The Reactivity of Atoms and Groups in Organic Compounds. XIX. The Relative Reactivities of the Chlorine Atoms in Certain Derivatives of Benzoyl Chloride

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In previous papers from this Laboratory[2] are given the results of the study of the influence of substituents on the relative reactivities of the carbon–chlorine bond in a number of monosubstitution products of benzoyl chloride. The rates at which the compounds react with methyl alcohol and with ethyl alcohol at 0 and 25° were determined by measuring the electrical conductivity of the solution as the reaction proceeded. Conclusions were drawn in regard to the effect on the rates of the chemical nature of the substituent and its position relative to the COCl group.

In this paper are given the results of the investigation of additional mono derivatives selected to show the effect of replacing in part hydrogen atoms in a substituent by methyl, chlorine or oxygen. Certain di- and trisubstituted derivatives were studied to compare the effect of the simultaneous action of the groups with the effect produced by each group alone.

In the discussion which follows the number placed after each substituent is the relative rate with which the acyl chloride containing this substituent reacts with ethyl alcohol at 0° compared with benzoyl chloride. In the ortho position the replacement of a hydrogen atom in methyl by methyl decreases reactivity: o-CH$_3$(3.7), o-CH$_2$-CH$_3$ (2.7). A similar replacement in the o-CH$_3$O compound increases reactivity: o-CH$_3$O (29), o-CH$_3$CH$_2$O (42).

In the meta series replacement by phenyl and by chlorine increases reactivity: m-CH$_3$ (0.85), m-C$_6$H$_5$·CH$_2$ (1.0), m-CH$_2$Cl (1.6). In the para series the effect of replacement is less: p-CH$_3$ (0.78), p-C$_6$H$_5$CH$_2$ (0.75), p-CH$_2$Cl (1.3).

The replacement of two hydrogen atoms in the benzyl group by oxygen increases reactivity: m-C$_6$H$_5$CH$_2$ (1.0), m-C$_6$H$_5$CO (4.4), p-C$_6$H$_5$CH$_2$ (0.75), p-C$_6$H$_5$CO (4.3). We were unable to prepare o-benzylbenzoyl chloride; the ortho benzoyl derivative reacted so rapidly that it was impossible to determine the rate of the reaction.

When the new results are combined with those published the increasing activating influence of substituents in the three positions are as follows:

Ortho Compounds: NO$_2$ (2.2), C$_2$H$_5$ (2.7), I (2.9), Br (3.4), Cl (3.5), CH$_3$ (3.7), CH$_3$O (29), C$_2$H$_5$O (42), C$_6$H$_5$CO (> 42).

Meta Compounds: CH$_3$ (0.85), C$_6$H$_5$CH$_2$ (1.0), CH$_3$O (1.1), CH$_2$Cl (1.6), I (4.1), C$_6$H$_5$CO (4.4), Br (4.6), Cl (5.6), NO$_2$ (20.6).

Para Compounds: C$_6$H$_5$CH$_2$ (0.75), CH$_3$ (0.78), CH$_3$O (0.81), CH$_2$Cl (1.3), Cl (1.9), I (1.9), Br (2.1), C$_6$H$_5$CO (4.3), NO$_2$ (21.2).

It appears from the above that the substituents fall into three classes: (I) those that exert the greatest influence on the reactivity when in the ortho position and show little difference in the meta and para positions, $o > m > p$, C$_6$H$_5$CO, C$_2$H$_5$O, CH$_3$O, CH$_3$; (II) those that are most effective in the meta positions, Cl, Br, I, $m > o > p$; (III) the NO$_2$ group is most effective in the para position, $p > m > o$.

The effect of the nitro group is opposite to that of the methyl group not only in the relative influence of the three positions but in the effect of these groups in the meta position. In the nitro compounds the meta position is almost as effective as the para in producing high reactivity; in the methyl derivatives the meta position resembles in influence the para position where the reactivity is reduced. In the effect of temperature on the reactions of the acyl chlorides with alcohols the groups differ: the methyl derivatives have a greater temperature coefficient than benzoyl chloride and the chloro and nitro derivatives a smaller coefficient.

Very few quantitative measurements have been made of the effect of the simultaneous action of two or more substituents on chemical reactivity. Knowledge of this phase of the subject would be of theoretical interest and would be very helpful in synthetic work in the laboratory and in industry. A previous paper[3] has reported the influence of substituents on the reactivity of the chlorine atom in derivatives of diphenyl chloromethane. Compounds were studied in which there was a

(1) From the thesis of Virgil W. Ware presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1935.

