic iodide the titration did not proceed smoothly. Apparently, some reaction with the iodine monochloride took place to a slight extent. To overcome this, the hydrochloric acid solution was extracted with chloroform before titrating. Preliminary experiments showed that this could be done without loss of inorganic iodide, and that the titration could then be carried out successfully. This led to a modified procedure in which the reaction tube was broken into a heavy-walled separatory funnel containing the usual mixture of ice and hydrochloric acid. The solution was extracted with three portions of 5 cc. each of chloroform. The titration was then performed in the usual manner. This modified procedure was used for the series of determinations given in this paper which were made with the ethyl chlorocarbonate and chloro-acetophenone. In the case of this latter substance the chloroform extraction was found necessary, not because the ω-iodo-acetophenone interfered with the titration, but because a small amount of iodine was liberated in the aqueous acid. This iodine was extracted by the chloroform, and was then titrated with sodium thiosulfate. The application of this correction is discussed below. It might be pointed out that in all the other cases there was no reduction in the aqueous acid, and no liberation of free iodine if the titrations were completed within a few hours; in all the experiments the titrations were carried out immediately.

Results

The following tables summarize the results obtained with the various compounds at the temperatures given. The molecular proportion of organic chloride to potassium iodide was in all cases 5 to 1. The concentrations are all expressed in moles per liter, and the constant is calculated from the equation for a bimolecular reaction which in this case takes the form:

$$k = \frac{1}{t4b} \log \frac{5 - z}{5(1 - z)}$$

where b is the concentration in moles per liter of the potassium iodide and z is the fraction of potassium iodide which has reacted in the time t meas-

TABLE III

RESULTS

REACTION BETWEEN *n*-BUTYL CHLORIDE AND POTASSIUM IODIDE AT 50° (±0.05°)
Titration cc. of 0.00301 *N* KIO_3

Time hours	Reaction Cc.	Blank Cc.	Per cent. reacted (100z)	*k*
2.00	34.22	35.62	3.9	0.0436
4.00	33.05	35.62	7.2	.0410
6.00	31.80	35.62	10.7	.0414
7.50	31.30	35.85	12.7	.0397
15.00	27.52	35.85	23.2	.0392
20.00	25.10	35.62	29.8	.0396
25.00	22.71	35.85	36.6	.0412
30.00	20.00	35.85	44.2	.0444
40.00	16.90	35.85	52.8	.0434
			Av.	.0415

n-BUTYL CHLORIDE AND POTASSIUM IODIDE AT 60° (±0.05°)

Time hours	Per cent. reacted	*k*
2.00	8.6	0.099
3.05	17.5	.142
4.00	19.6	.121
5.00	23.5	.119
6.00	27.4	.119
7.83	36.2	.130
15.03	50.8	.109
20.00	63.1	.117
25.00	70.2	.115
	Av.	.119

n-AMYL CHLORIDE AND POTASSIUM IODIDE AT 60°

2.0	12.02	0.142
4.0	21.72	.135
6.5	30.21	.125
15.75	55.60	.119
22.0	66.50	.117
	Av.	.128

BENZYL CHLORIDE AND POTASSIUM IODIDE AT 25°

0.50	15.90	0.760
1.00	29.21	.778
2.00	48.80	.772
3.00	63.60	.792
4.00	72.40	.767
	Av.	.774

δ-PHENYLBUTYL CHLORIDE AND POTASSIUM IODIDE AT 60°

Time hours	Per cent. reacted	*k*
2.00	11.88	0.137
4.00	21.82	.136
6.00	30.00	.133
8.00	38.04	.136
16.25	60.55	.136
20.00	67.70	.134
	Av.	.135

ε-PHENYLAMYL CHLORIDE AND POTASSIUM IODIDE AT 60°

2.50	13.71	0.131
5.00	25.23	.130
7.10	33.62	.130
15.50	58.10	.131
21.50	68.35	.127
22.00	68.00	.123
	Av.	.129

ζ-PHENYLHEXYL CHLORIDE AND POTASSIUM IODIDE AT 60°

2.50	15.08	0.144
2.50	14.81	.141
5.00	26.02	.134
8.00	37.82	.135
15.00	55.02	.124
24.00	70.85	.122
	Av.	.133

β-Phenylethyl Chloride and Potassium Iodide at 50°

2.00	4.07	0.0494
6.00	12.50	.0485
16.00	28.45	.0471
24.00	38.80	.0477
29.33	40.50	.0402
	Av.	.0466

