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CONVERSION OF NITRILES TO AMIDES ON THE SURFACE OF ALUMINA

A Thesis Presented for the Master of Science Degree

The University of Tennessee, Knoxville

Catherine Pala Wilgus

December 1994

This thesis is lovingly dedicated to my husband, John.

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ABSTRACT

The conversion of nitriles to amides is difficult to achieve, generally requiring harsh reaction conditions. It is the goal of this research to demonstrate that amides can be produced from nitriles by means of a fairly simple method using alumina and an acid catalyst.

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CHAPTER I

INTRODUCTION

The conversion of nitriles to amides is a challenging synthetic task (eq. 1)[1] because the amides are often more easily hydrolyzed than the nitriles from which they are made.

(1)

R= alkyl or aryl group

A number of methods for nitrile hydrolysis have been reported; most are carried out using acid or base catalysis at elevated temperatures.[2,3,4,5] Figure 1 illustrates some of these methods: (a) hydrogen peroxide[2], (b) boron trifluoride in acetic acid[3], (c) polyphosphoric acid (PPA)[3], and (d) water in the presence of a copper catalyst[4]. Under vigorous conditions, the formation of the corresponding carboxylic acids usually is favored (eq. 2).[5,12,13,14] A few successful nitrile to amide conversions have been performed under more moderate conditions. Raadt, Griengl, and Klempier reported, for example, a simple conversion using the "SP409" nitrile hydratase enzyme (eq. 3).[6] Although the conversions were successful, the reactions took between 7 and 14 days.[6]

(a)

$$C_6H_5CN + 2H_2O_2 \xrightarrow[24\ hr.]{40\ ^\circ C} C_6H_5-\overset{O}{\overset{\|}{C}}-NH_2 + O_2 + H_2O$$

(b)

$$CH_3CN \xrightarrow[C_6H_5COOCH_3]{NaNH_2} C_6H_5COCH_2CN$$

$$\xrightarrow[140\ ^\circ C/\ 1\ hr.]{BF_3(CH_3COOH)} C_6H_5COCH_2CONH_2$$

(c)

$$CH_3CN \xrightarrow[C_6H_5COOCH_3]{NaNH_2} C_6H_5COCH_2CN$$

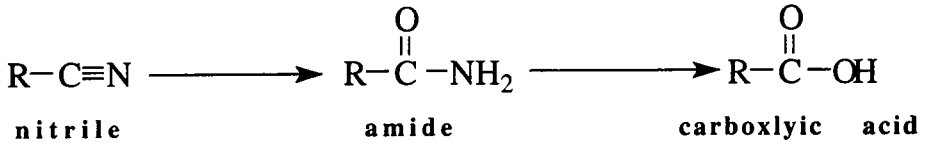
$$\xrightarrow[100\ ^\circ C/\ 30\ min.]{PPA} C_6H_5COCH_2CONH_2$$

(d)

$$C_6H_5CN \xrightarrow[90\ ^\circ C/\ 2\ hrs.]{Cu(0)/H_2O} C_6H_5-\overset{O}{\overset{\|}{C}}-NH_2$$

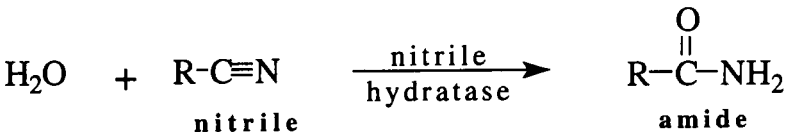
Figure 1

Various Nitrile to Amide Conversions



(2)

R= alkyl or aryl group



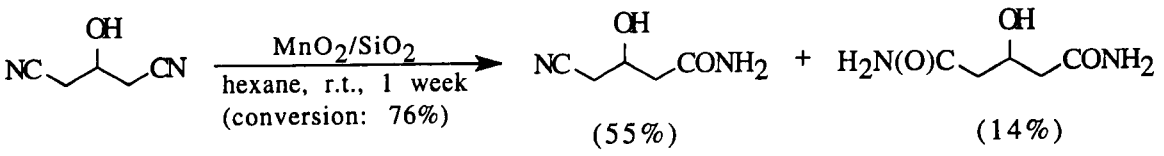
(3)

R= alkyl or aryl group

Breuilles, Leclerc, and Uguen also described a mild hydration of nitriles but this procedure required a 10-day reaction period (eq. 4)[1]; they did not mention if carboxylic acids were formed as a by-product. A successful nitrile hydrolysis which transpires under mild conditions in a short period of time has yet to be reported. This research was performed in order to determine if such a procedure could be developed.

Since, the chemical literature does not contain any references to a succinct and mild solvent-based nitrile hydrolysis, it may be necessary to carry out the nitrile hydrolysis in a medium different from what has been previously reported. Inorganic oxides have been used as media for bimolecular reactions in the absence of solvents.[7] Pagni, Kabalka and co-workers have reported various

(4)



reactions run on the surface of alumina.[8] Many of these reactions were superior to their solution analogs. The heterogeneous phase of the alumina surface is believed to promote and often catalyze the reactions.[7] Neutral alumina should be a good environment for nitrile-to-amide conversions. In order to determine if alumina would be suitable for the hydrolysis reactions, the properties of alumina have to be understood.

Knözinger and Ratnasamy[9] and Peri[10] have developed theories describing the surface of alumina. They have presented detailed studies regarding the nature, structure, and properties of alumina.[9] The term alumina describes a conglomeration of anhydrous and hydrated aluminum oxides.[15] Most are prepared from the aluminum ore, bauxite by the Bayer process and are commercially available.[11] Entirely unique chemistry often occurs on the surface of alumina because it has properties which are not reproduced in the solution or gas phase.[7] Because of its ability to support a wide variety of substrates including oxides, transition metals, and saturated hydrocarbons, alumina is being used to catalyze such diverse reactions as the isomerization of paraffins and the hydrodealkylation of aromatics.[9]

A naturally occurring form of anhydrous alumina (α-alumina) does exist, but this form is chemically inert.[16] The forms of alumina

which are catalytically important are the transition aluminas: $\gamma, \delta, \kappa, \eta, \chi$, and θ. Transition aluminas are produced from the dehydration, by heat, of hydrated aluminas with the end result of dehydration being α-alumina.[15] Synthetic, γ-alumina is the most important for catalytic operations and the most frequently utilized of all the transition aluminas.[11]

γ-Alumina possesses distinct chemisorption characteristics.[9] It has a maximum surface area of 200 m^2/g made up of both acidic and basic sites.[9] The actual form of γ-alumina was described by Knözinger and Ratnasamy using a spinel defect model.[9] The following paragraphs contain a brief description of their findings.

γ-Alumina has a slightly tetragonally distorted spinel lattice which is strongly disturbed. The lattice is composed of unit cells built up by oxygen and aluminum atoms. Each unit cell contains 32 oxygen atoms and 21-1/3 aluminum atoms, which creates vacant cation positions throughout the lattice. The oxygen lattice is made up of a fairly well ordered arrangement of 4 distinct oxygen layers: A, B, C, and D, stacked in a cubic close-packed pattern. The A-layer is the top of the lattice while the B-layer, C-layer, and D-layer lie deeper into the alumia (Fig. 2).[11]

The Al^{3+} cations are distributed throughout the lattice in both octahedral and tetrahedral sites. The lattice layers (A, B, C, D) are distinguished by the type of cation distribution they contain. The A-layer consists of 24 cation positions, 8 octahedral and 16 tetrahedral; the B-layer is made up of 24 octahedral positions. The C-layer

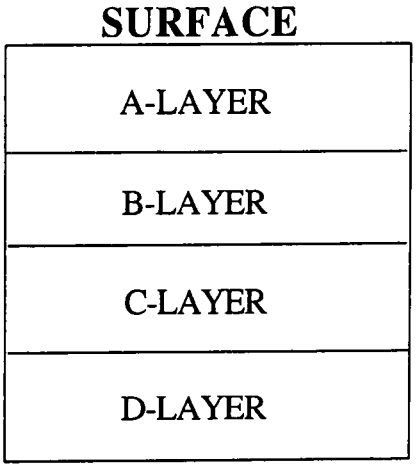


Figure 2

Layering of Alumina.

contains an equal number of octahedral and tetrahedral interstices, while the D-layer contains only octahedral positions. Figure 3 depicts two-dimensional representations of the three-dimensional layers of alumina. Energetic reasons dictate that the surface layer will usually be terminated by hydroxide groups. Infrared spectrophotometry showed that five different types of hydroxide groups existed on the surface of alumina (Fig. 4). Alumina is thermally stable and can withstand large influxes of heat. It was found that alumina is most catalytically active when it has been heated higher than 200 °C. Heating removes the surface hydroxyl groups and exposes aluminum cations and coordinatively unsaturated oxygen anions (Fig.5).[16] The exposed ions, Brønsted acids and Lewis bases, are involved as catalytically active sites and components of chemisorption. Alumina which has been heated to an elevated temperature is termed

