On the Studies of the Friedel-Crafts Acylation. II. The Relative Reactivity for Some Acyl Halides

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In Part I[1] the relative reactivities for benzoyl halides, phenylacetyl halides, and mesitoyl halides were measured by Calloway's method and Olivier's method; it was confirmed that the order of reactivity observed is not always in agreement with the order for acetyl halides obtained by Calloway,

$$CH_3COF < CH_3COCl < CH_3COBr < CH_3COI$$

In the present study the relative reactivities for acetyl halides, propionyl halides, isobutyryl halides, cyclohexanecarbonyl halides, and trimethylacetyl halides in the Friedel-Crafts acylation were measured by Calloway's method, and the effect of structure on the order of reactivity for acyl halides was examined. From the observation, it was found that on replacement of the methyl group in acetyl halides with a group with great steric requirement, the order of reactivity for acyl halides varies and does not agree with the order for acetyl halides, but when the methyl group is replaced with a group with a greater steric requirement, the order of reactivity for acyl halides again agrees with the order for acetyl halides.

On the other hand, it was observed that the order of reactivity for acyl halides remains the same in acylation of various aromatic compounds, even when a sterically hindered

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[1] Y. Yamase and R. Goto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 1906 (1960).

or activated aromatic position is to be substituted, and is influenced by the structure of acyl halides.

Experimental

Methods. — In measuring the relative reactivity for acyl halides by Calloway's method, the apparatus was the same as that used in Part I, and also in the same manner as that mentioned in Part I the measurement of the temperature was carried out at which the velocity of reaction for various acyl halides becomes sufficient to cause visible bubbles to be evolved. The temperature at which the first visible evolution of hydrogen halide occurred was taken as the temperature at which the measurable reaction began, and it was designated as the temperature of incipient reaction. The inverse order of this temperature, therefore, was regarded as the order of reactivity for the acyl halides.

Materials. — The acyl halides used in the acylation were acetyl halides(I), propionyl halides(II), isobutyryl halides (III) cyclohexanecarbonyl halides (IV), and trimethylacetyl halides (V). The fluorides of I, II, and IV were prepared by the reaction between the acyl chlorides and antimony trifluoride, and those of III and V by the interaction between the corresponding carboxylic acids and benzoyl fluoride. The chlorides of II, III, and V were prepared by the interaction between the corresponding carboxylic acids and benzoyl chloride, and that of IV by the interaction between the corresponding carboxylic acid and thionyl chloride. The bromides of I, III, and IV were prepared by the interaction between the corresponding carboxylic acids and phosphorous tribromide, and that of V by the interaction between the corresponding carboxylic acid and benzoyl bromide. The iodides of I, II, III and IV were prepared by the interchange of halogens between the acyl chlorides and hydrogen iodide. The physical constants of these compounds are summarized in Table I.

TABLE I. BOILING POINTS ACYL HALIDES

	Acyl halides		
X	CH_3COX	CH_3CH_2COX	$(CH_3)_2CHCOX$
F	22°C	42.5∼43.5°C	55∼56°C
	(20∼23°C)	(44°C)	(—)
Cl	50∼51°C	77∼78°C	90°C
	(50.9°C)	(80°C)	(92°C)
Br	75∼76°C	98∼100°C	114∼115°C
	(76.7°C)	(96∼98°C)	(116∼118°C)
I	104∼105°C	32∼34°C/ 16 mmHg	43∼44°C/ 21 mmHg
	(108°C)	(127∼128°C)	(—)

	Acyl halides	
X	$C_6H_{11}COX$	$(CH_3)_3CCOX$
F	146∼148°C	67.5∼68°C
	(—)	(—)
Cl	180∼182°C	102∼104°C
	(184°C)	(104°C)
Br	197∼198°C	124∼126°C
	(—)	(—)
I	103∼105°C/11 mmHg	—
	(—)	(—)

The values in parentheses are those reported in the literature.

Results and Discussion

The orders of reactivity of various acyl halides obtained by Calloway's method are described below.

Reactivity of Acetyl Halides. — *Acylation of Benzene.* — A mixture of aluminum chloride (0.1 mol.), benzene (0.3 mol.), and carbon disulfide (95 ml.) was cooled to about −60°C. To the solution was added the acetyl halide (0.1 mol.) in carbon disulfide (5 ml.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. Results are shown in Table II.

Acylation of Mesitylene.—A mixture of aluminum chloride (0.01 mol.), mesitylene (0.01 mol.), and carbon disulfide (150 ml.) was cooled to about −60°C. To the solution was added the acetyl halide (0.01 mol.) in carbon disulfide (10 ml.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. Results are shown in Table II.

Acylation of Anisole.—A mixture of aluminum chloride (0.01 mol.), anisole (0.01 mol.), and carbon disulfide (150 ml.) was cooled to about −60°C. To the solution was added the acetyl halide (0.01 mol.) in carbon disulfide (10 ml.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. Results are shown in Table II.

