

## *The Hydrogen Fluoride-Catalyzed Reaction between Phenol and Nitriles*

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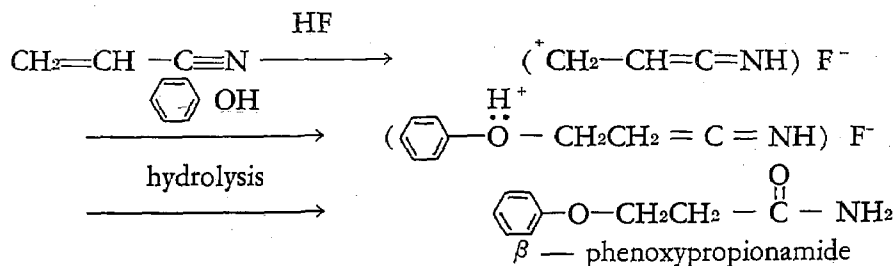
and

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EXTENSIVE WORK has been done by MacKenzie, Schmidt, and Webb (1951) in the preparation of imidoester hydrochlorides by Pinner's method. The basic structure of the compounds obtained by these workers was reported as  $R-C(OR')=NH \cdot HCl$  in which R is a saturated hydrocarbon, a halo-monosubstituted hydrocarbon, or phenyl group. It was of interest to us to determine whether or not anhydrous hydrogen fluoride would cause the formation of this type of salt in the reaction of acrylonitrile with phenols since other data (Johnston and Gross, 1957; Johnston, 1960) were available concerning these reactants and various catalysts of the stronger Lewis acid type.

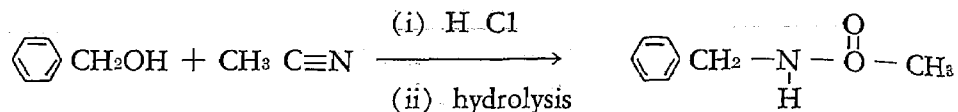
It was found that when HF was used as a catalyst hydrofluoride salts of imidoester were not found in the reaction between phenol and acrylonitrile. Instead, all experimental evidence indicated the following route of reaction:



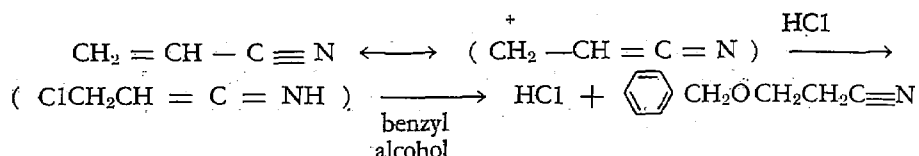
Under the same experimental conditions (24 hours at 80° C), no reaction was observed between phenol and acetonitrile. Therefore, 1,2-addition of hydrogen fluoride to acrylonitrile is precluded, and the small amount of amide found after hydrolysis may be accounted for by the resonance stability of the 1,4-addition complex.

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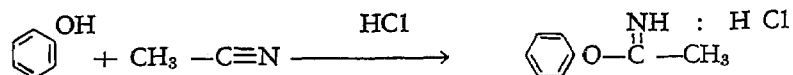
That the modes of reaction of acetonitrile and acrylonitrile are different due to the resonance state of the latter is further supported by the fact that in a group of experiments in which the nitrile and benzyl alcohol were mixed prior to the addition of HCl, different results were obtained. When acetonitrile was used, N-benzyl-acetamide was found:



This was in accordance with the experimental data of Parris and Christenson (1960), who used concentrated sulfuric acid as a catalyst. However, when acrylonitrile was used,  $\beta$ -benzyloxypropionitrile was found. Hence, the latter reaction proceeded in the 1,4-addition manner:



It is apparent that anhydrous hydrogen fluoride is too weak a catalyst to promote carbon-carbon addition but strong enough to bring about carbon-oxygen addition in the 1,4-manner coupled with conversion of the cyano group to the amide (or an intermediate imidoester which would be hydrolyzed in subsequent operations). This is in marked contrast to the action of anhydrous hydrogen chloride, which will attack both acetonitrile and acrylonitrile to cause 1,2-addition to the oxygen atom of phenol (McElvain and Nelson, 1942):



Previous work in this laboratory has demonstrated that a stronger Lewis acid such as anhydrous aluminum chloride at about 15° C caused 1,4-addition to the ring of phenol to give a small amount of dihydrocoumarin (in which instance the cyano group was hydrolyzed because of the formation of a stable ring) and a much larger amount of  $\beta$ -(*p*-hydroxyphenyl)-propionitrile. Aluminum phenoxide behaved in a similar manner at 180° C, but under this condition of elevated temperature, polymerization took place and infrared analysis indicated participation of the cyano group in a cross-linking reaction similar to the well-known Houben-Hoesch reaction.

*Para*-cresol in the presence of anhydrous hydrogen fluoride was found to react with acrylonitrile to form  $\beta$ -(*p*-methylphenoxy)-propionamide but in lower yield than in the case of phenol and acrylonitrile.