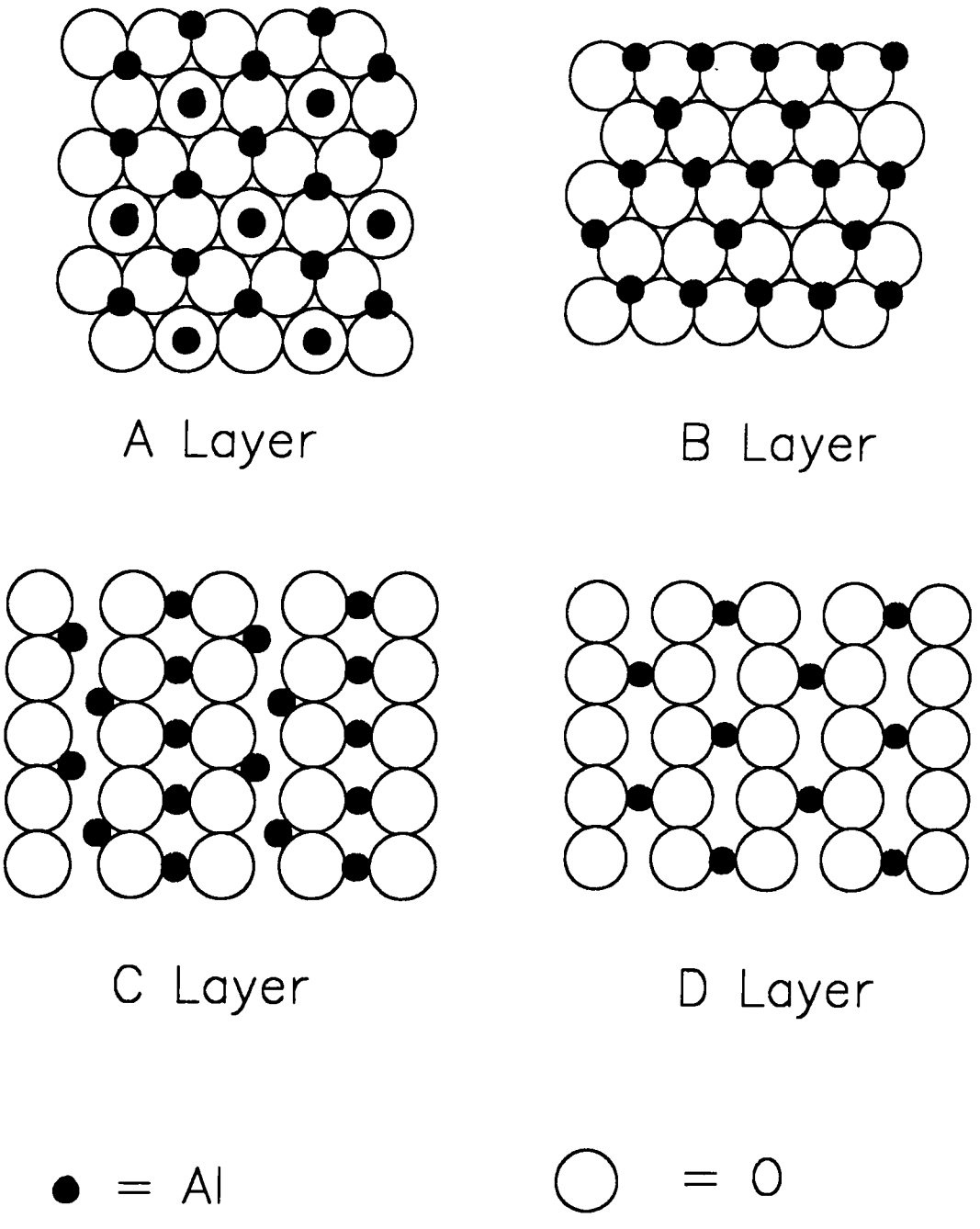


Figure 3

The Knözinger and Ratnasamy Layers of γ-Alumina

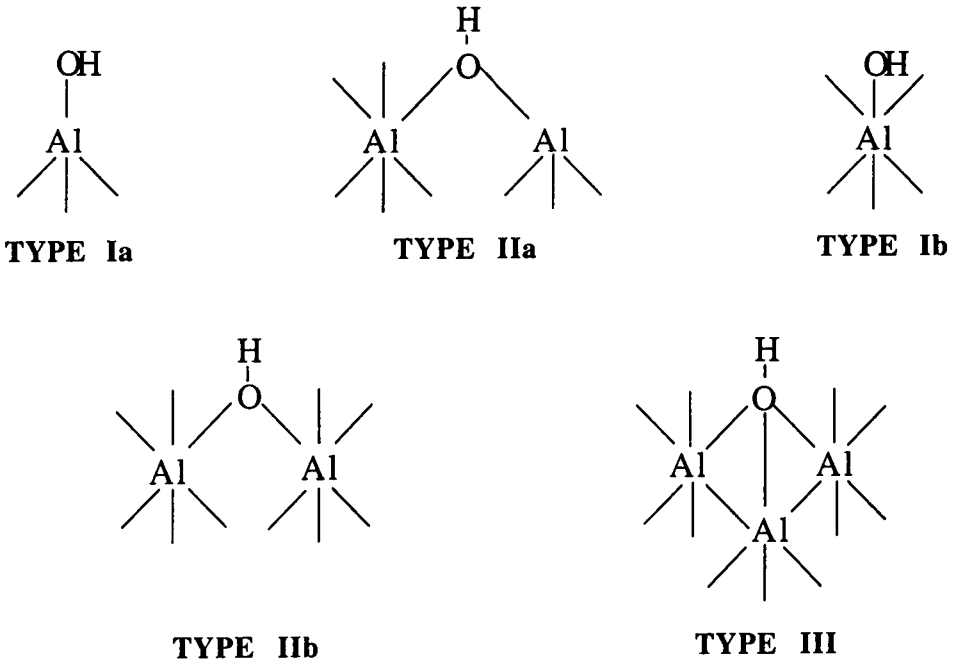


Figure 4

Surface Hydroxyl Types

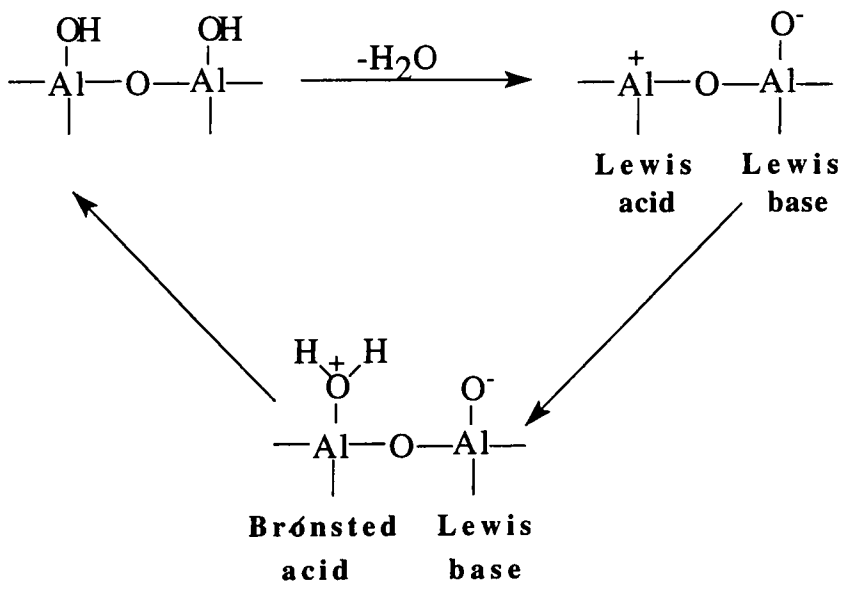


Figure 5

Acidic and Basic Sites on Alumina

"activated". Hence, alumina which has not been exposed to heat and still contains its surface hydroxyl groups is "unactivated". The activity of alumina depends upon the concentration of accessible Brønsted acid and Lewis base sites.

The surface of unactivated alumina contains an ample supply of hydroxyl groups which could be utilized for nitrile hydrolysis. Assuming that two hydroxyl groups are required to form the water needed to hydrolyze a nitrile, the apparent concentration of water can be calculated. Using the density of hydroxyl groups on the surface of unactivated alumina, from the theory of Knözinger and

Ratnasamy,[9] and a surface area of 155 m^2/g for the alumina used in this study, the concentration of 1.87 mmol of water per gram of alumina is calculated. In order to obtain this amount of water, the alumina must remain unactivated for nitrile hydrolysis. By remaining unactivated, the catalytically active sites would not be exposed as they are when the hydroxyl groups are thermally removed from the surface, so the alumina would not be expected to act as a catalyst for the nitrile reactions. In solution, nitrile hydrolysis is often brought about with the aid of a catalyst.[3] In the same manner, nitrile hydrolysis could occur on the surface of unactivated alumina with the addition of a catalyst. The most common catalysts of solution reactions are strong Brønsted acids. Some reactions are catalyzed by Lewis bases as well. Therefore, it could be assumed that the same type of catalysts could catalyze the nitrile reactions on alumina.

As already discussed, most methods of nitrile hydrolysis in solution require harsh conditions. Although milder methods do exist, these require lengthy reaction periods. It was hoped that alumina would be a useful medium for amide synthesis without using harsh reagents or requiring prolonged reaction periods.

CHAPTER II

RESULTS AND DISCUSSION

Amides are produced from the hydrolysis of nitriles in solution.[2,3,4,5] Often the resulting amides do not survive the vigorous conditions of nitrile hydrolysis and are in turn hydrolyzed to the corresponding carboxylic acids.[14] In order to obtain amides under milder conditions, nitriles were hydrolyzed on the surface of unactivated alumina. It has been noted that, in solution, when the conditions of the hydrolysis were mild, amides were less likely to be hydrolyzed to the corresponding carboxylic acids.[1] However, all the documented mild nitrile-to-amide conversions require lengthy reaction periods.[1,6] Alumina might provide the ideal environment for nitrile hydrolysis without subsequent amide hydrolysis. The following chapter describes the results of a study of nitrile to amide conversions on alumina.

Most of the reactions in this study were run using 5.0 grams of alumina per mmole of nitrile which, from the theory of Knözinger and Ratnasamy[9], provides 9.35 mmoles of water per mmole of nitrile for the hydrolysis reaction. Many reactions had to be performed, however, before a satisfactory yield of amide was obtained.

This study was performed using eight nitriles: acetonitrile, benzonitrile, hexanenitrile, isobutyronitrile, 4-methoxybenzonitrile, 4-nitrobenzonitrile, propionitrile, and *p*-tolunitrile. The reactions were performed on unactivated, activity grade 1, Brockmann, neutral

alumina. The majority of the reactions were catalyzed by one of the following acids: chemisorbed boron tribromide (BBr_3), hydrogen bromide (HBr), trifluoromethanesulfonic acid (CF_3SO_3H), or trifluoroacetic acid (CF_3CO_2H). A few reactions were also performed without catalyst. Most of the reactions were carried out at a temperature of 60 °C. Other reactions were carried out under sonication (ultrasound). The test substrate was benzonitrile.

The reaction mixtures involving benzonitrile, isobutyronitrile, hexanenitrile, propionitrile, and *p*-tolunitrile were analyzed by gas chromatography/mass spectrometry (GC/MS). The yields were obtained using either a decane (isobutryonitrile, propionitrile) or a tetradecane (benzonitrile, hexanenitrile, *p*-tolunitrile) internal standard. The reactions of 4-methoxybenzonitrile and 4-nitrobenzonitrile were analyzed by high performance liquid chromatography (HPLC) and thin layer chromatography (TLC). The yields were determined, in these instances, by the weight of the products. The yields of the acetonitrile reactions were also obtained using the weight of the product. ^{13}C and ^{1}H nuclear magnetic resonance spectrometry (NMR) were used to verify the structures of the products from all the nitrile reactions. A few of the benzonitrile reactions were also analyzed using TLC, as well as fourier transform infrared (FT-IR), and C-13 solid state (SS) NMR spectroscopy.

Benzonitrile

The rate equation for acid-catalyzed nitrile hydrolysis (Fig. 6) shows that the rate of the reaction depends on the basicity of nitrile as reflected in K_{eq}, the equilibrium constant for the reversible protonation of RCN, and the intrinsic reactivity of the protonated nitrile ($RCNH^+$), as reflected in k_2.

Two theories of nitrile reactivity in acidic solutions exist. A well known hypothesis of organic chemistry is that more basic nitriles will be more reactive in acid because a greater concentration of the protonated nitrile will be present to react with the nucleophile;[14] in other words, K_{eq} dominates the rate. According to Deno, Gaugler, and Wisotsky[17], however, less basic nitriles are more reactive because their protonated forms are intrinsically more

$$RCN + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RCNH^+$$

$$H_2O + RCNH^+ \xrightarrow[\text{slow}]{k_2} RCONH_2$$

$$\text{Rate} = k_1 K_{eq} [RCN][H_2O][H^+]$$

$$\text{where } K_{eq} = \frac{k_1}{k_{-1}}$$

Figure 6

Rate Equation For Nitrile Hydrolysis*

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* Derivation of Rate Equation contained in Appendix.

reactive with water.[17] Here k_2 dominates the rate. Deno and coworkers found that various nitriles, when dissolved in 98-100% sulfuric acid, were long lived enough to evaluate their basicity by NMR spectroscopy. They showed that both acetonitrile and propionitrile were more reactive than benzonitrile in the subsequent hydrolysis even though benzonitrile is more basic than the aliphatic nitriles.[17] It is believed that the increased reactivity of the protonated forms of weaker bases compensates for their lower concentrations. Since it is *apriori* unclear how to apply these concepts to the reactions on the surface of alumina, there was no way to predict nitrile reactivity. Based on Deno's work, however, it is reasonable to assume that benzonitrile will be in the middle range of reactivities exhibited by the eight nitriles studied. Thus, the test reactions were performed with benzonitrile because of its anticipated median reactivity. Once a method for producing benzamide in high yield was discovered, it was applied to the other nitriles.