(2) Norris, Fasce and Staud, THIS JOURNAL, 57, 415 (1935); Norris and Young, ibid., 57, 1420 (1935).

(3) Norris and Banta, THIS JOURNAL, 50, 1804 (1928).

substituent in one ring and those in which the same substituent was in both rings in similar positions. The relative reactivities of these derivatives were as follows (taking diphenylchloromethane as 1): *p*-chloro 0.42, *p,p'*-dichloro 0.15, *p*-methyl 16.2, *p-p'*-dimethyl 413. In the case of chlorine, which reduced reactivity, the reactivity of the di-derivative was less than the product, 0.42 × 0.42 = 0.18; in the case of methyl that increased reactivity, the reactivity was greater than the product: 16.2 × 16.2 = 262.

In this paper are given the results of the study of the effect of the introduction of two and of three atoms of a substituent into the single ring of benzoyl chloride. In the case of certain compounds the acyl chloride reacted so rapidly that it was impossible to measure the rate. Results were obtained with a chloride which reacted 41 times as fast as did benzoyl chloride; in this case the reaction was 75% complete in five minutes. The relative reactivities are given in Table I.

TABLE I

RELATIVE REACTIVITIES OF THE C–CL BOND IN DI- AND TRI-SUBSTITUTION PRODUCTS OF C_6H_5COCl, MEASURED WITH ETHYL ALCOHOL AT $0°$

Deriv. of benzoyl chloride	Relative reactivity, $C_6H_5COCl = 1$	Product of reactivities of mono derivatives
2,4-Dimethyl	6.8	2.9[a]
2,6-Dimethyl	F[b]	13.7
2,6-Dimethoxy	F	784
2,4-Dichloro	7.7	6.7
2,5-Dichloro	14.1	19.6
3,4-Dichloro	7.2	10.6
2,4-Dinitro	31.8	46.6
3,5-Dinitro	F	424
2,6-Dinitro	S[b]	4.8
2,4,6-Triethyl	F	..
2,4,6-Trichloro	S	20
2,4,6-Tribromo	S	24

[a] The relative reactivity of 2-$CH_3C_6H_4COCl$ is 3.7 and of 4-$CH_3C_6H_4COCl$ is 0.78, the product 3.7 × 0.78 = 2.9.

[b] F signifies too fast to measure; S too slow to measure.

The following conclusions can be drawn from Table I. (a) The substituents fall into three classes: (1) when two or three CH_3, C_2H_5 or CH_3O groups are present the reactivity is greater than the product of the reactivities of the corresponding monosubstituted acyl chlorides. (b) When two or three nitro groups are present the reactivities are less than the products. (c) When the substituent is chlorine the reactivities are less than the product except in one case in which reactivity is slightly greater. The activating effect of chlorine resembles more closely that of the nitro group than the alkyl group.

These differences are probably traceable to the differences shown by the mono derivatives: the greatest activating effect of CH_3 is in the ortho position, of Cl in the meta position and of NO_2 in the para position.

The effect of the presence of substituents in both ortho positions is of particular interest in connection with the theories of steric hindrance and the diortho effect. When the substituent was CH_3, C_2H_5, or CH_3O the acyl chloride reacted with ethyl alcohol at $0°$ so fast it was impossible to measure the rate of reaction. When the substituent was Cl or NO_2 the reaction was too slow to permit measurement. These facts have led to the study, which is now in progress, of other so-called sterically hindered reactions from the point of view of the nature of the substituents in the inactive compounds and the mechanism of the reactions.

Experimental Details

Compounds Used.—The ethyl alcohol used had the density 0.78508^{25}_4; it was kept under dry nitrogen and was transferred for use in the absence of air.

The acyl chlorides were prepared by heating the pure acid with pure thionyl chloride in an all glass vessel, provided with a drying tube, until the evolution of sulfur dioxide and hydrogen chloride ceased. The excess thionyl chloride was removed at $70°$ or lower. The liquid acyl chlorides were distilled through a fractionating column at from 1 to 5 mm. and the fraction taken boiled within $0.2°$. The solid chlorides were recrystallized. All operations were carried out in an atmosphere of dry air or dry carbon dioxide. The chlorides which have not been described contain the following substituents: m-CH_2Cl, p-CH_2Cl, 2,4-di-CH_3. In these cases, for further identification, the chlorides were converted into the acids by water and amides by ammonia.

