of 5-*n*-butyl-5-acetophenonyl-barbituric acid, precipitation occurred during the heating period; with all the others, the reaction product crystallized only after removal of part of the solvent, and cooling.

The compounds are colorless, and crystallize from alcohol or water in characteristic plates. Other data are given in Table I.

Summary

1. Acetophenonyl-substituted barbituric acids have been prepared by the action of bromo-acetophenone on certain 5-alkyl-substituted barbituric acids.
2. In contrast to acetophenone, these new substances, with the exception of the ethyl derivative, are surprisingly lacking in hypnotic properties, and all are moderately toxic.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE RICE INSTITUTE]

THE EFFECT OF STRUCTURE OF ORGANIC HALIDES ON THEIR RATE OF REACTION WITH INORGANIC HALIDES. I. THE EFFECT OF THE HYDROXYL, PHENOXYL AND BENZOXYL GROUPS

BY W. R. KIRNER

RECEIVED AUGUST 30, 1926 PUBLISHED OCTOBER 6, 1926

Introduction

The influence of the benzoyl, carbethoxyl, phenyl and acetoxyl groups upon the reactivity of a chlorine atom placed at various distances from the functional group in a typical series such as ACl, ACH_2Cl, ACH_2CH_2Cl, $ACH_2CH_2CH_2Cl$, etc., has already been determined.[1]

The purpose of this paper is to extend the list of these groups, which now includes the effect of the hydroxyl, phenoxyl and benzoxyl groups. The results obtained are in general agreement with those already published; that is, in the new series that have been studied it has again been found that there are indications of an alternation in the reactivity of the chlorine atom as the distance between A and Cl is regularly increased by the insertion of methylene groups. The degree and extent of this alternation in reactivity is a function of the character of the group A; in the case of certain groups the alternation is well defined, in other cases it is feeble. This is brought out by a study of Table I which contains a summary of the results.

From a consideration of this table together with summarizing tables previously published[1a,2] one may arrange the groups in the following order of decreasing activity: C_6H_5CO—, > C_2H_5OCO—, > CH_3COO—, > HO—,

---

[1] (a) Conant and Kirner, THIS JOURNAL, **46**, 232 (1924). (b) Conant, Kirner and Hussey, *ibid.*, **47**, 488 (1925).

[2] Conant and Hussey, *ibid.*, **47**, 477 (1925). Ref. 1 b, pp. 489, 494.

TABLE I

SUMMARY OF RESULTS

Compound	K_{25}	K_{35}	K_{45}	K_{50}	K_{60}	A	Relative reactivity at 50° *n*-Butyl chloride taken as unity R
n C_4H_9Cl	..	...	....	0.0415[c]	0.119	4920	1.00[c]
$HOCH_2CH_2Cl$	..	...	....	.070	.201	4925	1.69
$HOCH_2CH_2CH_2Cl$	..	0.016	0.0497	(.0853)[a]	...	4820	(2.06)[a]
$C_6H_5OCH_2CH_2Cl$	..	...	....	.0124	.034	4710	0.30
$C_6H_5OCH_2CH_2CH_2Cl$	..	...	....	.0694	.186	4600	1.67
$C_6H_5OCH_2CH_2CH_2CH_2Cl$	..	...	....	.0572	.157	4715	1.37
$C_6H_5COOCH_2Cl$	0.17	.326	....	(2.455)[b]	...	(2597)?	(59.1)[b]
$C_6H_5COOCH_2CH_2Cl$	..	...	....	0.0186	.0484	4465	0.45
$C_6H_5COOCH_2CH_2CH_2Cl$	.00451	.0275	....	(.0651)[b]	...	(7210)?	(1.57)[b]

[a] Calculated value.

[b] Calculated value using K_{25} and 4465 for value of A.

[c] See Ref. 1 a.

> C_6H_5—, > C_6H_5COO—, > C_6H_5O—, > CH_3—. This is not an absolute arrangement, for certain inversions occur when the groups are at some distance from the chlorine atom. This seems to be due to the fact that two different forces are at work. One group may activate the chlorine atom, when it is fairly close to it, to a greater extent than another group, but the latter group may have the property of impressing an alternating influence a greater distance through the carbon chain.