Reactions Performed with Chemisorbed Boron Tribromide

The first benzonitrile-to-benzamide conversions were attempted on bromoboronated unactivated alumina (BBr_3/Al_2O_3) which Pagni, Kabalka, and coworkers have shown to be a very strong Lewis acid[23] that functions as a catalyst (Fig. 7).

^{11}B and ^{27}Al SS NMR and FT-IR show that BBr_3/Al_2O_3 contains trigonal boron connected by two oxygen atoms to the surface of the alumina with a bromine atom above the surface.[11] It is noteworthy

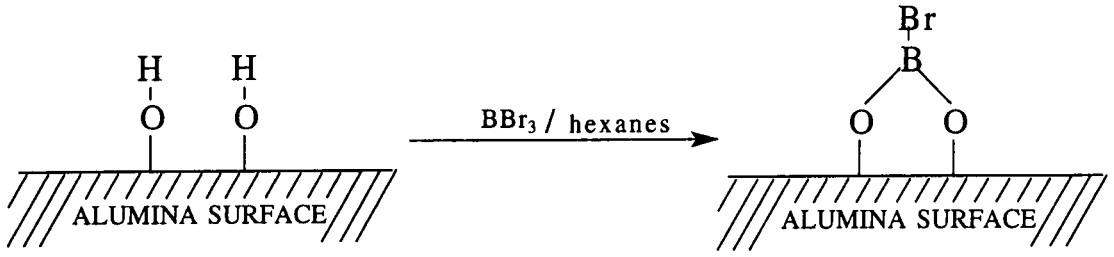
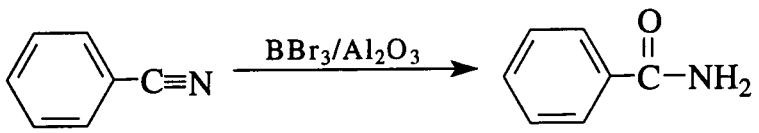


Figure 7

Bromoboronated Alumina

that nitrile-to-amide conversions had been accomplished in solution using boron trifluoride.[3,5] Bromoboronated alumina was shown to be more catalytically active than fluoroboronated and chloroboronated functionalized aluminas in the Diels-Alder reaction.[11] On the basis of the work done with boron trihalogen compounds, both in solution and on alumina, BBr_3/Al_2O_3 was the first catalyst utilized in the nitrile hydrolysis reactions (eq. 5).



benzonitrile benzamide (5)

Several reactions were performed on bromoboronated alumina; unfortunately, none of these reactions produced benzamide. Table 1 lists the various conditions employed with these reactions.

In order to understand why these reactions were not successful, the proposed mechanism for the expected hydrolysis

TABLE 1

REACTION CONDITIONS FOR THE HYDROLYSIS OF BENZONITRILE ON BROMOBORONATED ALUMINA

	Alumina (grams)	Nitrile (mmoles)	BBr_3 (mL)	Time (hours)	Temp. (°C)
A	40	40	40	36	25
B	40	40	40	36	55
C	40	20	20	36	25
D	40	40	18	72	25

must be studied (Fig. 8). BBr_3/Al_2O_3 should catalyze this reaction, since it had catalyzed other reactions.[23] However, none of these reactions required the presence of the surface hydroxyl groups.

When BBr_3 is chemisorbed onto the surface of the alumina, by reaction with surface hydroxyl groups, the surface density of the hydroxyl groups, and thus water, is reduced significantly.

Most of the attempted BBr_3-catalyzed reactions were carried out with a 1:1 ratio of alumina to benzonitrile. As discussed previously, the alumina used in this study had a surface area of 155 m^2/g. Therefore, 1.87 mmoles of water per gram of alumina were formed from surface hydroxyl groups. Because of the displaced hydroxyl groups from the reaction with BBr_3, there is even less water on the surface of bromoboronated alumina. Apparently, there were too few hydroxide groups on the surface of all of the BBr_3/Al_2O_3 studied to bring about the reaction.

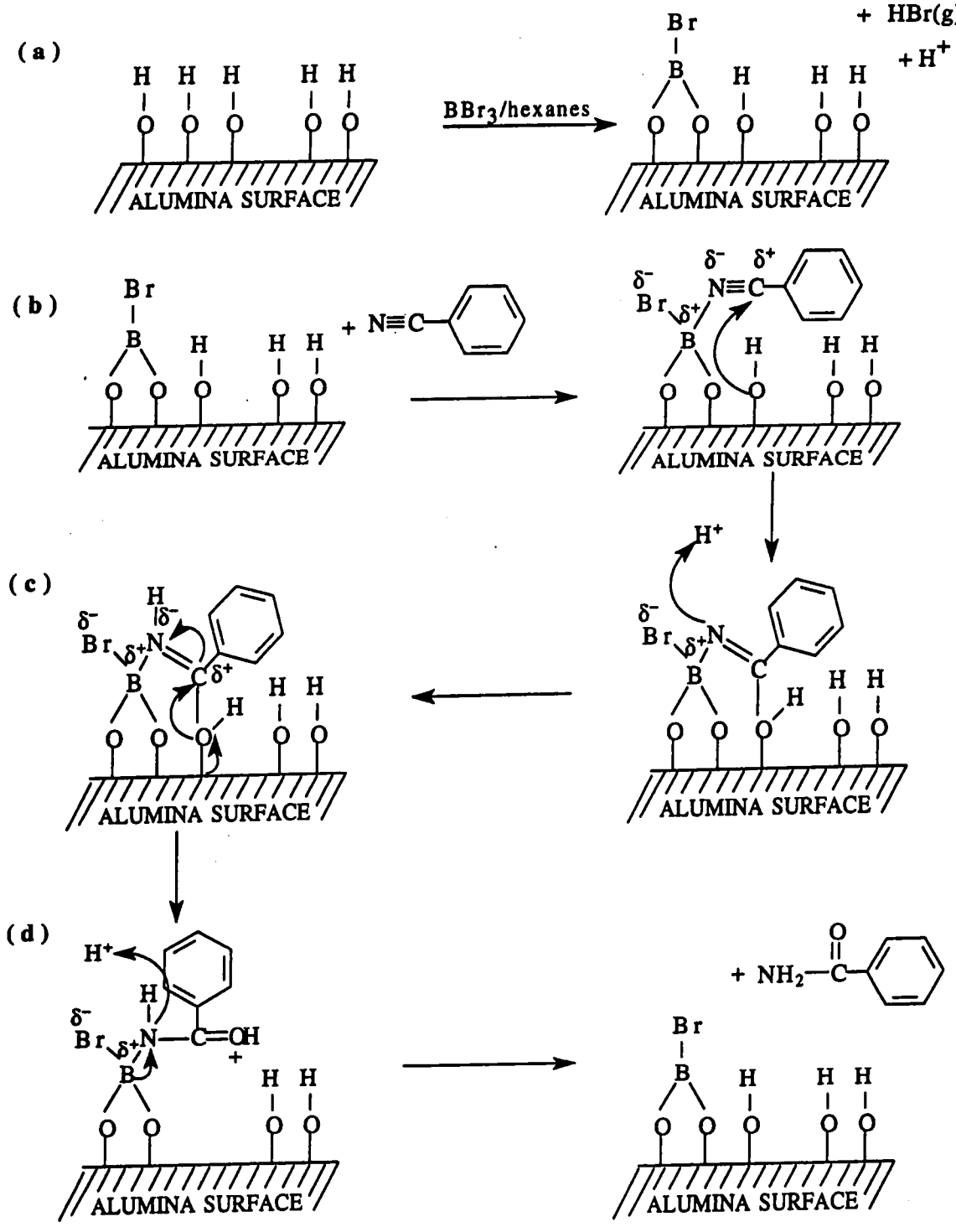
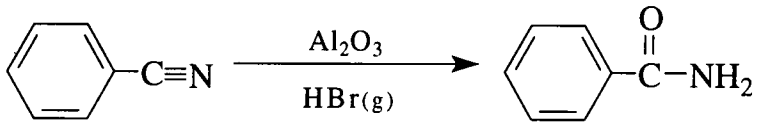


Figure 8

Proposed Mechanism for the Formation of Benzamide on Bromoboronated Alumina

Reactions Performed with Hydrogen Bromide Gas

Even though the BBr_3-catalyzed reactions were unsuccessful, it was believed, nonetheless, that the hydrolysis reaction could be achieved if catalyzed with a sufficiently strong Brønsted acid. HBr was chosen for this purpose (eq. 6). The hydrogen bromide gas was



benzonitrile benzamide (6)

generated by the reaction of bromine with xylene and was added directly onto alumina containing benzonitrile.

The results of the benzonitrile-to-benzamide conversions, shown in Table 2, were at first difficult to explain because only two of the reactions produced benzamide. One reaction gave a 3% yield and the other gave 56%. The reason for the erratic results is probably due to the fact that hydrogen bromide gas leaked out of the apparatus which was sealed with a glass stopper. Since the HBr gas had to be added to the flask, there was no simple way to run these reactions in a sealed apparatus which could prevent the gas from escaping. Unfortunately, it was also not possible to monitor the amount of HBr in the flask to see if this hypothesis was true. It is also possible that the reactions which produced benzamide contained more HBr gas than those which did not yield any product.

TABLE 2

REACTION CONDITIONS FOR THE HBr-CATALYZED REACTIONS OF BENZONITRILE ON ALUMINA[a]

Reaction	Time of Reaction (hours)	Amide Produced (mmoles)	Percent Yield[b]
A	1	0. 00	0.00%
B	5	0.00	0.00%
C	12	0.00	0.00%
D[c]	15	0.00	0.00%
E	24	0.00	0.00%
F[d]	24	0.00	0.00%
G	36	0.00	0.00%
H	48	0.15	3.0%
I	72	0.00	0.00%
J	120	2.8	56%
K	168	0.00	0.00%
L[e]	168	0.00	0.00%
M[f]	168	0.00	0.00%

[a]All reactions were run with 20 g of alumina and 20 mmoles of benzonitrile at 60 °C unless noted otherwise.

[b]Reactions analyzed by GC/MS; yield determined with a tetradecane internal standard.

[c]Reaction performed with 20 g of alumina and 10 mmoles of benzonitrile.

[d]Reaction performed with 20 g of alumina and 20 mmoles of benzonitrile at 25°C.

[e]Reaction performed with 10 g of alumina and 5 mmoles of benzonitrile.