β-Phenylethyl Chloride and Potassium Iodide at 60°

2.00	9.71	0.112
3.933	18.18	.114
6.00	23.90	.102
8.167	31.10	.102
15.33	51.40	.108
20.00	60.40	.108
	Av.	.108

γ-Phenylpropyl Chloride and Potassium Iodide at 50°

3.50	11.89	0.0790
7.00	19.68	.0707
16.083	39.81	.0726
20.00	44.90	.0674
24.00	50.30	.0670
	Av.	.0713

γ-Phenylpropyl Chloride and Potassium Iodide at 60°

2.00	13.62	0.164
4.166	26.38	.163
6.00	35.00	.162
8.00	42.20	.156
15.10	63.35	.156
	Av.	.160

δ-Phenylbutyl Chloride and Potassium Iodide at 50°

6.00	16.39	0.0664
15.00	33.22	.0609
20.00	40.15	.0585
24.00	48.60	.0638
26.50	49.10	.0587
	Av.	.0617

η-Phenylheptyl Chloride and Potassium Iodide at 60°

2.60	14.98	0.137
5.00	26.02	.134
7.50	34.65	.129
15.00	54.98	.124
20.00	64.40	.122
24.00	68.70	.115
	Av.	.127

Ethyl Chlorocarbonate and Potassium Iodide at 25°

5.167	20.58	0.099
17.50	50.93	.094
22.167	58.45	.093
	Av.	.095

Ethyl Chloro-acetate and Potassium Iodide at 25°

0.0833	22.75	6.95
.1667	38.98	6.75
.25	50.40	6.46
.333	59.20	6.29
.50	71.05	5.90
.50	70.90	5.87
	Av.	6.37

Ethyl β-Chloropropionate and Potassium Iodide at 50°

2.0	6.375	0.0688
4.0	11.81	.0690
7.75	20.60	.0662
16.0	37.63	.0674
24.0	47.70	.0621
	Av.	.0667

Ethyl γ-Chlorobutyrate and Potassium Iodide at 50°

2.0	6.59	0.074
6.0	17.49	.071
16.0	36.95	.0653
24.0	48.55	.0639
	Av.	.0686

Ethyl δ-Chlorovalerate and Potassium Iodide at 50°

2.0	5.59	0.0638
6.0	14.10	.0565
16.0	31.30	.0529
26.0	44.40	.0516
	Av.	.0562

ured in *hours*. This value of z is obviously the difference between the "blank" titration and the titration of the reaction mixture divided by the "blank" titration. In the first table the actual titrations are given; in the others only the percentage of potassium iodide which has reacted, and the value for k. The small correction for the change in volume on mixing the acetone solution of potassium iodide and organic halide has been neglected in calculating the concentrations given in the tables and the value for b in the above equation.

In every experiment reported in the following tables 0.001 mole of organic halide, 0.0002 mole of potassium iodide and 5 cc. of acetone were employed. The concentration of the reactants was, thus, KI, 0.04 *M*; organic halide, 0.2 *M*.

In determining the speed of the reaction with ω-chloro-acetophenone it was necessary to work at 0° as the reaction was too rapid at higher temperatures. Very little, if any, reduction took place during the reaction, as the reaction mixture was colored only a very faint yellow. However, when the tube was broken in the ice-hydrochloric acid mixture a certain amount of iodine was liberated as shown by the color of the solution. This is undoubtedly due to a reaction of the ω-iodo-acetophenone with the hydrogen iodide in aqueous solution. Preliminary experiments showed that the ω-chloro-acetophenone was not responsible for the difficulty as it did not interfere with the titration of a known amount of iodide by the usual procedure. The error introduced by the liberation of iodine was corrected by extracting with chloroform and titrating the iodine in the chloroform layer. It was assumed that the reaction in aqueous solution was $RI + HI \longrightarrow RH + I_2$. If this is the case, half of the free iodine formed came from the inorganic iodine we were endeavoring to determine and our titrations with potassium iodate were corrected for this loss. The correction is not very large, as can be seen from an inspection of the following results. As might be expected the results with

TABLE IV

REACTION BETWEEN ω-CHLORO-ACETOPHENONE AND POTASSIUM IODIDE AT 0°

KIO_3 = 0.00301 *N*; 1 cc. of $Na_2S_2O_3$ is equivalent to 0.688 cc. of KIO_3

Time hours	Reaction cc. KIO_3	$Na_2S_2O_3$ cc.	Titration cc. KIO_3 corr.	Blank cc. KIO_3	Per cent. reacted	k
0.0667	14.80	2.42	16.47	37.20	55.7	28.4
.10	11.92	1.92	13.24	37.20	64.4	24.4
.10	12.02	1.60	13.12	37.20	64.8	24.6
.1334	9.90	1.90	11.21	37.20	69.9	21.4
.1334	9.53	1.95	10.87	37.20	70.6	21.8
.1667	9.6	1.0	10.29	34.60	70.2	17.3
.1667	8.95	1.60	10.05	37.20	72.9	18.7
					Av.	22.4

