centage of hydrogen bromide was 23 and of hydrogen chloride 77; for each mole of hydrogen bromide there was formed 3.3 moles of hydrogen chloride. When acetyl chloride and aluminum bromide were used the mole percentage of hydrogen chloride was 30 and of hydrogen bromide 70; for each mole of hydrogen chloride there was 2.3 moles of hydrogen bromide. The yields of acetophenone in the two cases were nearly the same, 72 and 76%, respectively.

Summary

1. The preparation and some of the properties of the complexes having the following formulas are described: $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot HBr$, $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot C_2H_5Br$, $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot C_2H_5Br$.

2. The complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$ did not react with CO_2 at 60 atmospheres, but a mixture of Al_2Br_6 and $s\text{-}C_6H_3(CH_3)_3$ under the same conditions gave high yields of the dimesityl ketone and *s*-trimethylbenzoic acid.

3. When a complex which contains aluminum chloride and benzene, toluene, triethylbenzene or nitrobenzene was treated with hydrogen bromide at room temperature an exchange of halogen atoms took place. When the complex which contained aluminum bromide was treated with hydrogen chloride, exchange also took place.

4. When acetyl chloride was condensed with benzene by means of aluminum bromide 77 mole per cent. of the hydrogen halides formed was hydrogen bromide. When acetyl bromide and aluminum chloride were used the mole per cent. of hydrogen chloride was 70.

CAMBRIDGE, MASS.

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The Preparation of Nitriles and Amides. Reactions of Esters with Acids and with Aluminum Chloride. The Use of the Salt NaCl·AlCl$_3$ in the Friedel and Crafts Reaction

BY JAMES F. NORRIS AND ALBERT JOHN KLEMKA[1]

In a former paper[2] the preparation was described of benzonitrile from benzamide or ammonium benzoate by means of aluminum chloride. Since the results were satisfactory, the method has been studied further and applied to the preparation of a number of typical compounds. As a guide in the use of the method the steps involved in the reaction were investigated. The results are indicated as follows

$$C_6H_5CONH_2 + AlCl_3 \xrightarrow{\text{heated}} HCl + C_6H_5CONHAlCl_2 \xrightarrow{\text{higher temperature}} C_6H_5CN + HCl + AlOCl$$

In one experiment a part of the product formed after the first evolution of hydrogen chloride had ceased was decomposed by water; benzamide was recovered. The second part was heated to a higher temperature; more hydrogen chloride was formed and the nitrile distilled.

Eleven nitriles were prepared by this method; the yields were from 63 to 97%. In most cases, the double salt of aluminum chloride and sodium chloride ($NaCl \cdot AlCl_3$) was used. This compound can be prepared easily, is convenient to handle and has the added advantage that it gives higher yields and does not melt during the reaction and cause frothing. The method cannot be applied to amides containing functional groups which react with aluminum chloride; unsatisfactory yields were obtained from amides of dibasic acids.

A simple procedure was devised for a semimicro method to be used in the identification of certain amides by converting them into nitriles and determining the melting point of the latter; about 10 milligrams of the amide is sufficient for the identification.

When ammonium salts of the acids were used the yields were low. It was shown that the first step in the reaction with aluminum chloride was not the formation of an amide.

Since this method of preparing nitriles involved the use of amides, the preparation of the latter directly from acids was studied. Biehringer and Borsum[3] have reported the interaction of an acid and an amide, as the result of which there is an interchange of the hydroxyl and amino groups. The reactions were carried out in sealed tubes at a high temperature and the yields were low.

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[1] From a part of the thesis of Albert John Klemka presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1939.

[2] Norris and Sturgis, THIS JOURNAL, **61**, 1413 (1939).

[3] Biehringer and Borsum, *Ber.*, **39**, 3348 (1906).

In our experiments a mixture of the acid and acetamide was heated in a flask and the volatile material was condensed and collected; the latter consisted chiefly of acetic acid.

When the method was applied to 2,6-dichlorobenzoic acid a quantitative yield of *m*-dichlorobenzene was obtained in two hours. The acid was heated with acetamide at the temperature (225–235°) at which decomposition takes place to a slight extent in six hours. The effect of acetamide on other acids that lose carbon dioxide when heated will be investigated.