[f]Reaction performed wit 20 g of alumina and 20 mmoles of benzonitrile at 100°C.

The proposed mechanism for the HBr catalyzed reactions is illustrated in Figure 9. The first step (a) is the reversible protonation of the nitrile by HBr, which should be facilitated on the polar surface. The protonation of nitrogen creates a partial positive charge on the nitrile carbon which is attacked by an oxygen of a surface hydroxyl group in step (b). The hydroxyl group breaks its bond with the surface and imidic acid, i.e., the *N*-enol of benzamide is freed in step (c). Tautomerization of the enol gives benzamide, however, it is not known whether the enol or the amide actually is freed from the surface. The bromine generated in step (a) abstracts a proton from a surface hydroxyl group to reform as HBr in step (d).

It was shown that the hydrogen bromide was acidic enough to catalyze the conversion of benzonitrile to benzamide. However, due to the uncertainties associated with the use of a gas, higher boiling catalysts were used for the duration of this research.

Reactions Performed with Trifluoromethanesulfonic Acid

Due to the erratic results of the HBr catalyzed reactions, the decision was made to attempt the nitrile-to-amide conversions using liquid acid catalysts. Hauser and Eby[3] reported a nitrile hydrolysis that was successfully catalyzed by a strong Brønsted acid, polyphosphoric acid (PPA). It was hoped that Brønsted acid-catalyzed nitrile hydrolyses could be achieved on unactivated alumina treated with a strong Brønsted acid. Trifluoromethanesulfonic acid (CF_3SO_3H), which has a Hammet H_o value of -14.1,[18] was the first acid chosen for this purpose (eq. 8)

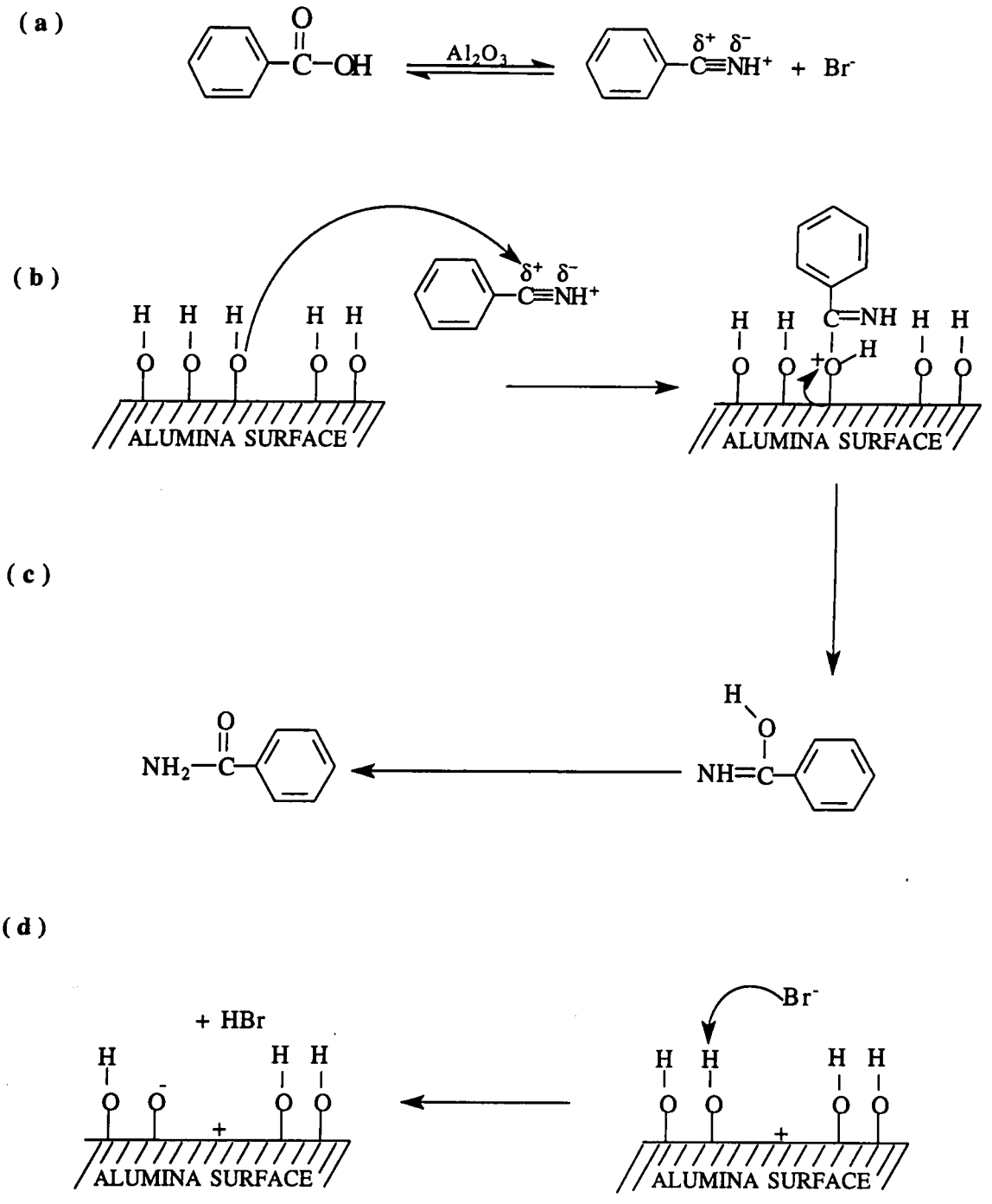
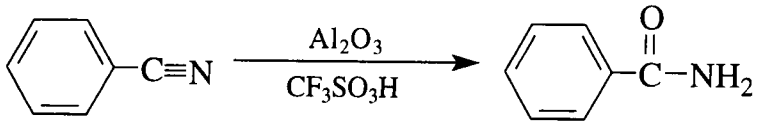


Figure 9

Mechanism for the HBr-Catalyzed Hydration of Benzonitrile



benzonitrile benzamide **(8)**

Because some of the previous acid-catalyzed hydrolyses were run under harsh conditions and produced more of the corresponding carboxylic acid than the amide,[5,13,14] only 4 drops (0.10 mL) of CF_3SO_3H were added to the alumina in order to try to prevent amide hydrolysis. However, two reactions were performed with 1 mL of acid in order to see what effect "excess" acid had on the reaction.

In order for the surface hydrolysis not to be limited by the amount of available water, the amount of alumina used must be greater than the amount of nitrile added to the surface. Since there are 1.87 mmoles of water on the surface for each gram of alumina, a 1:1 ratio of grams of alumina to mmoles of nitrile would limit the amount of amide produced to 1.87 mmoles. Therefore, excess alumina would be necessary to obtain the maximum yield of amide, but too much surface water could encourage amide hydrolysis. Different ratios of alumina to benzonitrile (wt. to mmole) were tested in the CF_3SO_3H-catalyzed reactions in order to determine which ratio favored the production of benzamide without the generation of benzoic acid.

The majority of the CF_3SO_3H-catalyzed reactions were performed at 60 °C, although two reactions were run at 100 °C. It was believed that at higher temperatures the reactions were more

likely to produce carboxylic acids from hydrolysis of the amide intermediates. The two reactions were performed at 100 °C to see if this hypothesis was true.

The effects of reaction time were also explored to see if the ideal reaction time for producing amides could be determined. Reactions were run for times ranging from 1 to 10 days.

Table 3 contains the results of all of the CF_3SO_3H catalyzed reactions.

Several conclusions concerning nitrile hydrolysis on alumina can be drawn from an analysis of these results. It is clear that there are certain conditions which significantly affect the outcome of the reaction. The largest effect arises from the amount of catalyst. Two reactions, *I* and *K*, were performed with 1.0 mL of CF_3SO_3H, while the rest of the reactions were catalyzed with 0.10 mL of acid. Reactions *I* and *K* did not produce any benzamide. The benzamide produced from the nitrile hydrolysis is quantitatively hydrolyzed to benzoic acid which is not isolated on work-up. The polar nature of benzoic acid prevents it from being removed from alumina; thus it is not detected on product analysis. The behavior of benzoic acid on alumina is described in a subsequent section.

The effect of acid concentration on yield of amide is shown by a comparison of reactions *J* and *K*. The reaction conditions of *J* were the same as those of *K* except for the amount of catalyst used. An 86% yield of benzamide was isolated from *J*, but no benzamide was obtained from *K*. Benzamide is not isolated from *I* or *K* because the

TABLE 3

REACTION CONDITIONS FOR THE TRIFLUOROMETHANESULFONIC ACID-CATALYZED HYDRATIONS OF BENZONITRILE ON ALUMINA[a]

	Al_2O_3 (grams)	C_6H_5CN (mmoles)	Time (hours)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A	15	3.0	24	0.60	0.33	11%	14%
B	15	3.0	48	0.028	0.63	21%	21%
C	40	2.0	48	0.012	0.63	32%	32%
D	15	3.0	72	0.046	2.1	70%	71%
E	5.0	5.0	120	0.087	1.2	24%	24%
F	10	5.0	120	0.41	4.0	80%	87%
G	9.0	3.0	120	0.42	1.0	33%	39%
H	15	3.0	120	0.20	1.5	50%	54%
I[d]	5.0	5.0	120	1.6	0.00	0.00%	0.00%
J	5.0	5.0	168	0.00	4.3	86%	86%
K[e]	5.0	5.0	168	0.50	0.00	0.00%	0.00%
L[f]	15	3.0	192	0.10	0.34	11%	12%
M	5.0	5.0	240	0.00	2.6	52%	52%

[a]Reactions run at 60 °C with 0.10 mL of trifluoromethanesulfonic acid unless otherwise noted.

[b]Reactions analyzed by GC/MS; yields obtained from a tetradecane internal standard.

[c]Yield corrected for remaining starting material.

[d]Reaction performed at 100°C with 1.0 mL of trifluoromethanesulfonic acid.

[e]Reaction performed at 60°C with 1.0 mL of trifluoromethanesulfonic acid.

[f]Reaction performed at 100°C with 0.10 mL of trifluoromethanesulfonic acid.

higher concentration of acid causes all of the benzamide to be hydrolyzed to benzoic acid.

The highest yields of benzamide were obtained from reactions *F* and *J*. These reactions differed in the fact that *F* was run for 120 hours with a 5:1 ratio of alumina to benzonitrile (wt. to mmole), while *J* was run for 168 hours with a 1:1 ratio. *F* produced 80% benzamide with 0.41 mmoles (0.043g) of recovered benzonitrile, while *J* produced 86% benzamide with no recovered benzonitrile. The exact reason for the success of these reactions cannot be determined because more than one variable differs for each reaction. If reactions *F* and *J* are compared with reactions performed under like conditions, the reason for their success may be understood.

TABLE 4

COMPARISON OF REACTIONS RUN FOR DIFFERENT AMOUNTS OF TIME[a]

	Time (hours)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield
E	120	0.087	1.2	24%
J	168	0.00	4.3	86%
M	240	0.00	2.6	52%

[a]Reactions run at 60 °C with 5.0 g of alumina, 5.0 mmols of benzonitrile, and 0.10 mL of trifluoromethanesulfonic acid.

