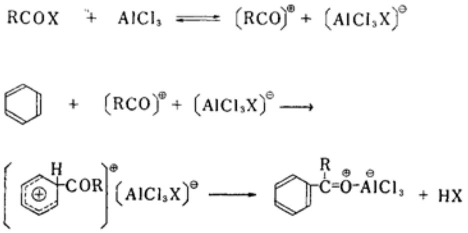
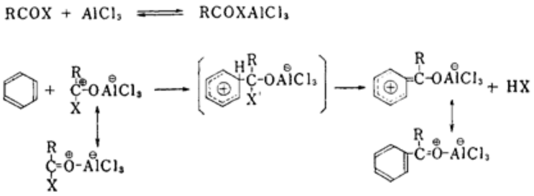
On the Studies of the Friedel-Crafts Acylation. III. The Reaction Mechanism

By Yoshiaki YAMASE

(Received September 12, 1960)

The two types of mechanism, ionic and substitution mechanisms, are generally accepted at the present time for the Friedel-Crafts acylation. The concept of an ionic mechanism[1-3] is that the attacking agent is an acylium ion produced by ionization of an acyl halide under the catalytic influence of aluminum chloride. The concept of a substitution mechanism[4-8] is that the attacking agent is an addition complex produced by the interaction of an acyl halide and aluminum chloride.





Since some evidence exists for both ionic and substitution mechanisms, they may not be dismissed.

Recently, a duality of mechanism for the Friedel-Crafts acylation, the concept of which is that the acylation by acyl halides under the influence of aluminum chloride takes place by both ionic and substitution mechanisms, seems to offer an attractive hypothesis[9-12], and it appears likely that the acylation by acyl halides under the influence of aluminum chloride takes place by one of two mechanisms, depending on the reactivity of aromatic substances and acyl halides; that is, the normal Friedel-Crafts acylation may proceed mainly by the substitution mechanism, but when a sterically hindered acyl halide is used, or when a sterically hindered aromatic position is to

---

1) F. Fairbrother, *J. Chem. Soc.*, **1937**, 503.
2) G. Baddeley et al., ibid., **1954**, 418.
3) F. Fairbrother, *Trans. Faraday Soc.*, **37**, 763 (1941).
4) R. Pajean, *Bull. soc. chim. France* [5] **13**, 544 (1946).
5) J. C. Butler et al., *J. Am. Chem. Soc.*, **76**, 1906 (1954).
6) H. Burton et al., *J. Chem. Soc.*, **1950**, 2034.
7) P. H. Groggins, "Unit Processes in Organic Synthesis" McGraw-Hill, New York (1952), p. 866.
8) H. C. Brown et al., *J. Am. Chem. Soc.*, **76**, 605 (1954).
* The above formulas were quoted from P. H. Gore, *Chem. Revs.*, **54**, 232 (1955).

9) H. Burton et al., *Chemistry & Industry*, **1954**, 90.
10) J. M. Tedder, ibid., **1954**, 630.
11) P. H. Gore, ibid., **1954**, 1385.
12) P. H. Gore, *Chem. Revs.*, **54**, 229 (1955).

be substituted, the ionic mechanism becomes important.

The order of reactivity for acetyl halides in the Friedel-Crafts acylation has been found by Calloway to be $\mathrm{CH_3COF < CH_3COCl < CH_3COBr < CH_3COI}$, and it has been inferred from this evidence that the order of reactivity for acyl halides is the same as that for acetyl halides[13,14].

Now, if the Friedel-Crafts acylation proceeds by the ionic mechanism, the reactivity for acyl halides depends on the equilibrium concentration of the acylium ion produced by ionization of acyl halides in the presence of aluminum chloride,

$$\mathrm{RCOX + AlCl_3 \rightleftarrows [RCO]^+ + [AlCl_3X]^-}$$

and the concentration of the acylium ion depends on the lability of the carbon-halogen bond in acyl halides. Therefore, the order of reactivity of acyl halides should be

$$\mathrm{RCOF < RCOCl < RCOBr < RCOI}$$

On the other hand, if the Friedel-Crafts acylation proceeds by the substitution mechanism, the reactivity for acyl halides should be identical with the reactivity for the addition complexes produced from acyl halides and aluminum chloride, because the attacking agent in this case is the addition complex. Then, the reactivity for acyl halides must be influenced not only by the lability of the carbon-halogen bond, but also by the steric effect of the halogen atom which reduces the reactivity of acyl halides as follows,

$$\mathrm{RCOF > RCOCl > RCOBr > RCOI}$$

Therefore, it is possible that the order of reactivity for acyl halides does not always agree with the order of reactivity for acetyl halides.