Procedure

The purification of the reagents, the procedure used in making the reaction-velocity determinations, the concentration and the method of calculation of the reaction velocity constant K and the temperature coefficient A was identical with that previously described.[1a]

Results

I. The Hydroxyl Series

Only two members of the hydroxyl series were studied; methylene chlorohydrin is too unstable to permit its measurement, and the higher homologs are not available and difficult to synthesize. Of the two substances measured, it is observed that the one containing an odd number of methylene groups is more reactive than the one containing an even number. This is in agreement with all of the work published in this and in our previous papers, for the case when an activating group is present in the molecule, and is fairly close to the chlorine atom. It seems clear that if methylene chlorohydrin were capable of existence, it would possess a quite reactive chlorine atom when its reactivity is measured by the metathetical reaction used in this work.

A. Purification of the Chlorohydrins

The ethylene and trimethylene chlorohydrin were from samples available on the market. Systematic fractionation of the former gave an analytically pure material boiling at 127–127.5°. The trimethylene chlorohydrin, however, after standing over anhydrous sodium sulfate for six months and being submitted to six vacuum fractionations, did not yield an analytically pure product. An average of four analyses indicated it to be approximately 97% pure trimethylene chlorohydrin. This sample was used for the velocity determinations despite the fact that it was slightly impure.

B. Reaction-Velocity Measurements

TABLE II

REACTION BETWEEN ETHYLENE CHLOROHYDRIN AND POTASSIUM IODIDE

At 50°			At 60°		
Time, hours	Percentage reacted (100z)	K	Time, hours	Percentage reacted (100z)	K
18	42.97	0.0712	2.1	18.22	0.213
25	52.50	.0690	5.0	35.98	.202
			7.33	45.87	.192
	Av.	.070	10.0	57.40	.198
				Av.	.201

TRIMETHYLENE CHLOROHYDRIN AND POTASSIUM IODIDE

At 35°			At 45°		
Time, hours	Percentage reacted (100z)	K	Time, hours	Percentage reacted (100z)	K
26.1	15.65	0.0144	12.1	17.81	0.0356
50.0	28.50	.0151	24.0	40.85	.0498
73.05	44.65	.0185	38.1	56.35	.0504
			49.0	72.60	.0629
	Av.	.016			
				Av.	.0497

II. The Phenoxyl Series

In the phenoxyl series the first member is also missing. The data indicate that the phenoxyl group induces alternation in the reactivity of the chlorine atom, but the effect is decidedly weak and the reactivity of the halogen in these compounds is low.

A. Preparation of the ω-Phenoxy Alkyl Chlorides

1. **Attempt to Prepare Phenoxymethyl Chloride.**—This substance is unknown. Bentley, Haworth and Perkin[3] attempted to prepare it by treating methylene chloride with sodium phenoxide. They found that even when these substances were present mole for mole only half of the chloride reacted and the sole product obtained was diphenoxymethane. Their attempts to split just one of the ether linkages of this last mentioned substance, using the theoretical amount of hydrobromic acid dissolved in acetic acid, resulted in the reaction of half the material only, to form methylene bromide, the remaining half being unattacked.

Because of the interest in this substance as the first member of the ω-

---

[3] Bentley, Haworth and Perkin, *J. Chem. Soc.*, **69**, 166 (1896).

phenoxy alkyl chloride series, an attempt was made to prepare it more or less indirectly. It was proposed to prepare phenoxymethyl acetate and then to hydrolyze the ester and obtain phenoxymethyl alcohol, which was then to be converted into the chloride. However, treatment of α-chloromethyl acetate with a cold aqueous solution of sodium phenoxide gave a 45% yield of phenyl acetate instead of the anticipated phenoxymethyl acetate. A possible mechanism to explain the formation of phenyl acetate in this reaction has been given by Descudé,[4] who carried out an analogous reaction using chloromethyl acetate and methyl alcohol. Other methods are being investigated for the synthesis of this compound.

2. **Preparation of β-Phenoxyethyl and γ-Phenoxypropyl Chlorides.**—These substances have been prepared by treating ethylene and trimethylene chlorobromide with sodium phenoxide,[3,5] and by treatment of ethylene chloride with sodium phenoxide.[6] The first mentioned method of preparation was not suitable for the purpose for which these compounds were intended, for it is quite likely that the final chloro compound would be contaminated with the bromo compound, inasmuch as it would not be expected that the sodium phenoxide would react exclusively with the bromine atom. Contamination of the chloro compound with the corresponding bromo compound would undoubtedly cause marked irregularities in the reaction-velocity determinations. The second method gives low yields (35%), unless run under pressure, when the yield is 48%, but is slow and tedious.