Reactions *E, J,* and *M* were run under identical conditions except for differing lengths of time: *E* for 120 hours, *J* for 168 hours, and *M* for 240 hours. The results of these three reactions are listed in Table 4. Benzonitrile was recovered from *E* but not from *J* or *M*. Reaction *J* generated the most benzamide followed by *M*, with *E* producing significantly less amide than the other reactions. As soon as any amide is produced from the nitrile hydrolysis, it is hydrolyzed to the corresponding carboxylic acid. Reaction *J* was stopped before much benzamide was hydrolyzed to benzoic acid (15% based on corrected yield); because *M* was allowed to run longer, more benzamide was hydrolyzed than in *J* (48.7% acid based on corrected yield). Reaction *E* ran for less time than either *J* or *M*, but of the three reactions, it produced the lowest yield of benzamide and hardly any benzonitrile was recovered. There is not a definite explanation for the anomalous behavior of reaction *E*.

The fact that there are two consecutive surface hydrolyses, nitrile then amide, can also be used to explain the results of reactions *A, B, D,* and *H* (Table 5). These reactions were also run under identical conditions except for different times. The highest yield of amide was produced in reaction *D* which ran for 72 hours. The amount of amide produced in *H* is less than that produced in *D*, even though *H* had a longer reaction period. The amounts of amide produced in *A* and *B* are also less than the amount produced in *D*, but *A* and *B* had shorter reaction periods than *D*. A relationship between reaction period and yield of amide is seen for reactions *A, B,* and *D*; more amide is produced when the reaction is performed for a longer

period of time. The behavior of reaction *H* cannot be explained in light of the behavior of reactions *A*, *B* and *D*.

Reactions *B* and *C* were both run for 48 hours at 60 °C and catalyzed with 0.10 mL CF_3SO_3H. Reaction *B* was performed with a 5:1 ratio of alumina to benzonitrile (wt. to mmol), while *C* utilized a 20:1 ratio of alumina to benzonitrile. As noted in Chapter 1, the concentration of water on the surface of alumina is equal to 1.87 mmol of H_2O per gram of Al_2O_3. Therefore, in *B*, there were 9.35 mmoles of water for every mmole of benzonitrile, while in *C* there were 37.4 mmoles of water per mmole of benzonitrile. Reaction *C*

TABLE 5

COMPARISON OF SEVERAL NITRILE HYDRATIONS WITH DIFFERENT REACTION PERIODS[a]

	Time (hours)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield	% Yield[b]
A	24	0.60	0.33	11%	14%
B	48	0.028	0.63	21%	21%
D	72	0.046	2.1	70%	71%
H	120	0.20	1.5	50%	54%

[a]Reactions run at 60 °C with 15 g of alumina, 3.0 mmoles of benzonitrile and 0.10 mL of trifluoromethanesulfonic acid.

[b]Yield corrected for remaining starting material.

produced 11% more benzamide than reaction *B*, which shows that the additional water did aid the nitrile hydrolysis.

Reactions *E, F, G,* and *H* also differed only in the ratio of alumina to benzonitrile (wt. to mmol) used for the reaction: *E* was performed with a 1:1 ratio, *F* with a 2:1 ratio, *G* with a 3:1 ratio, and *H* with a 5:1 ratio. Of these reactions, *F* produced the most benzamide, followed by *H, G,* and *E* . The amount of water available on the surface per mmole of nitrile is calculated for these reactions and shown in Table 6. Actually, there is slightly more water on the surface than these values suggest due to the fact that alumina absorbs atmospheric moisture. The exact amount of additional water is unknown. Reaction *E,* which produced the lowest yield, contained only 1.87 mmoles of water per mmole of benzonitrile. The production of benzamide in reaction *E* was limited by the low concentration of water. Thus, there must be a sufficient quantity of water on the surface to generate a high yield of amide from the alumina reactions. The results of reactions *E, F, G,* and *H*, show that the most amide was produced when there were 3.74 mmoles of water available for hydrolysis. Too much water must, therefore, encourage amide hydrolysis. From 3.0 mmoles of benzonitrile starting material in *G* and *H,* 0.42 mmoles were recovered from *G* and 0.20 mmoles from *H*. Reaction *H* did produce more benzamide, but less starting material was recovered. Therefore, more benzamide was apparently hydrolyzed to benzoic acid.

TABLE 6

COMPARISON OF REACTIONS RUN WITH DIFFERENT RATIOS OF ALUMINA TO BENZONITRILE[a,b]

	Al_2O_3 (grams)	C_6H_5CN (mmoles)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	Surface Water (mmoles)	% Yield	% Yield[c]
E	5.0	5.0	0.087	1.2	1.87	24%	24%
F	10.0	5.0	0.41	4.0	3.74	80%	87%
G	9.0	3.0	0.42	1.0	5.61	33%	39%
H	15.0	5.0	0.20	1.5	9.35	50%	54%

[a]Reactions run for 120 hours at 60 °C with 0.10 mL of trifluoromethanesulfonic acid.

[b]Ratio is by weight to mmoles.

[c]Yield corrected for recovered starting material.

In a reaction where no amide hydrolysis occurs, the sum of the amount of recovered starting material and the amount of product should equal the amount of initial starting material. It is obvious that the sum of the recovered starting material and product does not equal the amount of initial starting material for any of the reactions. The question is, what happened to the rest of the starting material? FT-IR was used to see if traces of benzamide, benzonitrile or benzoic acid remained on the alumina after the work-up of the reactions.. Spectra of pure samples of benzonitrile, benzamide, and benzoic acid were first obtained. Then, the alumina from reaction *D* (Table 3) was analyzed after it had been rinsed with 650 mL of methanol. The spectrum of the alumina from reaction *D* was compared with those

of the pure nitrile, amide, and carboxylic acid. Figure 10 is the FT-IR spectrum of benzonitrile chemisorbed on alumina. The characteristic carbon-nitrogen triple bond stretch is very evident at 2226 cm^{-1}. In Figure 11, the FT-IR spectrum of benzamide* chemisorbed on alumina, the amide C-N stretch at 1400 cm^{-1} is clear. Several peaks in the range of 1710-1620 cm^{-1} also indicate the presence of benzamide. These peaks are from both the carbonyl C=O stretch and the amide H-N-H bend; unfortunately, it is impossible to distinguish between the two. Figure 12, the FT-IR spectrum of benzoic acid**, shows several distinguishing peaks of the carboxylic acid. For example there are the C-O-H in plane bend at 1428 cm^{-1}, the C-O stretch at 1207 cm^{-1}, and the out of plane O-H bend at 825 cm^{-1}. In Figure 13, the spectrum of the alumina from reaction *D*, the benzonitrile peak at 2226 cm^{-1} is distinguishable but very small; unfortunately, the descriptive benzamide and benzoic acid peaks overlap with each other. It is definite that either benzamide or benzoic acid or a combination of the two is present on the alumina from reaction *D*. However, because of the absorbance similarities it is impossible to determine with FT-IR exactly what is on the surface.

The expected mechanism for the reactions catalyzed with CF_3SO_3H is identical to that depicted in Figure 9 on page 21 for the HBr catalyzed reactions. The nitrile nitrogen is first protonated by CF_3SO_3H to yield a cation which is attacked by an oxygen from a

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* Benzamide was dissolved in methanol before addition to the alumina.

** Benzoic acid was dissolved in diethyl ether before addition to the alumina.

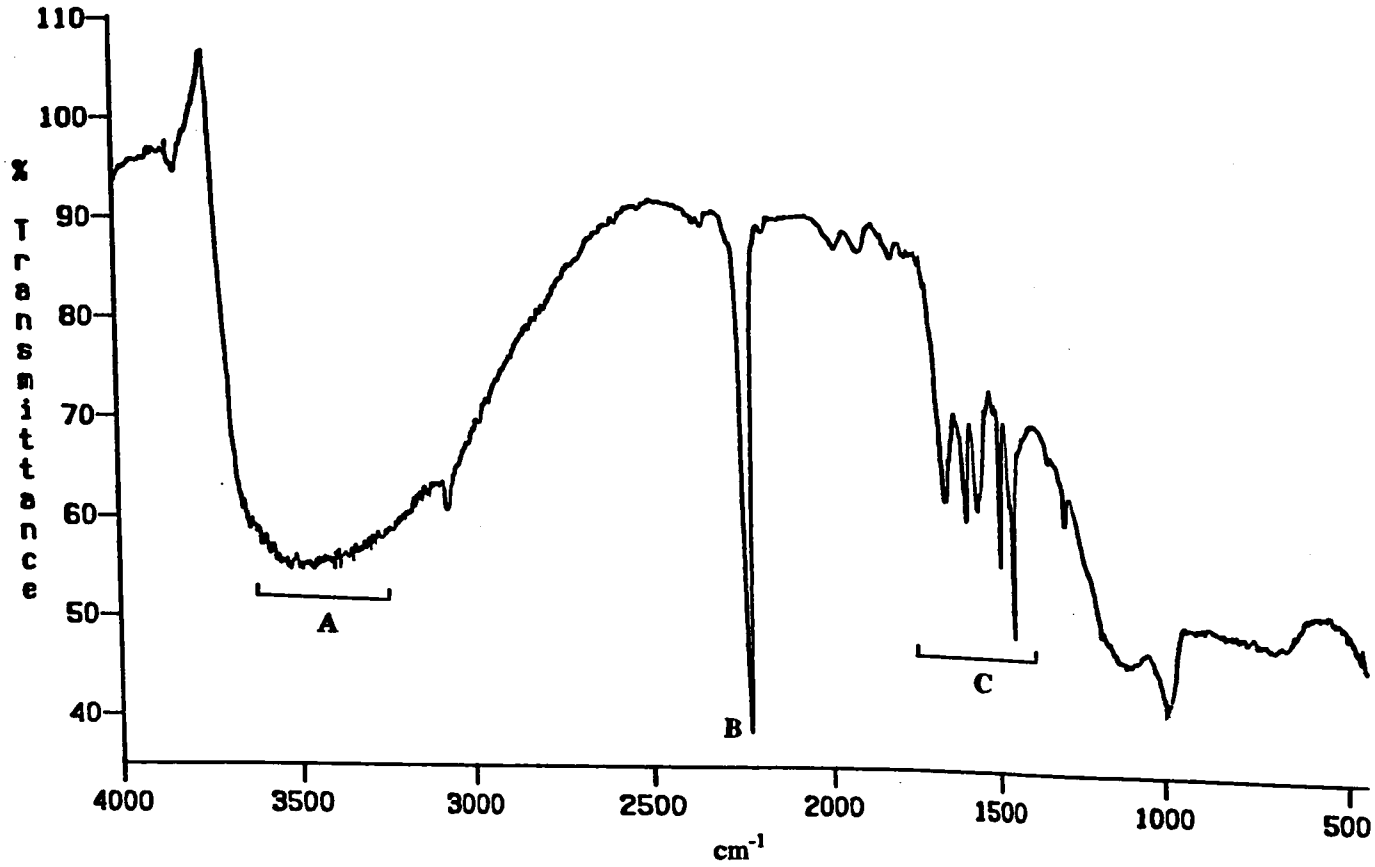


Figure 10
FT-IR of Benzonitrile Chemisorbed on the Surface of Alumina

A. Aromatic C-H stretch (3500-3000 cm^{-1}) overlapped by free O-H stretch (3500-3250 cm^{-1}) of the surface hydroxyl groups. **B.** Nitrile C≡N stretch (2226 cm^{-1}), intensified by aryl conjugation. **C.** Out of plane O-H bend (1710-1680 cm^{-1}) of surface hydroxyl groups.