The interchange reaction between an acid and amide was shown to be a reversible one; an interchange took place between benzoic acid and acetanilide as the result of which benzanilide was formed. Certain esters were shown to interchange groups with acids; for example, benzoic acid and phenyl acetate were converted by heating into phenyl benzoate and acetic acid.

The use of the compound of aluminum chloride and sodium chloride in Friedel and Crafts condensations was studied in a few cases. Since the reagent was found to be much less reactive than aluminum chloride, it could be used with advantage in the case of halogen compounds that are decomposed by aluminum chloride. A good yield of diphenylmethane was obtained from benzyl chloride. With chloroform and carbon tetrachloride the condensation took place to a slight degree only.

A number of miscellaneous reactions related to the work being done in this Laboratory are described in the Experimental Part of this paper. These include the reaction between ethyl 2,6-dichlorobenzoate and aluminum chloride as the result of which the ester was quantitatively converted into a salt of the acid and ethyl chloride; the reaction between benzoyl chloride and ammonium chloride; and the condensation of benzoic acid with toluene.

Details of Experiments

Preparation of Nitriles.—The double salt NaCl·AlCl$_3$ was prepared as follows. Thirty grams of dry sodium chloride was intimately mixed with 68 g. of pulverized aluminum chloride (equal molecular quantities) and heated in a flask for one hour at 230–250°. The liquid was poured into a beaker and stirred as it solidified to a meal. The product was kept in a tightly stoppered bottle and ground before use.

The process used in making nitriles was as follows. A mixture of the amide and the salt NaCl·AlCl$_3$ was heated in a flask connected with a condenser and a receiver. The mixture was heated cautiously with a free flame until the evolution of hydrogen chloride had nearly ceased; it was then heated at a higher temperature until no more distillate was obtained and a charred solid remained in the flask. The volatile product was the nitrile in pure condition. The liquids were redistilled to free them from a small amount of dissolved hydrogen chloride. The boiling and melting points agreed closely with those given in the literature.

The yields of pure nitriles were as follows. CH$_3$CN (b. p. 81–82°) 91% (moles amide to moles NaCl·AlCl$_3$, 0.2 to 0.26; decrease in NaCl·AlCl$_3$ gave lower yields; aluminum chloride alone, 0.2 to 0.2 mole gave 43%). (C$_6$H$_5$)$_2$CHCN (m. p. 72–73°) 52% (0.031 to 0.044 mole). *n*-C$_5$H$_{11}$CN (b. p. 158–159°) 63% (0.052 to 0.068 mole). C$_6$H$_5$CN (b. p. 190.7° (cor.) (97% (0.2 to 0.2 mole). *o*-ClC$_6$H$_4$CN (m. p. 43–44°) 93% (0.03 to 0.036 mole). *p*-CH$_3$-C$_6$H$_4$CN (b. p. 217–220° (cor.)) 89% (0.062 to 0.077 mole). *p*-NO$_2$C$_6$H$_4$CN (m. p. 149–150°) 29%. 2,6-Cl$_2$C$_6$H$_3$CN (m. p. 142.5–143.5°) 67% (0.026 to 0.029 mole). 2,4,6-Cl$_3$C$_6$H$_2$CN (m. p. 75–76°) (50 mg. of acid used). α-C$_{10}$H$_7$CN (m. p. 31–32°) 79% (1 g. of amide used). β-C$_{10}$H$_7$CN (m. p. 65–66°) 80% (2 g. amide and 2.3 g. NaClAlCl$_3$).

In the study of the mechanism of the reaction, equal molecular quantities of benzamide and NaCl·AlCl$_3$ were heated; when the temperature reached 140–150° hydrogen chloride began to be evolved. When the reaction ceased the temperature was raised to 290–295° before any more gas was formed. At this temperature hydrogen chloride was evolved freely and benzonitrile distilled from the flask; two moles of hydrogen chloride was formed.