The method chosen for the synthesis of these compounds was first to prepare the phenoxy alcohols and then to convert them into the chlorides. The alcohols were prepared from sodium phenoxide and ethylene and trimethylene chlorohydrin, respectively. Powell[7] used this method for the preparation of γ-phenoxypropyl alcohol and reported an 80% yield, which was verified. Application of the method to the preparation of β-phenoxyethyl alcohol was successful and gave an 84% yield. The boiling point of β-phenoxyethyl alcohol was 128–130° at 20 mm., and that of the γ-phenoxypropyl alcohol was 147–148° at 25 mm.

The alcohols were converted into the chlorides by means of Darzens' method,[8] using thionyl chloride and pyridine. The yields in each case were 88%.

β-Phenoxyethyl chloride: b. p., 122.3° (26 mm.). Calcd. for C_8H_9OCl: Cl, 22.65. Found: 22.75.

---

[4] (a) Descudé, *Bull. soc. chim.*, [3] **27,** 1215 (1902); (b) **29,** 47 (1903).

[5] (a) Henry, *Bull. soc. chim.*, **40,** 323 (1883); [3] **15,** 1224 (1896). (b) Gabriel, *Ber.*, **25,** 416 (1892). (c) Granger, *Ber.*, **28,** 1198 (1895). (d) Günther, *Ber.*, **31,** 2136 (1898).

[6] Wohl and Berthold, *Ber.*, **43,** 2179 (1910).

[7] Powell, THIS JOURNAL, **45,** 2709 (1923).

[8] Darzens, *Compt. rend.*, **152,** 1314 (1911).

γ-Phenoxypropyl chloride: b. p., 139° (25 mm.). Calcd. for $C_9H_{11}OCl$: Cl, 20.79. Found: 21.02.

3. Preparation of δ-Phenoxybutyl Chloride

δ-Phenoxybutyl alcohol was prepared according to the directions of Marvel and Tanenbaum,[9] with approximately the same yields in each step as reported by them. The alcohol was converted into the chloride by Darzens' method with a yield of 80%.

δ-Phenoxybutyl chloride: b. p., 157° (24 mm.). Calcd. for $C_{10}H_{13}OCl$: Cl, 19.21. Found: 19.27.

B. Reaction-Velocity Measurements

TABLE III

REACTION BETWEEN β-PHENOXYETHYL CHLORIDE AND POTASSIUM IODIDE

At 50°			At 60°		
Time, hours	Percentage reacted (100z)	K	Time, hours	Percentage reacted (100z)	K
25.0	13.27	0.0125	7.1	9.63	0.0312
47.5	23.23	.0125	15.5	20.78	.0334
75.0	33.80	.0124	25.0	31.42	.0342
100.0	41.97	.0124	50.0	55.40	.0374
	Av.	.0124		Av.	.034

γ-PHENOXYPROPYL CHLORIDE AND POTASSIUM IODIDE

At 50°			At 60°		
6.1	17.31	0.0693	2.0	14.99	.178
18.0	42.40	.0698	4.0	29.62	.198
25.0	52.68	.0692	6.5	42.75	.195
			9.0	49.10	.172
	Av.	.0694			
				Av.	.186

δ-PHENOXYBUTYL CHLORIDE AND POTASSIUM IODIDE

At 50°			At 60°		
6.0	14.07	0.0561	2.0	12.53	0.147
13.4	28.35	.0560	5.0	29.53	.158
18.75	37.75	.0575	7.2	39.95	.161
25.0	47.60	.0593	10.0	49.65	.158
			10.0	50.60	.163
	Av.	.0572			
				Av.	.157

III. The Benzoxyl Series

The measurements on the benzoxyl series were not so satisfactory as usual, particularly in case of the compounds containing one and three methylene groups. It was found that there was a decided "drift" in the velocity constants. This was not due to any reaction of the organic material during the titration, for the constants were essentially the same

---

[9] Marvel and Tanenbaum, THIS JOURNAL, **44**, 2647 (1922).

whether or not the organic material was extracted before titration in the manner already described.[10]

By close observation of the amount of potassium chloride that precipitated, it was apparent that the reaction between the potassium iodide and the organic chloride was gradually being retarded. The exact reason for this has not been discovered although it seems probable that a simple replacement was not taking place as in the case of all of the compounds previously studied. A large-scale reaction with isolation of the products will probably determine the difficulty. It is known that α-chloromethyl benzoate and α-chloromethyl acetate react abnormally in many replacement reactions. Thus, in the reaction between chloromethyl acetate and methyl alcohol,[4a,4b] instead of obtaining a simple replacement reaction resulting in the formation of methoxymethyl acetate, there was formed methoxymethyl ether (dimethylformal), methyl acetate, hydrochloric acid, and formaldehyde, although methoxymethyl acetate is indicated as an intermediate product. When sodium methylate is used,[4a] methoxymethyl ether and acetic acid are obtained. Adams and Ulich[11] also found that simple replacement reactions did not take place when these compounds were treated with reagents such as water, alcohols, ammonia and amines.