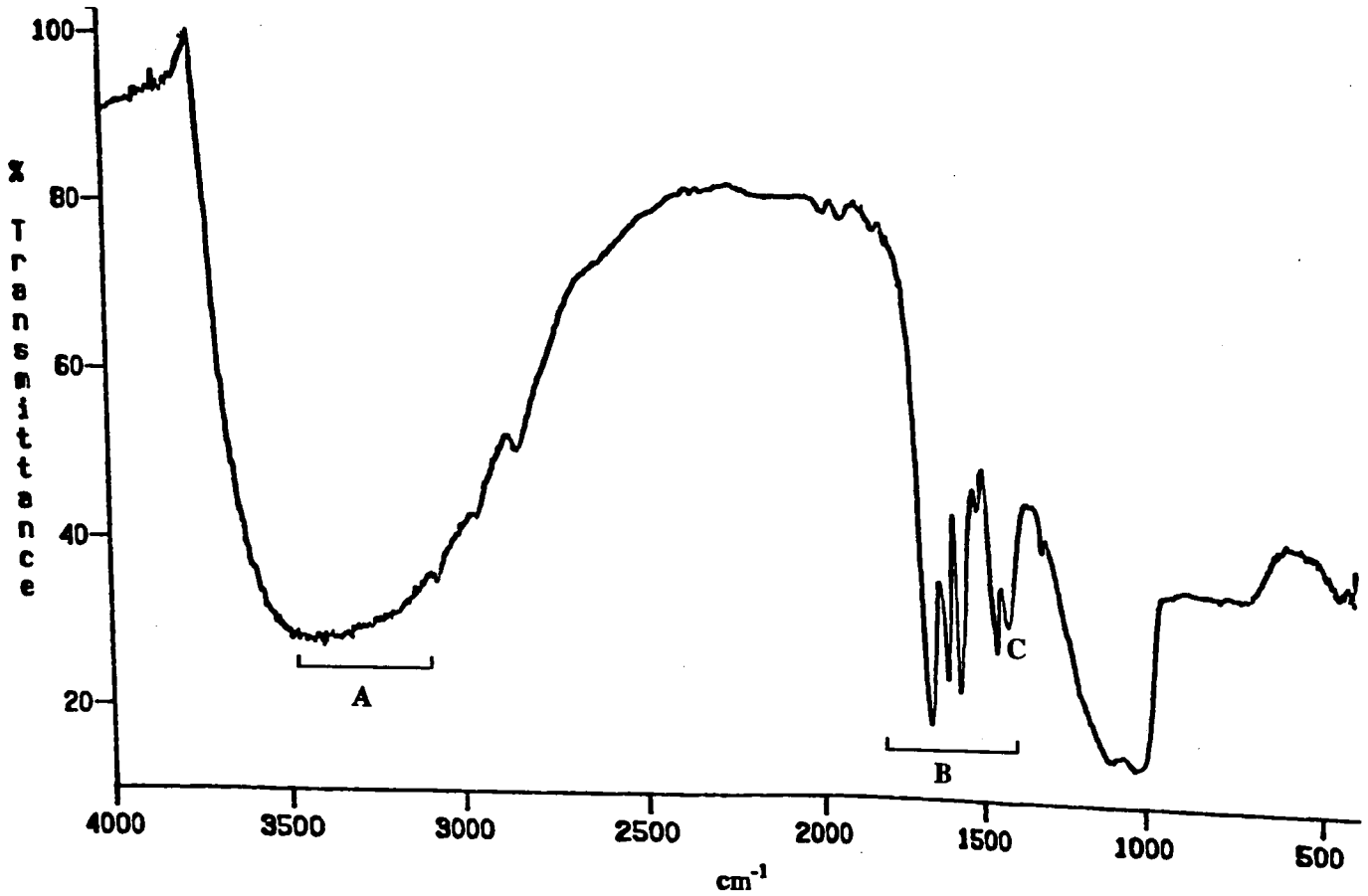


Figure 11
FT-IR of Benzamide Chemisorbed on the Surface of Alumina

A. Amide N-H stretch (3352 cm^{-1}) overlapped by free O-H stretch (3500-3250 cm^{-1}) of the surface hydroxyl groups. **B.** Area of overlapping O-H out of plane bend (1710-1680 cm^{-1}) of surface hydroxyl groups, N-H_2 bend (1655-1620 cm^{-1}), and C=O stretch (1650 cm^{-1}). **C.** Amide C-N stretch (1400-1350 cm^{-1}).

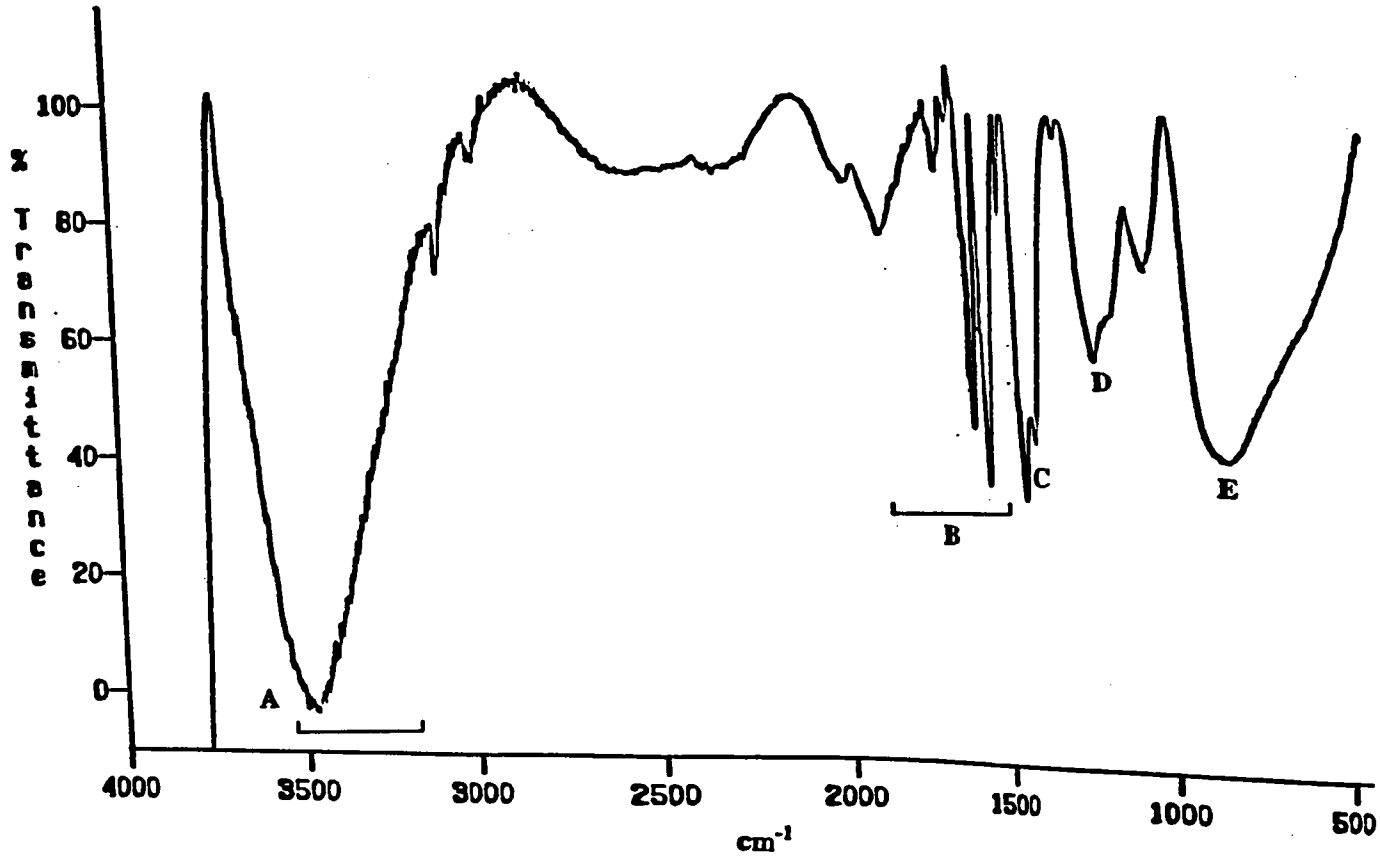


Figure 12

FT-IR of Benzoic Acid Chemisorbed on the Surface of Alumina

A. Aromatic C-H stretch (3500-3000 cm^{-1}) overlapped by free O-H stretch (3500-3250 cm^{-1}) of the surface hydroxyl groups. **B.** Carbonyl C=O stretch (1710-1680 cm^{-1}) overlapped with out of plane O-H bend (1710-1680 cm^{-1}) of surface hydroxyl groups. **C.** In plane bend of C-O-H (1428 cm^{-1}). **D.** C-O stretch (1207 cm^{-1}). **E.** Characteristic carboxylic acid out of plane O-H bend (825 cm^{-1}).