Equal molecular quantities of benzamide and aluminum chloride were heated. At the melting point of the amide hydrogen chloride was evolved and the aluminum chloride dissolved in the liquid. The product, after solidification, was hydrolyzed by water; 86% of the amide was recovered.

p-Nitrobenzamide was heated with NaCl·AlCl$_3$ (equal moles) at 180° until one mole of hydrogen chloride was formed. More of the salt was added but no additional hydrogen chloride was formed. The product was steam distilled; no nitrile was obtained. The amount of amide recovered was 94% of the amount used.

The Semi-micro Procedure.—The following procedure is recommended. A powdered mixture of 10 mg. of the amide and the equivalent weight of NaCl·AlCl$_3$ or aluminum chloride is introduced into a 6-mm. tube closed at one end. In order to prevent the mixture from coming into contact with the sides of the tube, it is introduced through a second tube drawn out so that it can be placed in the reaction tube. The latter is then heated about 4 cm. from the closed end and drawn down to the diameter of a melting point tube. The mixture is heated cautiously above a flame until the hydrogen chloride has been given off. It is then heated slowly at a higher temperature until the nitrile formed has sublimed into the narrow part of the tube. When cold, the narrow tube is cut off and the melting point of the nitrile determined in a melting point block. The observed and the recorded melting points (in parentheses) are given of the nitriles made in this way; *o*-ClC$_6$H$_4$ 45–46° (42–43°); 2,6-Cl$_2$C$_6$H$_3$CN 144.5–146.5° (143°); 2,4,6-Cl$_3$C$_6$H$_2$CN 75–76° (77.5°); 4-NO$_2$C$_6$H$_4$CN

144.5–146.5° (149°); α-$C_{10}H_7CN$ 31–32° (33.5°); β-$C_{10}H_7CN$ 63–64° (66°).

Nitriles from Ammonium Salts.—Attempts were made, without success, to isolate an amide as an intermediate product in the formation of nitriles from ammonium salts. In all cases the acid was recovered, although much hydrogen chloride was formed. The yields of acetonitrile (50%) and benzonitrile (48%) were about one-half of those obtained from the amides, when the ammonium salts and $NaCl \cdot AlCl_3$ were heated together in the molecular ratio of 1 to 2.

The Reaction between Acids and Amides.—The reactions were carried out in a 125-cc. distilling flask in the neck of which was placed a 3 cm. layer of glass beads. The latter served to prevent the acetamide used from distilling from the flask which was connected with a condenser and heated in a metal-bath.

One-tenth mole of benzoic acid was heated for two and one-half hours at 220–230° with 0.125 mole of acetamide. The distillate contained a little water, acetic acid and a small amount of benzonitrile. The benzamide formed in three experiments was 46, 51, and 53% of the theoretical yield. When equal molecular quantities of the acid and amide were refluxed for seven hours, the yield of benzamide was 30%.

The reaction was shown to be a reversible one. When equal molecular quantities of acetic acid and benzamide were refluxed for twenty-four hours, 42% of the benzamide and 31% of the acetic acid were recovered. The amount of benzoic acid formed showed that the interchange had taken place to the extent of 35%.

o-Chlorobenzoic acid gave 39% of its amide when heated with acetamide. The acid which did not react was recovered. When 16.1 g. of 2,6-dichlorobenzoic acid was heated at 225–235° for six hours with acetamide, the distillate was 93% of the theoretical yield of *m*-dichlorobenzene. When aliphatic dibasic acids were heated with acetamide the yield of amides was small. When formamide or urea was substituted for acetamide the yields were unsatisfactory.

An interchange of groups took place when benzoic acid was heated with acetanilide for three hours at 230–240°. The acetic acid formed was 65% of the theoretical and the benzanilide 50% after recrystallization.

Interchange between an Acid and an Ester.—An interchange of groups took place when 0.1 mole each of benzoic acid and phenyl acetate and 4 drops of sulfuric acid were heated at 175–177° for two and one-half hours; 49% of the benzoic acid was converted into phenyl benzoate.

The interchange reaction between benzoic acid and ethyl acetate gave 15% ethyl benzoate. No reaction took place between benzoic acid and phenetole.