β-Chloropropiophenone and Potassium Iodide at 50°

Time hours	Per cent. reacted	k
0.1667	23.92	3.66
.25	30.65	3.28
.50	55.70	3.76
.667	64.75	3.69
.50	54.25	3.63
		Av. 3.60

γ-Chlorobutyrophenone and Potassium Iodide at 25°

Time hours	Per cent. reacted	k
0.50	17.80	0.862
1.00	33.56	.915
1.00	33.25	.910
1.50	41.60	.816
2.00	51.30	.829
3.00	62.00	.756
		Av. .848

β-Chloropropiophenone and Potassium Iodide at 40°

Time hours	Per cent. reacted	k
0.50	20.43	1.02
1.00	39.85	1.17
1.50	55.49	1.25
2.00	67.45	1.33
		Av. 1.19

ω-chloro-acetophenone were not as consistent as with the other compounds and for the present must be considered only as somewhat preliminary values.

Because of the rapid hydrolysis of benzoyl iodide it was found impossible to apply the usual procedure in measuring the speed of the reaction between benzoyl chloride and potassium iodide. A rough indication of the speed was made by noting the amount of precipitated potassium chloride which had formed in the reaction tube from time to time. From our previous experiments with a variety of compounds we could estimate how far the reaction had proceeded from the appearance of this precipitate. Such approximations are given below as merely rough indications of the speed of this reaction.

Table V

Estimate of the Speed of the Reaction between Benzoyl Chloride and Potassium Iodide at 0°

The concentrations of materials were the same as in all the experiments with the other halides.

Time, hours	1	3.25	6.5	8.5		..
Per cent. reacted	10	20	30	40		..
k	0.23	0.15	0.12	0.14	Av.	0.16

Summary

1. A method of wide applicability has been developed for comparing the reactivities of the halogen atoms in organic compounds. This method consists in measuring the speed of the reaction between the organic halide and potassium iodide in acetone solution.

2. The reactivity of the chlorine atom in three series of compounds of the type $A(CH_2)_nCl$ has been measured and compared with the reactivity of the chlorine atom in *n*-butyl chloride.

3. The halogen atom is more reactive in the compounds ACH_2Cl than in ACl or ACH_2CH_2Cl in the three series studied in which A is benzoyl, phenyl and carbethoxy, respectively. The influence of the group on the chlorine atom in the compounds of the type ACH_2Cl is roughly proportional to the effect of the same group on the activity of the hydrogen atom in the compounds of the type ACH_3.

4. In the benzoyl series the compound ACH_2CH_2Cl is 80 times more reactive than a simple normal alkyl chloride; in the phenyl and carbethoxy series the activity of the corresponding compound is of the same order as that of the alkyl chlorides. The compounds $ACH_2CH_2CH_2Cl$ in the benzoyl and phenyl series are more reactive than the compounds ACH_2CH_2Cl, this increase being large in the benzoyl series; in the carbethoxy series no such increase is apparent. The chlorine atom in the next higher homolog in the phenyl and carbethoxy series is only as reactive as that in butyl chloride; no higher homologs were available in the benzoyl series. Phenylamyl, phenylhexyl and phenylheptyl chlorides do not differ significantly in their reactivity from one another or from *n*-butyl or *n*-amyl chlorides.

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ACETONYL-BARBITURIC ACID AND SOME OF ITS DERIVATIVES

By Arthur W. Dox and Bruce Houston

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Monochloro-acetone, notwithstanding its cheapness, ease of preparation and reactivity, has seldom been used as an alkylating agent. The acetonyl group, CH_3COCH_2, has many properties in common with the simple alkyls, and its introduction into certain types of compounds, particularly those of pharmaceutical interest, where the ethyl or the allyl group is ordinarily employed, might be expected to yield derivatives similar in character though perhaps with somewhat modified physiological properties.

In the barbituric acid series, for example, some 60 or more alkyl substitutions have been made on the 5-carbon atom, and in addition to these, various alkoxyl, alkoxyalkyl, hydroxyalkyl and dialkylamino-alkyl substitution products have been described. Apparently, however, the preparation of keto-alkyl-barbituric acids has not been attempted. This is rather surprising in view of the fact that the ketones in general have hypnotic properties, at least two of them, diethylketone and acetophenone,