## *Experimental*

### I. Phenol and Acrylonitrile

#### 1. *Reaction Conditions*

Equi-moles of freshly distilled phenol and anhydrous acrylonitrile were mixed and poured into a steel bomb at 0° C. The equivalent amount of anhydrous hydrogen fluoride was collected in a polyethylene bottle at 0° C and poured over the mixture. The bomb was sealed, wrapped in a heating mantle, and placed on a shaker. The reaction was allowed to proceed with constant shaking at 80° C for about 24 hours. The bomb was opened and the mixture poured over a mixture of cracked ice and water. Enough sodium bicarbonate was added in small portions with vigorous stirring until pH of the aqueous phase reached 6-7. The phenolic layer was removed and the aqueous layer extracted with small portions of toluene. The extracts and the phenolic fraction were combined, giving a volume of about 200 ml per mole of each reactant and processed through a chromatographic separation as described below.

#### 2. *Chromatographic Separation*

*A. The adsorbent and its treatment.* Nontreated alumina was found to be inadequate in that no crystals were obtained, apparently because of excessive basicity. However, a column packed with deactivated alumina (1 cc/30 gram freshly opened Baker Reagent Grade alumina) yielded crystals. This result led to the adoption of a weaker adsorbent, charcoal on an asbestos support. Fifty grams of bone charcoal and 50 grams of asbestos fibers were boiled separately in enough distilled water for 15 minutes and filtered by suction. The two cakes were well mixed in a liter of boiling water in which three ml of concentrated HCl had been added until a homogeneous mixture was observed. This mixture was filtered by suction. The cake was placed in a suction flask and as much water as possible removed by aspirating the flask and contents over a small, hot plate (approximately 8-10 hours). The material after drying in a desiccator was ready for use. Paper and "Super-Cel" with charcoal were also satisfactory and were prepared similarly.

*B. Column preparation and characteristics.* The packing was introduced into the column as a slurry in petroleum ether.

A glass column of one-inch internal diameter was used. An estimated amount of 80 gram of absorbent gave a column length of about 18 inches before the introduction of hydrolyzed mixture.

*C. Elution.* The column was assembled over an automatic fraction collector set for 15-ml fraction collection. Satisfactory results were obtained both at atmospheric pressure and at pressures up to 910 mm Hg. The solvent system was petroleum, benzene chloroform in the order mentioned. The semi-automatic gradient set-up as reported by Donaldson, Tulane, and Marshall (1952) was used. The volume of reaction mixture put through the column was 100 ml.

*D. Results.* Most of the unreacted starting materials were eluted by petroleum ether. This fraction was re-chromatographed, but only a few, barely visible crystals were found. This suggested that the capacity of the column for the amide has been reached. In no case was phenol found after the benzene elution. Crystals came down with benzene-chloroform mixture or later with chloroform. The use of a stronger eluent such as methanol following the chloroform was found unnecessary since it only brought down low molecular weight polymeric material. The yield of crystalline m.p. 117-118 material was 0.10 gm (0.13 per cent based on acrylonitrile). Its identity was established as  $\beta$ -phenoxypropionamide by the following procedure.

The compound was dissolved in 10 per cent sulfuric acid and the solution gently warmed at approximately 60° C for two hours, after which the solution was extracted three times with small portions of benzene. The combined extract was dried over anhydrous MgSO<sub>4</sub>, filtered, and the solvent removed by evaporation. The resulting colorless crystals melted at 95-96° C. A mixed-melting point determination with an authentic preparation of  $\beta$ -phenoxypropionic acid gave a reading of 94-95° C.

Principal infrared absorption lines of the spectrum of  $\beta$ -phenoxypropionamide were found to be: 3380, 3220, 1650, 1610, 1260, and 1085.

## II. Acrylonitrile and Benzyl Alcohol

Equi-moles of benzyl alcohol (reagent grade) and dried acrylonitrile were mixed in a three-necked flask fitted with a condenser and a mechanical stirrer. HCl was passed into the mixture under constant stirring. A white precipitate was observed almost immediately. After the addition of about the same number of moles of HCl, the mixture was stoppered and placed in a refrigerator pending further operations (Thorpe, 1960).

The mixture was poured over cracked ice, and NaHCO<sub>3</sub> was added until the pH of the aqueous portion reached 7; then the organic layer was removed

and the aqueous layer extracted four times with ether. The combined organic phase was dried with saturated salt solution followed by anhydrous  $\text{MgSO}_4$  overnight.

The distillation temperature of main fraction was  $61-62^\circ\text{C}$  at 18 mm. Nitrile and ether functional groups were indicated by infrared spectrographs. The yield was about 62 per cent.

### *Summary*

The catalytic effect of anhydrous hydrogen fluoride in the system phenol-acrylonitrile has been discussed. The resulting compound is  $\beta$ -phenoxypropionamide. A discussion of the effects of the catalyst, the phenol, and the nitrile has also been presented.

### *Acknowledgements*

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