The Use of the Compound $NaCl \cdot AlCl_3$ in Friedel and Crafts Condensations. Preparation of Diphenylmethane.—Into a mixture of 32 g. of $NaCl \cdot AlCl_3$ and 100 cc. of benzene was allowed to drop, during one hour, a solution of 63 g. of $C_6H_5CH_2Cl$ in 75 cc. of benzene, the temperature being held at 15–20°. Dry air was drawn over the mixture for one hour. It was then hydrolyzed. The product was distilled at 33 mm. pressure. The yield of diphenylmethane (b. p. 154–155°) obtained was 44 g. Diphenylmethane, which is converted into a tar by aluminum chloride, was not appreciably affected when a solution of 5 g. of the hydrocarbon in 15 cc. of benzene was allowed to stand with 3.5 g. of $NaCl \cdot AlCl_3$ for one hundred hours at room temperature. Stilbene and phenanthrene are rapidly changed by aluminum chloride; they were unaffected by $NaCl \cdot AlCl_3$ at room temperature.

Benzene condensed with chloroform or carbon tetrachloride in the presence of $NaCl \cdot AlCl_3$ at room temperature to only a very slight extent. The salt was active enough to bring about the usual reaction between benzene and alkyl halides.

Benzoyl Chloride and Ammonium Chloride.—The acyl chloride (0.20 mole) was refluxed with 0.34 mole of ammonium chloride for two hours; at the end of this time the odor of benzoyl chloride was no longer apparent. The product was treated with a solution of sodium hydroxide; the oil formed (9.8 g.) was shown to be benzonitrile; 10.2 g. of benzoic acid was recovered from the alkaline solution. An explanation of the reaction was evident from the results of Titherly and Holden,[4] who showed that benzoyl chloride and benzamide react and form benzonitrile and benzoic acid. In our experiment the benzamide probably formed from the chloride and ammonium chloride reacted with benzoyl chloride. The yield of nitrile obtained was close to that theoretically possible.

Reaction between Esters and Aluminum Chloride.—The study of this reaction[5] has been extended. Ethyl benzoate (0.1 mole) and aluminum chloride (0.1 mole) were mixed and heated cautiously in a flask, placed in a metal-bath, until the heat generated by the formation of the molecular compound had been given off. The flask was connected with a receiver cooled by dry-ice. The temperature was raised at the rate of about 1° per minute. At about 150–155° the solid melted. At 165° ethyl chloride began to condense. At the end of five hours the reaction ceased. The ethyl chloride obtained was 95% of the theoretical yield. The residue in the flask melted at 245°. When twice the amount of aluminum chloride was used only a few drops of ethyl chloride were obtained; a viscous mass was left in the flask.

Ethyl 2,6-Dichlorobenzoate and Aluminum Chloride.—The ester was prepared by treating the acid with thionyl chloride, removing the excess of the latter by heating and final heating with alcohol. The yield of the pure ester was 82%. To 7.1 g. of the ester 4.5 g. of aluminum chloride was added slowly while the mixture was cooled. The molecular compound melted at 90–95°; at 110° the rate of formation of ethyl chloride was appreciable. The temperature was raised to 120–130°. At the end of two and one-half hours reaction ceased. The weight of ethyl chloride formed was 91% of the theoretical. The residue was treated with water and acidified. The weight of 2,6-dichlorobenzoic acid (m. p. 141.5–142.5°, recorded 139–140°) was 92% of the theoretical yield. It should be noted that this ester of a diortho acid reacted with aluminum chloride at a much lower temperature than did ethyl benzoate or ethyl acetate. This fact is added evidence of the lability of the alkyl–oxygen bond produced by two groups in the ortho position to the carboxyl group. Treatment of these esters with hydrobromic acid or aluminum chloride

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[4] Titherly and Holden, *J. Chem. Soc.*, **101**, 1876 (1912).

[5] Norris and Arthur, THIS JOURNAL, **62**, 874 (1940).

appears the best method of converting them into acids, since hydrolysis is effected with difficulty.

The ester and acetamide were distilled slowly at 200–210° for three hours to discover whether an interchange of groups would take place. Twenty-eight per cent. of the ester was converted into *m*-dichlorobenzene and the rest was recovered. The temperature used (200–210°) was below that at which the acid first loses carbon dioxide (235°).