From these results, the order of reactivity of the acetyl halides is independent of the nature of aromatic compounds to be acylated and increases in the following order,

$$CH_3COF < CH_3COCl < CH_3COBr < CH_3COI.$$

This order is consistent with that of acetyl halides observed by Calloway[2].

Reactivity of Propionyl Halide. — A mixture of aluminum chloride (0.1 mol.), benzene (13.4 g.), and carbon disulfide (100 ml.) was cooled to about −60°C. To the solution was added the propionyl halide (0.1 mol.) in benzene (10 g.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. The reaction mixture was warmed to 30°C over a period of 5 min. from the initiation of hydrogen halide evolution and was maintained at 30°C for 55 min. The yields of ketone from various propionyl halides were obtained by the ordinary method. Results are shown in Table III.

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[2] N. O. Calloway, *J. Am. Chem. Soc.*, **59**, 1474 (1937).

TABLE II. REACTIVITY OF ACETYL HALIDES

	Acetyl halides			
The temp. of incipient reaction	CH_3COF	CH_3COCl	CH_3COBr	CH_3COI
In acylation of benzene, °C	13	6	0	−5
In acylation of mesitylen, °C	15	0	−5	—*
In acylation of anisole, °C	5 ; 3	−10 ; −8	−14 ; −14	—*

* The temperature of incipient reaction for acetyl iodide could not be measured, as only a very small amount of it was used in the acylation and also it was readily hydrolyzed.

TABLE III. REACTIVITY OF PROPIONYL HALIDES

	Propionyl halides			
	CH_3CH_2COF	CH_3CH_2COCl	CH_3CH_2COBr	CH_3CH_2COI
The temp. of incipient reaction, °C	5	−1	−5	−2
The max. reaction temp. reached, °C	30	30	30	30
Reaction time, hr.	1	1	1	1
Ketone isolated, g.	8.0	11.0	12.0	2.5
Yields of ketone, %	59.7	82.2	89.6	18.7

TABLE IV. REACTIVITY OF ISOBUTYRYL HALIDES

	Isobutyryl halides			
	$(CH_3)_2CHCOF$	$(CH_3)_2CHCOCl$	$(CH_3)_2CHCOBr$	$(CH_3)_2CHCOI$
The temp. of incipient reaction, °C	12	5	6	20
The max. reaction temp. reached, °C	30	30	30	30
Reaction time, hr.	1	1	1	1
Ketone isolated, g.	5.9	11.2	11.0	1.0
Yields of ketone, %	39.8	75.7	74.3	6.8

TABLE V. REACTIVITY OF CYCLOHEXANECARBONYL HALIDES

	Cyclohexanecarbonyl halides			
	$C_6H_{11}COF$	$C_6H_{11}COCl$	$C_6H_{11}COBr$	$C_6H_{11}COI$
The temp. of incipient reaction, °C	12	0	2	22
The max. reaction temp. reached, °C	30	30	30	30
Reaction time, hr.	1	1	1	1
Ketone isolated, g.	4.4	10.5	10.0	1.0
Yields of ketone, %	23.4	55.9	53.2	5.3

From these results, the order of reactivity of the propionyl halides is given as follows,

$$CH_3CH_2COF < CH_3CH_2COCl < CH_3CH_2COBr > CH_3CH_2COI$$

The yields of ketone were in good agreement with the reactivity observed.

Reactivity of Isobutyryl Halides.—A mixture of aluminum chloride (0.1 mol.), benzene (18.4 g.), and carbon disulfide (100 ml.) was cooled to about −60°C. To the solution was added the isobutyryl halide (0.1 mol.) in benzene (5 g.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. The yield of ketone was obtained in the usual manner. Results are shown in Table IV.

From these results, the order of reactivity of the isobutyryl halides is as follows,

$$(CH_3)_2CHCOF < (CH_3)_2CHCOCl \fallingdotseq (CH_3)_2CHCOBr > (CH_3)_2CHCOI$$

The yields of ketone were in good agreement with the reactivity observed.

Reactivity of Cyclohexanecarbonyl Halides.—A mixture of aluminum chloride (0.1 mol.), benzene (15.4 g.), and carbon disulfide (100 ml.) was cooled to about −60°C. To the solution was added the cyclohexanecarbonyl halide (0.1 mol.) in benzene (8 g.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. The yield of ketone was obtained by the same method. Results are shown in Table V.