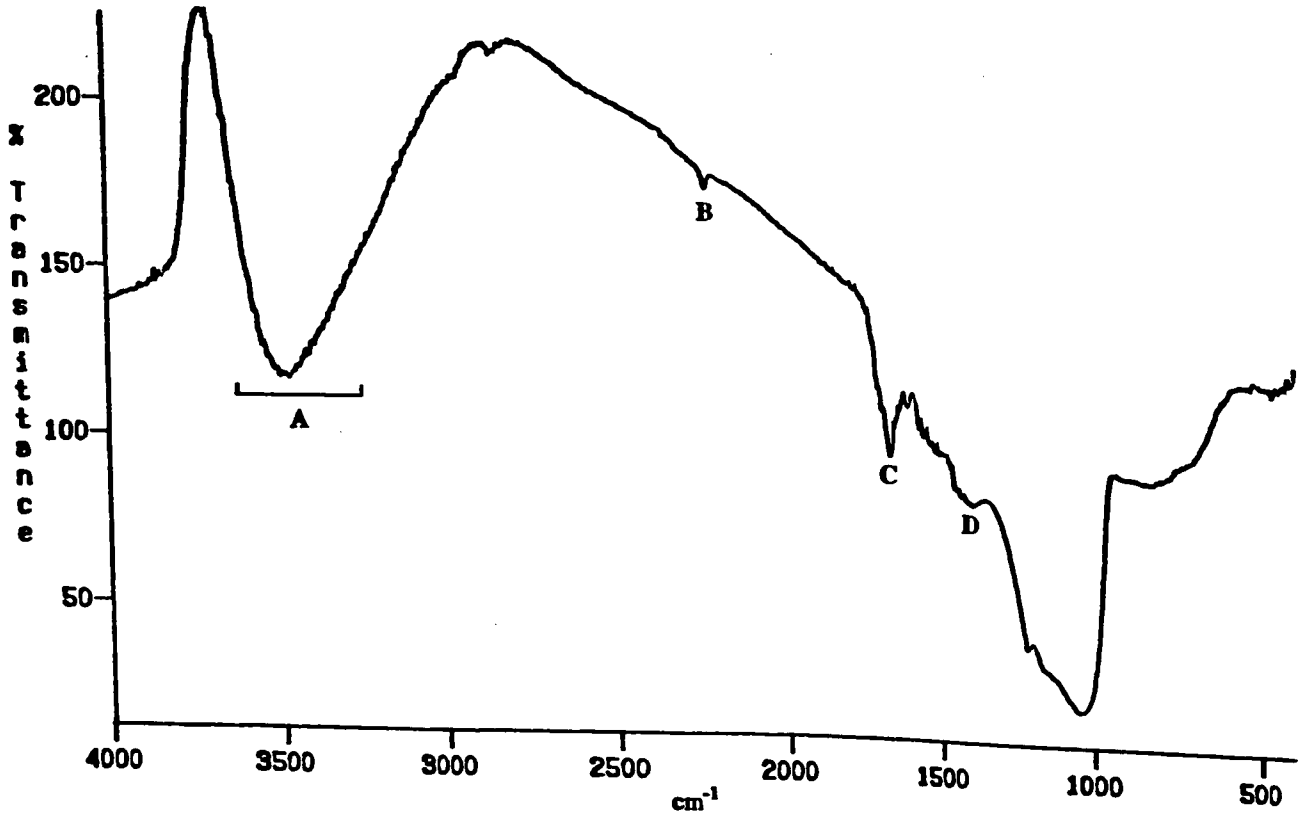


Figure 13

FT-IR of Alumina from Reaction *D* (Table 3)

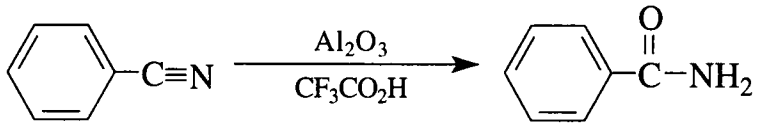
$$C_6H_5CN + Al_2O_3 \xrightarrow[72\ hr./60\ ^\circ C]{CF_3SO_3H} C_6H_5C(O)NH_2$$

A. Aromatic C-H stretch (3500-3000 cm^{-1}) and Amide N-H stretch (3352 cm^{-1}) overlapped by free O-H stretch (3500-3250 cm^{-1}) of the surface hydroxyl groups. **B.** Nitrile C≡N stretch (2226 cm^{-1}), intensified by aryl conjugation. **C.** Area of overlapping O-H out of plane bend (1710-1680 cm^{-1}) of surface hydroxyl groups, N-H_2 bend (1655-1620 cm^{-1}), and C=O stretch (1710-1680 cm^{-1}). **D.** In plane C-O-H bend (1428 cm^{-1}) or amide C-N stretch (1400-1350 cm^{-1}).

surface hydroxyl group. Removal of the hydroxyl group from the alumina frees the amide enol which on tautomerization gives benzamide. The conjugate base of trifluoromethanesulfonic acid abstracts a proton from a neighboring hydroxyl group to regenerate the CF_3SO_3H.

Reactions Performed with Trifluoroacetic Acid

In order to determine wheter acid strength affected the nitrile to amide conversions, several reactions (eq.9) were run using



benzonitrile benzamide **(9)**

trifluoroacetic acid. The Hammet H_0 value for CF_3CO_2H is 0.04[21]. Because H_0 decreases with increasing acid strength, CF_3CO_2H is not nearly as strong a Brønsted acid as CF_3SO_3H.

The reactions catalyzed by CF_3CO_2H were basically performed under the same conditions as the CF_3SO_3H-catalyzed reactions: 0.10 mL of CF_3CO_2H was added to the majority of the reactions, although three reactions were also run with 1.0 mL of acid. Most of the reactions were run at 60 °C. Various ratios of alumina to benzonitrile (wt. to mmole) were utilized with the CF_3CO_2H-catalyzed reactions, as were various reaction periods.

One difference from the CF_3SO_3H-catalyzed reactions involved the use of sonication. Sonication had been used to produce a 12% increase in yield from a nitrile hydrolysis performed in solution by Breuilles, Leclerc, and Uguen (eq 10).[1] In order to see if the yields of the surface reactions could also be improved as well, several reactions were performed in a sonicated water bath held at 60 °C.

As with the CF_3SO_3H-catalyzed reactions, the results of the CF_3CO_2H-catalyzed reactions, shown in Table 7, can be analyzed to give information regarding the relationship between reaction conditions and yield of amide. Two reactions were run under sonication for different lengths of time. The 20-hour reaction (*A*) did not produce any benzamide, while the 72-hour reaction (*B*) produced 1.0 mmoles of benzamide to give a 33% yield. Reaction *E*, which was run for 120 hours without sonication, yielded only 17% of benzamide even though it had a longer reaction period. The sonicated reaction yielded a higher percent of benzamide in less time so, for this particular case, sonication is beneficial for the production of amides.

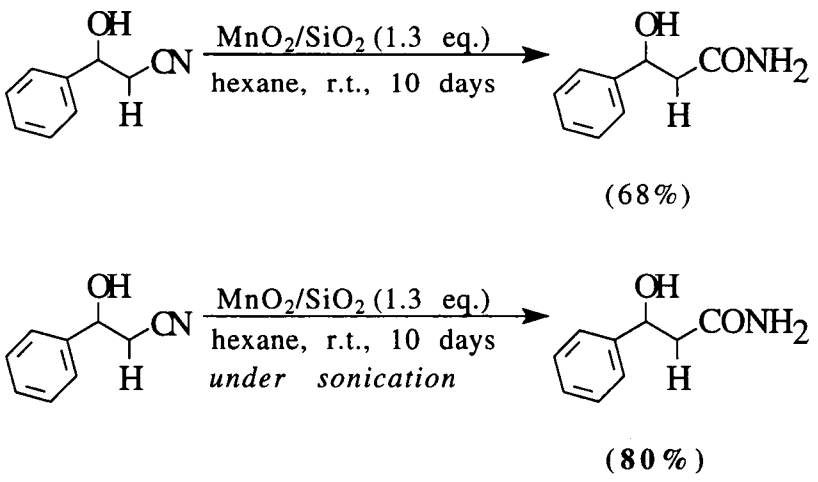


TABLE 7

REACTION CONDITIONS FOR THE HYDROLYSIS OF BENZONITRILE ON ALUMINA CATALYZED WITH TRIFLUOROACETIC ACID[a]

	Al_2O_3 (grams)	C_6H_5CN (mmoles)	Time (hours)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A[d]	15	3.0	20	1.3	0.0	0.00%	0.00%
B[d]	15	3.0	72	0.52	1.0	33%	40%
C[e]	5.0	5.0	96	1.9	0.31	6.2%	10%
D[f]	5.0	5.0	96	0.83	0.58	12%	14%
E	5.0	5.0	120	1.2	0.84	17%	22%
F	10	5.0	120	0.23	2.1	42%	44%
G	15	3.0	120	0.24	1.5	50%	54%
H[g]	5.0	5.0	120	0.33	0.17	3.4%	3.6%
I[h]	5.0	5.0	120	0.94	0.00	0.00%	0.00%
J	9.0	3.0	144	0.12	0.76	25%	26%
K[g]	15	3.0	168	0.00	0.23	7.7%	7.7%
L[d]	5.0	5.0	168	0.30	1.0	20%	21%

[a]Reactions run at 60 °C with 0.10 mL of trifluoroacetic acid unless otherwise noted.

[b]Reactions analyzed by GC/MS; yields calculated with a tetradecane internal standard.

[c]Yield corrected for remaining starting material.

[d]Reaction performed under sonication.

[e]Reaction performed with 1.0 mL of trifluoroacetic acid at 60 °C.

[f]Reaction performed with 1.0 mL of trifluoroacetic acid at 100°C.

[g]Reaction performed at 100°C with 0.10 mL of trifluoroacetic acid.

[h]Reaction performed at 25°C with 0.10 mL of trifluoroacetic acid.

As previously mentioned, none of the reactions which were catalyzed with 1.0 mL of CF_3SO_3H produced benzamide. The reactions, *C, D,* and *L,* which were catalyzed with 1.0 mL of the weaker acid, CF_3CO_2H, did produce some benzamide. However, sincethe yields of reactions *C, D,* and *L* were low, it is obvious that an additional amount of acid-catalyst does not favor the production of benzamide. Therefore, all further acid-catalyzed nitrile hydrolyses were run with 0.10 mL of catalyst.

The reactions, *E, H,* and *I,* which were performed under identical conditions, except for temperature, can be compared to see the effect of temperature on nitrile hydrolysis: *H* was performed at 100 °C, *E* at 60 °C, and *I* at room temperature, 25 °C. Reaction *I* did not produce any benzamide; therefore, to obtain benzamide, the reactions must be run above ambient temperature. The low yield from reaction *H* (3.4%), demonstrated that the other extreme of temperature also is not favorable for amide production. Reaction *E* produced more benzamide than either *I* or *H*. This shows that the nitrile-to-amide conversions are most efficient at the median temperature of 60°C. Reaction *E* can also be compared with reactions *F* and *G* to see if a correlation exists between ratio of alumina to benzonitrile (wt. to mmole) and yield of benzamide. Reactions *E, F,* and *G* were performed under identical conditions except for the ratios of alumina to benzonitrile: *E* had a 1:1 ratio, *F* had a 2:1 ratio, and *G* had a 5:1 ratio. Of these reactions, *G* produced the greatest yield of benzamide (50%), followed by *F* (42%), and *E* (17%). For reaction *G*, there were approximately 9.35 mmoles of water per

gram of alumina, but for *E* there were only 1.87 mmoles of water per gram of alumina. (There was actually slightly more surface water due to the tendency for alumina to absorb atmospheric moisture.) For reaction *F* there was also an excess of water on the alumina (3.74 mmoles/g). It is obvious that there must be an excess of water on the surface to have a successful nitrile-to- amide conversion.

The results of the CF_3CO_2H-catalyzed reactions can be compared with the results of the CF_3SO_3H-catalyzed reactions to show that the strength of the acid catalyst does indeed affect the amount of amide produced. In general, the yields of the reactions catalyzed with trifluoroacetic acid were lower than those of the trifluoromethanesulfonic acid-catalyzed reactions. Table 8 contains data from a number of reactions whose only differences are the acids used to catalyze the reactions.

The mechanism for the CF_3CO_2H-catalyzed reactions is presumbly the same as the mechanism for the reactions catalyzed with HBr which is illustrated in Figure 9 on page 21.