Phenyl Tolyl Ketones from Toluene and Benzoic Acid.—Groggins[6] has shown that chlorobenzophenone can be prepared by condensing chlorobenzene with benzoic acid by means of aluminum chloride. We have applied the reaction to toluene. A mixture of 0.20 mole of benzoic acid, 0.40 mole of aluminum chloride and 0.44 mole of toluene was refluxed for six hours. About two-thirds of the 60% yield of ketones was a mixture which contained *p*-tolyl phenyl ketone and a smaller amount of the ortho isomer. When benzene was used with benzoic acid about 90% of the acid was recovered.

Summary

1. Eleven examples are given of the preparation with excellent yields of nitriles by the reaction between amides and aluminum chloride or the compound $NaCl \cdot AlCl_3$. The process can be used on a semi-micro scale as an aid in the identification of amides.

2. It has been shown that a reversible reaction takes place between an acid and an amide as the result of which the NH_2 and OH groups exchange places.

3. 2,6-Dichlorobenzoic acid loses its carboxyl group quantitatively when heated with acetamide at a temperature at which it is relatively stable when heated alone. The ester of the acid is quantitatively converted into the acid and ethyl chloride when it is heated at 110° with aluminum chloride.

4. The following are described: the reaction between benzoyl chloride and ammonium chloride, the use of the compound $NaCl \cdot AlCl_3$ in the Friedel and Crafts reaction and the condensation of benzoic acid with toluene by means of aluminum chloride.

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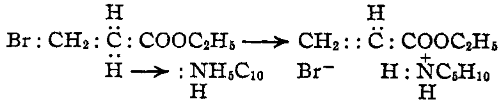
[6] Groggins, Nagel and Stearton, *Ind. Eng. Chem.*, **26**, 1317 (1934).

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reaction of Organic Halides with Piperidine. V. Negatively Substituted Ethyl Bromides

BY E. LEON FOREMAN AND S. M. MCELVAIN

In the preceding paper[1] of this series it was shown that esters with a β-bromo substituent are very much more reactive toward piperidine than are other types of bromo-esters. Also it was shown that the reaction involves, first, the elimination of hydrogen bromide from the β-bromo-ester, and then the addition of piperidine to the resulting acrylic ester. The mechanism by which the acrylic ester is formed was thought to be the removal of a proton from the α-carbon atom of the bromo-ester by the nucleophilic reagent, piperidine, followed by the release of the bromide ion from the molecule,[2] thus



$$\begin{array}{l} \qquad\qquad\quad\; H \qquad\qquad\qquad\qquad\qquad\quad\; H \\ Br:CH_2:\ddot{C}:COOC_2H_5 \longrightarrow CH_2::\ddot{C}:COOC_2H_5 \\ \qquad\qquad\quad\; \ddot{H} \longrightarrow :\underset{H}{NH_5C_{10}} \quad Br^- \quad H:\underset{H}{\overset{+}{N}}C_5H_{10} \end{array}$$

On the basis of such a mechanism it is obvious that the reactivity of β-substituted ethyl bromides, YCH_2CH_2Br, should parallel the electronegativity of the group Y.

The present paper reports the preparation and reactivity of a number of such negatively substituted ethyl bromides with piperidine. In the cases that Y is carbethoxy, cyano or benzoyl the rate of reaction of the bromide with piperidine is so rapid (*e. g.*, ethyl β-bromopropionate reacts to the extent of 94% in fifteen minutes at room temperature) that it cannot be measured readily. For this reason negatively substituted phenylethyl bromides, $YC_6H_4CH_2CH_2Br$, were used. These vinylogs of the more simply substituted ethyl bromides are, in most cases, more easily prepared and generally show a lower and more readily determined reaction rate.

Experimental

Preparation of β-Substituted Ethyl Bromides.—Ethyl β-Bromopropionate was prepared from ethylene cyano-

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[1] Drake and McElvain, THIS JOURNAL, **56**, 697 (1934).

[2] A similar idea as to the mechanism of this type of elimination reaction has been expressed in a footnote of a paper by Noller and Dinsmore, *ibid.*, **54**, 1025 (1932), and also by Hauser and coworkers, *ibid.*, **57**, 1056 (1935); **59**, 1823 (1937).