Taking the above facts into consideration, the determinations of reactivities for some acyl halides in the presence of aluminum chloride in the Friedel-Crafts acylation have been carried out in Parts I[15] and II[16], and it has been observed that the order of reactivity for acyl halides may be influenced by the structure of acyl halides.

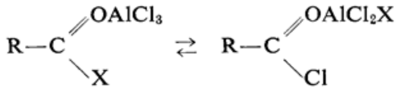
On the replacement of the methyl group in acetyl halides with a group with great steric requirement, the order of reactivity for acyl halides does not consist with the order for acetyl halides. But, when the methyl group is replaced with a group with greater steric requirement, the order of reactivity for acyl halides becomes consistent with the order for acetyl halides.

These phenomena can be explained reasonably on the basis of the concept that the normal Friedel-Crafts acylation proceeds mainly by the substitution mechanism, but when a sterically hindered acyl halide is used, the acylation proceeds by the ionic mechanism.

Discussion

The halogen exchange reactions have been observed between acetyl chloride and aluminum chloride in which some of the chlorine atoms are radioactive isotopes[1], and also between 2, 4, 6-tribromobenzoyl chloride, or 2, 4, 6-trimethylbenzoyl chloride and aluminum bromide[2].

If the acylation proceeds by the substitution mechanism, it is conceivable that the attacking agents are the complexes I and II, and in the complete halogen exchange the ratio of the concentration of the complexes I and II will be 1/3.



$$\mathrm{R{-}C}\genfrac{}{}{0pt}{}{\mathrm{/\!\!/OAlCl_3}}{\mathrm{\backslash X}} \rightleftarrows \mathrm{R{-}C}\genfrac{}{}{0pt}{}{\mathrm{/\!\!/OAlCl_2X}}{\mathrm{\backslash Cl}}$$

(I) (II)

On the assumption that there is scarcely any difference between the catalytic ability of $\mathrm{AlCl_3}$ and $\mathrm{AlCl_2X}$, it may be considered that of the two different kinds of complexes produced by the interaction between aluminum chloride and various acyl halides, the complexes II, $\mathrm{RCOClAlCl_2X}$, have similar reactivities regardless of the nature of X (F, Cl, Br and I).

From this assumption, the difference of reactivities of acyl halides is nothing but that of reactivities of the complex, I, $\mathrm{RCOXAlCl_3}$, and the order of reactivity of acyl halides can be explained by considering the difference of reactivity of the complex I.

The reactivity of the complex I is influenced by the lability of the carbon-halogen bond and the steric hindrance of the halogen atom; the effect of the carbon-halogen bond energy on the reactivity for the complex I increases in the following order, $\mathrm{F < Cl < Br < I}$, and the steric hindrance of the halogen atom may reduce the reactivity of the complex I as follows, $\mathrm{F > Cl > Br > I}$.

In the substitution mechanism, the order of reactivity of acyl halides is influenced by both the lability of the carbon-halogen bond and the steric hindrance of the halogen atom simultaneously and does not always agree with the order of acetyl halides.

On the other hand, in the ionic mechanism the reactivity of acyl halides depends on the equilibrium concentration of the acylium ion

---

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

[14] N. O. V. Sonntag, *Chem. Revs.*, **52**, 345 (1953).

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

[16] Y. Yamase, This Bulletin, **34**, 480 (1961).

TABLE I. REACTIVITY OF ACYL HALIDES

Acyl halides	Compound to be acylated	Solvent	The order of reactivity of acyl halides
CH_3COX	Benzene	CS_2	$F<Cl<Br<I$
〃	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	〃

which, in turn, depends on the lability of the carbon-halogen bond in acyl halides. Then, the order of reactivity of acyl halides is influenced by the magnitude of the carbon-halogen bond energy and increases as follows

$$F<Cl<Br<I$$

Upon these considerations, the experimental data of reactivities for some acyl halides summarized in Table I can be reasonably explained.

Acylation of Benzene in Carbon Disulfide or Benzene.—In acylation of benzene in a nonpolar solvent, carbon disulfide or benzene, the order of reactivity of acetyl halides was $RCOF<RCOCl<RCOBr<RCOI$; for propionyl and phenylacetyl halides it was $RCOF<RCOCl<RCOBr>RCOI$, and for isobutyryl, cyclohexanecarbonyl, and benzoyl halides it was $RCOF<RCOCl\fallingdotseq RCOBr>RCOI$.