In spite of the fact that good constants were not obtained in the velocity measurements of α-chloromethyl benzoate and γ-chloropropyl benzoate, it is quite clear from Table IV that the first mentioned compound reacts more rapidly than the latter, and that both react more rapidly than β-chloro-ethyl benzoate. There is, therefore, a distinct alternation in the reactivity of the ω-halogen atom and the benzoxyl group is a fairly potent activating group, of about the same order as the acetoxyl group.

A. Preparation of the ω-Chloro Alkyl Benzoates

1. **Preparation of α-Chloromethyl Benzoate.**—This substance was prepared according to the method of Adams and Ulich.[12] Although the synthesis was repeated several times, the yield reported by them could not be duplicated. There was always a much larger quantity of methylene dibenzoate formed than they indicated, and likewise a considerable amount of benzoyl chloride remained which necessitated tedious fractionation in order to obtain an analytically pure sample. The fraction finally used for the velocity measurements was fractionated four times in a vacuum, from a modified Claissen flask with a long fractionating column forming one of the necks. The side arm was fitted with a short water condenser which was then led to the customary receiver so that a regular, observable distillation rate could be maintained.

---

[10] Ref. 1 a, p. 247.

[11] Adams and Ulich, THIS JOURNAL, **43**, 661 (1921).

[12] Ref. 11, p. 662.

α-Chloromethyl benzoate: b. p. 89° (1 mm.). Calcd. for $C_8H_7O_2Cl$: Cl, 20.79. Found: 20.70.

2. **Preparation of β-Chloro-ethyl Benzoate.**—This compound was made by direct benzoylation of ethylene chlorohydrin. Fourneau and Page[13] also made it in this way but gave no details of the procedure, properties of the compound, nor the yield obtained. The corresponding bromo compound was prepared in a similar manner by Auwers.[14]

Forty-eight g. of benzoyl chloride and 25 g. of ethylene chlorohydrin were mixed and heated on a water-bath. When the temperature of the bath reached 60°, evolution of hydrogen chloride began. The water-bath was gradually brought to boiling and the heating continued until evolution of hydrogen chloride had ceased (two hours). After standing overnight, the reaction mixture was poured into a separatory funnel containing 50 cc. of water, and solid sodium bicarbonate was added in portions until all of the acid was neutralized. The oily layer was separated off and the aqueous layer was extracted once with 50 cc. of ether. The ethereal washings were added to the original oily layer and dried over anhydrous sodium sulfate. The ether was then distilled and the residue fractionated in a vacuum; yield, 84.5%.

β-Chloro-ethyl benzoate: b. p., 118–120° (2 mm.). Calcd. for $C_9H_9O_2Cl$: Cl, 19.21. Found: 19.25.

3. **Preparation of γ-Chloropropyl Benzoate.**—This is a new compound, though the corresponding bromo compound is known.[15] It was prepared in exactly the same manner as described above for its lower homolog; yield, 84%.

γ-Chloropropyl benzoate: b. p., 133–134° (2 mm.). Calcd. for $C_{10}H_{11}O_2Cl$: Cl, 17.86. Found: 17.94.

B. Reaction-Velocity Measurements

TABLE IV

REACTION BETWEEN α-CHLOROMETHYL BENZOATE AND POTASSIUM IODIDE AT 25°

Without extraction			With extraction		
Time, hours	Percentage reacted (100z)	K	Time, hours	Percentage reacted (100z)	K
1.0	12.37	0.290	1.0	11.82	0.276
1.25	13.13	.252	1.0	11.97	.281
2.0	17.91	.217	2.0	17.68	.215
2.0	18.22	.224	4.083	24.77	.156
4.0	22.84	.145	4.2	22.62	.137
4.1	25.62	.162	6.1	30.56	.135
6.0	25.21	.108	10.1	32.0	.086
			17.75	40.2	.066
	Av.	.20		Av.	.17

---

[13] Fourneau and Page, *Bull. soc. chim.*, [4] **15,** 546 (1914).

[14] Auwers, *Ann.*, **332,** 209 (1904).