The weights of the chlorides required for the experiments and for analysis were sealed in wafer glass tubes which were broken under the solvent. The chlorides were analyzed for chlorine. All compounds except those that contained chlorine in the ring were analyzed by heating the chloride with an alcoholic solution of silver nitrate and weighing the silver chloride formed. When chlorine was present in the ring total chlorine was determined by the Carius method. Two analyses were made of each compound; the results checked closely the theoretical values.

Determination of the Velocity Constants.—The apparatus, technique and method of calculating the constants were essentially those described in the paper of Norris, Fasce and Staud. Four determinations of the constant for benzoyl chloride were made. The greatest variation was 0.5% and the average was identical with the value already published.

The plotted results gave excellent straight lines up to a

high percentage of conversion. The results are given in Table II, which includes the physical constants of the chlorides used.

TABLE II

FIRST ORDER VELOCITY CONSTANTS OF THE REACTIONS BETWEEN CERTAIN DERIVATIVES OF BENZOYL CHLORIDE AND ETHYL ALCOHOL AT 0°

Constant for benzoyl chloride, $K^{25} = 0.00414$; time in minutes.

Deriv. of benzoyl chloride	Velocity constant	Constant with C_6H_5COCl taken as 1
o-C_2H_5, b. p. 101.2–101.4° at 1 mm.	0.01190 .01205	2.73
o-C_2H_5O—, b. p. 108.1–108.3° at 2 mm.	.1810 .1838	41.6
o-C_6H_5CO—, b. p. 170–171° at 1 mm., m. p. 82–83°	99.7% conversion in 1 min.	
m-C_6H_5CO—, m. p. 57°	0.01919 .01920	4.35
p-C_6H_5CO—, m. p. 93°	.01855 .01950	4.31
m-$C_6H_5CH_3$—, b. p. 151.2–151.3° at 4 mm.	.00462 .00459	1.04
p-$C_6H_5CH_3$, b. p. 151.2–151.3° at 1 mm., m. p. 0°	.00331 .00331	0.75
m·CH_2Cl—, b. p. 95.7–95.8° at 1 mm.	.00728 .00721	1.64
p-CH_2Cl—, b. p. 108.3–108.5° at 1 mm.	.00578 .00574	1.30
2,4-di-CH_3—, b. p. 99–99.1° at 5 mm., m. p. 26.5°	.0303 .0298	6.75
2,6-di-CH_3O—, m. p. 64–66°	99.7% converted in 1 min.	
2,4-di-NO_2, b. p. 164.1–164.3° at 3 mm.	0.1390 .1420	31.6
3,5-di-NO_2, m. p. 68–69°	100% converted in 1 min.	
2,4-di-Cl, b. p. 91.9–92.2° at 1.5 mm.	0.0344 .0338	7.7
2,5-di-Cl, b. p. 95.3–95.5° at 1 mm.	.0621 .0623	14.11
3,4-di-Cl, b. p. 88.0–88.3° at 1 mm.	.0317 .0319	7.22
2,4,6-tri-C_2H_5—, b. p. 120.1–120.4° at 3 mm.	99.4% complete in 1 min.	

Summary

1. In this and a previous paper are given the results of the determination of the first order velocity constants of the reaction between ethyl alcohol at 0° and benzoyl chloride and thirty-eight of its substitution products.

2. Conclusions are drawn from these results as to the nature of the substituent and its position on the reactivity of the carbon–chlorine bond in the compounds studied.

3. When the substituents in the ortho position are arranged according to increasing effect on reactivity, the order is the reverse of that obtained when the substituents are in the para position. The order in the meta position is close to that in the para position.

4. The substituents can be divided into three classes: (1) those that have their greatest effect in the ortho position and show only small differences in the meta and para positions $o > m > p$; (2) those that show their greatest effect in the meta position: $m > o > p$; and (3) the nitro group which has the greatest effect in the para position; with little difference in the para and meta positions, $p > m > o$.

5. When the reactivities of the derivatives which contain two or three identical substituents are compared the groups fall into three classes similar to those enumerated in (4) above. Those of the first class show reactivities greater than the product of the reactivities of the monosubstituted chlorides which have their substituents in the positions occupied by the substituents in the disubstituted chloride. In the case of the nitro group, which is in the third class, the di- and trinitro derivatives give reactivities less than the product. In the case of the second class the reactivity of one derivative was slightly greater and the others less than the product.

6. The differences between the three classes are strikingly shown in the di-ortho derivatives. When the substituent was of the first class, the acyl chloride reacted with alcohol so rapidly that the velocity constant could not be measured. In the case of the second and the third class, the reaction was so slow it could not be measured. These results are of interest in connection with the theory of steric hindrance.