These results may be explained reasonably by the substitution mechanism. It has generally been considered that in the substitution mechanism the addition complex $RCOXAlCl_3$ attacks the aromatic substance by the displacement reaction of S_N2 type. Then, it must be considered how much effect the lability of the carbon-halogen bond and the steric hindrance of the $OAlCl_3$, R, and X groups have on the reactivity of the complex. The $OAlCl_3$ group in the addition complex may be considerably bulky and be common to various addition complexes.

In acylation by acetyl halides the reactivity of the addition complex is influenced by the lability of the carbon-halogen bond alone, since the steric hindrance of the methyl group is small. Therefore, the order of reactivity for acetyl halides is $F<Cl<Br<I$.

In acylation by propionyl and phenylacetyl halides, the steric hindrances of ethyl and phenylmethyl groups become great, and the reactivities of the addition complexes are influenced not only by the lability of the carbon-halogen bond but also by the steric hindrance of the halogen atom caused by the sterically hindered R groups. Consequently, the orders of reactivities of these acyl halides become $F<Cl
I$.

In acylation by isobutyryl, cyclohexanecarbonyl, and benzoyl halides, the steric hindrances of isopropyl, cyclohexyl, and phenyl groups become considerably great, and the orders of reactivities of these addition complexes are influenced not only by the lability of the carbon-halogen bond but also by the steric hindrance of the halogen atom caused by the sterically hindered R groups. Accordingly, the orders of reactivities for these acyl halides become $F<Cl\fallingdotseq Br>I$.

Acylation of Anisole by Mesitoyl Halides and Trimethylacetyl Halides.—In acylation of anisole by mesitoyl(2) and trimethylacetyl halides(17), the reaction has been believed to occur by the ionic mechanism. As reported in the previous reports, in spite of the large steric hindrance of mesityl and *tert*-butyl groups, the orders of reactivities for these acyl halides were as follows, $RCOF<RCOCl<RCOBr<RCOI$.

These results are explained reasonably by the ionic mechanism; as a result of the great steric hindrance of acyl halides, the addition complex is not formed and the halide is completely ionized, giving the acylium ion. The acylium ion attacks anisole as an acylating agent, and the order of reactivities for these acyl halides agrees with the order of the lability of the carbon-halogen bond, $F<Cl<Br<I$.

Acylation of Benzene by Phenylacetyl Halides and Anisole by Mesitoyl Halides.—In acylation of benzene by phenylacetyl halides the reaction is believed to proceed by the substitution

---

17) E. Rothstein et al., *J. Chem. Soc.*, **1949**, 1950.

mechanism, and the order of reactivity of phenylacetyl halides was RCOF$<$ RCOCl$<$ RCOBr$>$RCOI in a non-polar solvent (carbon disulfide) and RCOF$<$RCOCl$>$ RCOBr$>$RCOI in a polar solvent (nitrobenzene).

When the polar solvent, nitrobenzene, is used in place of the non-polar solvent, carbon disulfide, aluminum chloride is solvated with nitrobenzene and it forms bulkier addition complexes with acyl halides. Then, the influence of the steric hindrance of the halogen atom on the reactivity of phenylacetyl halides becomes greater, and consequently the above orders are observed.

On the other hand, in acylation of anisole by mesitoyl halides the reaction is believed to proceed by the ionic mechanism. The order of the lability of the carbon-halogen bond would always be the same regardless of the nature of the solvent and, in fact, the order of reactivity of mesitoyl halides was RCOF$<$RCOCl$<$ RCOBr$<$RCOI.

Acylation of Benzene, Mesitylene, and Anisole by Acetyl Halides and Benzoyl Halides.—In acylation of benzene, mesitylene, and anisole by acetyl and benzoyl halides, the orders of reactivities of these acyl halides were $CH_3COF < CH_3COCl < CH_3COBr < CH_3COI$, and $C_6H_5COF < C_6H_5COCl \fallingdotseq C_6H_5COBr > C_6H_5COI$, respectively.

These results show that the orders of reactivities of these acyl halides are not influenced even when a sterically hindered or activated aromatic position is to be substituted and these acylations proceed by the same substitution mechanism.

From the above results, it may be considered that the normal Friedel-Crafts acylation by acyl halides proceeds mainly by the substitution mechanism. However, when sterically hindered acyl halides are used, the ionic mechanism becomes important as the formation of the addition complexes becomes difficult; that is, the mechanism of the Friedel-Crafts acylation by acyl halides is influenced by the structure of acyl halides, and not by the nature of the aromatic substances to be acylated.

The author wishes to express his sincere appreciation to Professor Ryozo Goto, Kyoto University, for his helpful discussions and criticisms.

Chemistry Institute
Faculty of Science
Kyoto University
Sakyo-ku, Kyoto