[15] Braun, *Ber.*, **46,** 1784 (1913); **49,** 968 (1916); Ger. pat. 192,035, **1907**; Merch, *Chem. Zentr.*, **79,** I, 781 (1908).

TABLE IV (*Concluded*)

AT 35°

With extraction		
Time, hours	Percentage reacted (100z)	K
1.5	32.62	0.593
3.0	39.40	.380
6.0	46.97	.243
9.0	55.15	.206
12.0	65.40	.208
	Av.	.326

β-CHLORO-ETHYL BENZOATE AND POTASSIUM IODIDE

At 50°			At 60°		
Time, hours	Percentage reacted (100z)	K	Time, hours	Percentage reacted (100z)	K
25.0	19.23	0.0191	5.33	11.38	0.0495
49.75	33.52	.0185	17.08	30.75	.0481
75.0	44.72	.0181	31.08	48.10	.0485
100.0	55.0	.0185	47.33	61.60	.0474
	Av.	.0186		Av.	.0484

γ-CHLOROPROPYL BENZOATE AND POTASSIUM IODIDE

At 25°			At 35°		
25.0	5.44	0.00489	15.35	19.57	0.0318
71.7	12.17	.00409	16.85	17.42	.0296
125.1	22.63	.00456	25.55	31.44	.0332
			50.55	38.80	.0220
	Av.	.00451	75.0	49.45	.0209
				Av.	.0275

The author wishes to express his gratitude to the University of Illinois for permission to use the Laboratory during the Summer of 1925.

Summary

1. The method previously developed for determining the effect of structure of organic halides on their rate of reaction with inorganic halides has been extended to include the influence of the hydroxyl, phenoxyl and benzoxyl groups.

2. Listing the groups which have now been studied in the order of their decreasing activity yields the following series: C_6H_5CO—, > C_2H_5OCO—, > CH_3COO—, > HO—, > C_6H_5—, > C_6H_5COO—, > C_6H_5O—, > CH_3—. This arrangement may vary somewhat when comparing compounds containing several methylene groups between the two functional groups. This appears to be due to the fact that one group may cause a greater alternation in reactivity than a second group, when the functional groups are close together, but it is not capable of impressing its effect through so great a distance of the chain as the second group.

3. An improved method for the preparation of pure β-phenoxyethyl and γ-phenoxypropyl chloride in good yields has been developed.

4. γ-Chloropropyl benzoate has been prepared for the first time and its properties have been described.

HOUSTON, TEXAS

NEW BOOKS

Physikochemisches Praktikum für Chemiker und andere Naturwissenschaftler. (Physicochemical Practice for Chemists and other Scientists.) Dr. A. THIEL, Professor of Physical Chemistry at the University of Marburg. Gebrüder Borntraeger, W 35 Schöneberger Ufer 12 a, Berlin, Germany, 1926. xv + 380 pp. 70 figs. 25 × 16 cm. Price, 16.80 G. M.

Professor Thiel justifies the publication of this laboratory guide in physical chemistry on the ground of the failure of all previous manuals to meet his own particular needs. For the same reason all instructors of physical chemistry will find much to criticize in the present volume.

We are told that the general student in chemistry having the necessary apparatus at his disposal can perform the described experiments in a period of six weeks, spending the whole of every day in the laboratory. It is seldom that American university conditions allow for a period of 240 continuous laboratory working hours.

The value of physical-chemical laboratory work is seen as a balance wheel at the time when the student, throwing aside the burdensome load of quantitative analysis, proceeds to "mess" in organic chemistry.

The table of contents reads surprisingly like those of similar books of the past three decades. Indeed, this fact may be taken as an indication that physical chemistry at present is content with the achievements of the past. Should not even the "general student" have experimental acquaintance with such phenomena as adsorption, gaseous equilibrium involving thermodynamical calculations, photochemical changes and heterogeneous catalysis?

The experiments are described in great detail, each group being introduced by a satisfactory explanation of the fundamentals involved. One feature that will find much favor with some is the presence, at the end of each experiment, of actual laboratory data together with the necessary numerical calculations that are required. A weakness common to most laboratory manuals is detected here, that is, insufficient use is made of the measurements. For example, an experiment measuring the heat of neutralization is performed. The result is a bare, uninspiring number. Let a few such measurements be made with acids and bases of various strengths, and the results interpreted in terms of heats of ionization and hydrolysis of salts, and the dull heat of reaction will then be transformed into a phenomenon of interest.

W. A. PATRICK