From these results, the order of reactivity of the cyclohexanecarbonyl halides is given

TABLE VI. REACTIVITY OF TRIMETHYLACETYL HALIDES

	Trimethylacetyl halides		
	$(CH_3)_3CCOF$	$(CH_3)_3CCOCl$	$(CH_3)_3CCOBr$
The temp. of incipient reaction, °C	−10	−19	−30

TABLE VII. REACTIVITY OF BENZOYL HALIDES

	Benzoyl halides			
The temp. of incipient reaction,	C_6H_5COF	C_6H_5COCl	C_6H_5COBr	C_6H_5COI
In acylation of mesitylene, °C	15	0	0	10
In acylation of anisole, °C	13; 15	3; 4	4; 4	12; 12

TABLE VIII. REACTIVITY OF ACYL HALIDES

Acyl halides	Compounds to be acylated	Solvents	The orders of reactivity for acyl halides
CH_3COX	Benzene	CS_3	$F<Cl<Br<I$
〃	Mesitylene	〃	〃
〃	Anisole	〃	〃
CH_3CH_2COX	Benzene	〃	$F<Cl I$
$C_6H_5CH_2COX$	〃	〃	〃
〃	〃	$C_6H_5NO_2$	$F<Cl>Br>I$
$(CH_3)_2CHCOX$	〃	CS_2	$F<Cl=Br>I$
$C_6H_{11}COX$	〃	〃	〃
C_6H_5COX	〃	〃	〃
〃	Mesitylene	〃	〃
〃	Anisole	〃	〃
$2,4,6\text{-}(CH_3)_3C_6H_2COX$	〃	〃	$F<Cl<Br<I$
〃	〃	$C_6H_5NO_2$	〃
$(CH_3)_3CCOX$	〃	CS_2	〃

as follows,

$$C_6H_{11}COF < C_6H_{11}COCl \fallingdotseq C_6H_{11}COBr > C_6H_{11}COI$$

The yields of ketone were in good agreement with the reactivity observed.

Reactivity of Trimethylacetyl Halides. — A mixture of alminum chloride (0.005 mol.), anisole (0.005 mol.), and carbon disulfide (140 ml.) was cooled to about −60°C. To the solution was added the trimethylacetyl halide (0.005 mol.) in carbon disulfide (10 ml.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. Results are shown in Table VI.

From these results, the order of reactivity of the trimethylacetyacetyl halides is given as follows,

$$(CH_3)_3CCOF < (CH_3)_3CCOCl < (CH_3)_3CCOBr\,(<(CH_3)_3CCOI)$$

Reactivity of benzoyl halides. — *Acylation of Mesitylene.* — A mixture of aluminum chloride (0.01 mol.) and carbon disulfide (90 ml.) was cooled to about −60°C. To the solution were added the benzoyl halide (0.01 mol.) and mesitylene (0.01 mol.) in carbon disulfide (10 ml.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. Results are shown in Table VII.

Acylation of Anisole.—A mixture of aluminum chloride (0.01 mol.), anisole (0.01 mol.), and carbon disulfide (100 ml.) was cooled to about −60°C. To the solution was added the benzoyl halide (0.01 mol.) in carbon disulfide (10 ml.). After addition, the mixture was warmed slowly and the temperature of incipient reaction was measured. Results are shown in Table VII.

From these results, it is seen that the order of reactivity for the benzoyl halides is independent of the nature of aromatic compounds to be acylated and is given as follows,

$$C_6H_5COF < C_6H_5COCl \fallingdotseq C_6H_5COBr > C_6H_5COI$$

These orders of reactivity for the acyl halides obtained in the present study and in Part I are summarized in Table VIII.

To summarize, it was observed that when R group in acyl halides RCOX is replaced successively with CH_3- group, CH_3CH_2- and $C_6H_5CH_2$- groups, and $(CH_3)_2CH$-, C_6H_{11}-, and C_6H_5- groups, the orders of reactivity vary as follows as a result of the steric hindrance of R group, $RCOF < RCOCl < RCOBr < RCOI$ ($R = CH_3$-), $RCOF < RCOCl < RCOBr > RCOI$

($R=CH_3CH_2$- and $C_6H_5CH_2$-), and $RCOF > RCOCl \fallingdotseq RCOBr > RCOI$ ($R=(CH_3)_2CH$-, C_6H_{11}-, and C_6H_5-) respectively. In the acylation by mesitoyl halides and trimethylacetyl halides, the orders of reactivity were observed as follows, $RCOF < RCOCl < RCOBr < RCOI$, in spite of the large steric hindrance of $(CH_3)_3C_6H_2$- and $(CH_3)_3C$- groups.

On the other hand, it was observed that in acylation of benzene, anisole, and mesitylene the orders of reactivity for benzoyl halides and acetyl halides do not change, and are given as follows, $C_6H_5COF < C_6H_5COCl \fallingdotseq C_6H_5COBr > C_6H_5COI$ and $CH_3COF < CH_3COCl < CH_3CBr < CH_3COI$ respectively.

Thus it may be suggested that the order of reactivity of acyl halides does not change even when a sterically hindered or activated aromatic position is to be substituted; that is, the order of reactivity depends only on the structure of acyl halides.

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