Reactions Performed without a Catalyst

A few reactions were also run without any acid catalyst in order to see if benzamide could still be produced from the surface hydrolysis reaction. The chemical literature states that alumina must be activated before it can be catalytically active;[9] however, for a hydrolysis reaction, the definition of catalytically active will be different. When alumina is activated, Al^{3+} sites and O^{2-} sites are

TABLE 8

A COMPARISON OF REACTIONS CATALYZED WITH CF_3SO_3H AND CF_3CO_2H[a,b]

	Al_2O_3 (grams)	C_6H_5CN (mmoles)	Catalyst	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield	% Yield[c]
E *Table 3*	5.0	5.0	CF_3SO_3H	0.087	1.2	24%	24%
E *Table 7*	5.0	5.0	CF_3CO_2H	1.2	0.84	17%	22%
F *Table 3*	10	5.0	CF_3SO_3H	0.41	4.0	80%	87%
F *Table 7*	10	5.0	CF_3CO_2H	0.23	2.1	42%	44%
H *Table 3*	15	3.0	CF_3SO_3H	0.20	1.5	50%	54%
G *Table 7*	15	3.0	CF_3CO_2H	0.24	1.5	50%	54%
K[d] *Table 3*	5.0	5.0	CF_3SO_3H	0.50	0.0	0.00%	0.00%
L[d] *Table 7*	5.0	5.0	CF_3CO_2H	0.30	1.0	20%	21%

[a]Reactions performed for 120 hours at 60 °C with 0.10 mL of acid catalyst unless noted otherwise.

[b]Reactions analyzed by GC/MS; yields obtained from a tetradecane internal standard.

[c]Yield corrected for remaining starting material.

[d]Reaction performed for 168 hours with 1 mL acid catalyst.

exposed by removal of the surface hydroxyl groups. For some reactions, these Lewis acidic and basic sites are necessary for catalysis, but hydrolysis is not one of those reactions. Surface hydroxyl groups are necessary for hydrolysis. Hence, all the nitrile-to-amide conversion reactions were performed on unactivated alumina.

Buck and Ide[19] catalyzed a nitrile to amide conversion with the Brønsted base, potassium hydroxide (eq. 11). Hall and Gisler[20] also

$$2(CH_3O)_2C_6H_3CN + 2H_2O_2 \xrightarrow{(KOH)} 2(CH_3O)_2C_6H_3CONH_2 + O_2 \quad \textbf{(11)}$$

reported a nitrile hydrolysis catalyzed with potassium hydroxide. It was hoped that alumina would be basic enough to induce nitrile hydrolysis.

Two uncatalyzed reactions of benzonitrile on alumina were performed at 60°C; three were also run under sonication. All of the reactions used 3.0 mmoles (0.36 g, 0.30 mL) of benzonitrile and 15 grams of alumina. The results of the uncatalyzed reactions (Table 9) do show that nitrile-to-amide conversions can be successfully accomplished on alumina without the addition of a catalyst. These results are most interesting when compared with the results of the corresponding catalyzed reactions. Table 10 contains the results of the uncatalyzed and the corresponding acid-catalyzed reactions.

Looking at Table 10, it can be seen that more amide was obtained from the uncatalyzed reactions *B* and *D*, than from the

TABLE 9

REACTION CONDITIONS OF THE UNCATALYZED REACTIONS OF BENZONITRILE ON THE SURFACE OF ALUMINA[a]

	Time of Reaction (hours)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A	24	0.00	0.73	24%	24%
B[d]	24	0.46	0.78	26%	31%
C	48	0.02	1.7	57%	57%
D[d]	48	0.28	0.82	27%	30%
E[d]	72	0.13	0.45	15%	15%

[a]Reactions run at 60 °C with 15 grams of alumina and 3 mmoles of benzonitrile.

[b]Reactions analyzed by GC/MS; yields calculated with a tetradecane internal standard.

[c]Yield corrected for remaining starting material.

[d]Reaction performed under sonication.

corresponding acid catalyzed reactions *A* and *C*. Therefore, to obtain more benzamide in less time, it is better to run the hydrolyses without the presence of an acid-catalyst. The uncatalyzed sonicated reaction *F* was not as successful as its acid-catalyzed counterpart. Sonication obviously interferes with the uncatalyzed hydrolysis reaction.

TABLE 10

COMPARISON OF UNCATALYZED REACTIONS OF BENZONITRILE WITH ACID-CATALYZED REACTIONS[a]

	Catalyst	Time (hours)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield	% Yield[b]
A	CF_3SO_3H	24	0.60	0.33	11%	14%
B	None	24	0.00	0.73	24%	24%
C	CF_3SO_3H	48	0.028	0.63	21%	21%
D	None	48	0.02	1.7	57%	57%
E[c]	CF_3CO_2H	72	0.52	1.0	33%	40%
F[c]	None	72	0.13	0.45	15%	15%

[a]Reactions performed at 60 °C with 15 g of alumina, 3 mmoles of benzonitrile, and 0.10 mL of catalyst (if listed).

[b]Yield corrected for remaining starting material

[c]Reaction performed under sonication

A possible mechanism for the uncatalyzed hydrolyses is shown in Figure 14. An oxygen of a surface hydroxyl group directly attacks the carbon of the nitrile and creates a bond between the nitrile and the alumina. The resultant negatively charged nitrogen easily abstracts a proton from a neighboring hydroxyl group. The enol of benzamide is then removed from the surface as the bond between the hydroxyl group and the surface is broken. Migration of the proton from the oxygen to the nitrogen leaves benzamide.

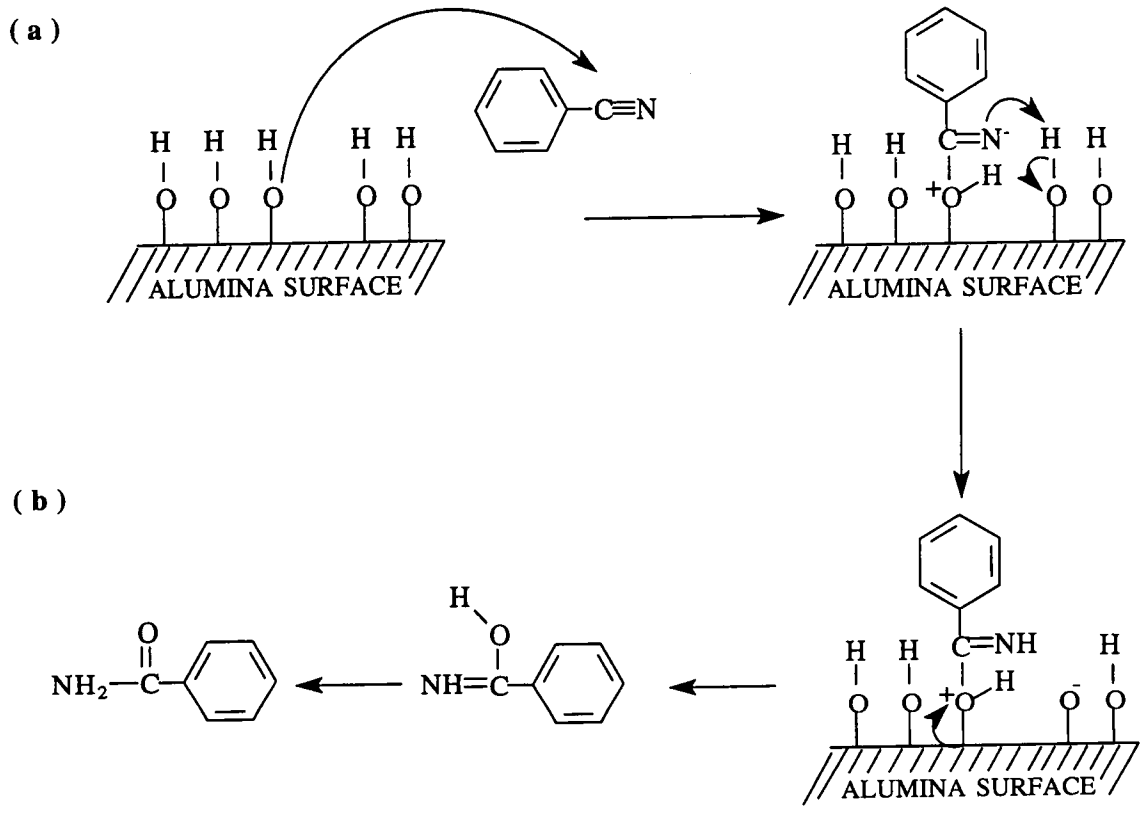


Figure 14

Mechanism for the Formation of Benzamide Induced by Alumina

Benzoic Acid

The previous studies assumed that benzoic acid is produced by the hydrolysis of benzamide, although it was never detected. As formerly mentioned, the reaction mixtures were analyzed by TLC, GC/MS, ^{13}C NMR, and ^{1}H NMR. Benzoic acid was not detected by any of these analytical methods. Hence, if it was being produced it remained on the alumina.

The FT-IR spectrum (Fig. 13) of the alumina from a 72 hour reaction of benzonitrile (*D* on Table 3) showed absorbance frequencies which could have been produced by either benzamide or benzoic acid. The alumina was analyzed after the reaction had been quenched and rinsed with 500 mL of methanol. All of the benzamide was thought to be in the methanol solution. FT-IR proved that either benzamide or benzoic acid, or a combination of the two, remained on the surface after the work-up. Unfortunately, since the absorbance frequencies of amides and carboxylic acids are similar there was no way to determine with FT-IR exactly what was on the alumina.

A control reaction was performed in order to determine whether benzoic acid could be extracted from alumina with methanol. The sample was prepared by adding 3 mmoles of benzoic acid dissolved in 3.0 mL of diethyl ether to 15 grams of unactivated alumina. Trifluoroacetic acid (0.10 mL) was also added to the alumina in order to simulate the acidic conditions of some of the benzonitrile reactions. The sample was left under sonication for 72 hours. The sample was then quenched and rinsed with methanol exactly as the previous benzonitrile reactions had been. To prepare

the mixture for analysis the methanol was evaporated *in vacuo*; no solid remained after the evaporation was completed. The sides of the flask were rinsed with 10 mL of methanol; this solution was then analyzed by GC/MS to see if a trace amount of benzoic acid may have been present. A comparison of the gas chromatogram of the sample reaction with a gas chromatogram of benzoic acid proved that benzoic acid was not present in the solution.

SS NMR was used to determine if benzoic acid remained on the surface of the alumina. Figure 15, the SS ^{13}C NMR spectrum from the benzoic acid sample reaction, shows a strong resonance peak at 167.338 ppm, indicative of the carbonyl carbon of benzoic acid.[22] Figure 16 is the SS NMR spectrum of the alumina from the 72-hour reaction of benzonitrile (*D* on Table 3). The peak at 165.723 ppm could arise from benzoic acid. However, when compared to the SS NMR spectra of pure benzonitrile (Fig. 17) and benzamide (Fig. 18), the actual identity of this peak is questionable. The spectra of benzonitrile and benzamide also show resonance peaks at 165.573 and 165.455 ppm, respectively. The FT-IR spectrum of the 72-hour reaction (Fig. 13), indicated that only a trace amount of benzonitrile remained on the surface. Therefore, the carbonyl peak in the SS NMR spectrum of this reaction is not due to benzonitrile. Unfortunately, it is not clear whether the peak is from benzoic acid or benzamide, or a combination of the two.

The control reaction proved that methanol was not able to remove benzoic acid from alumina. Unfortunately, because of the

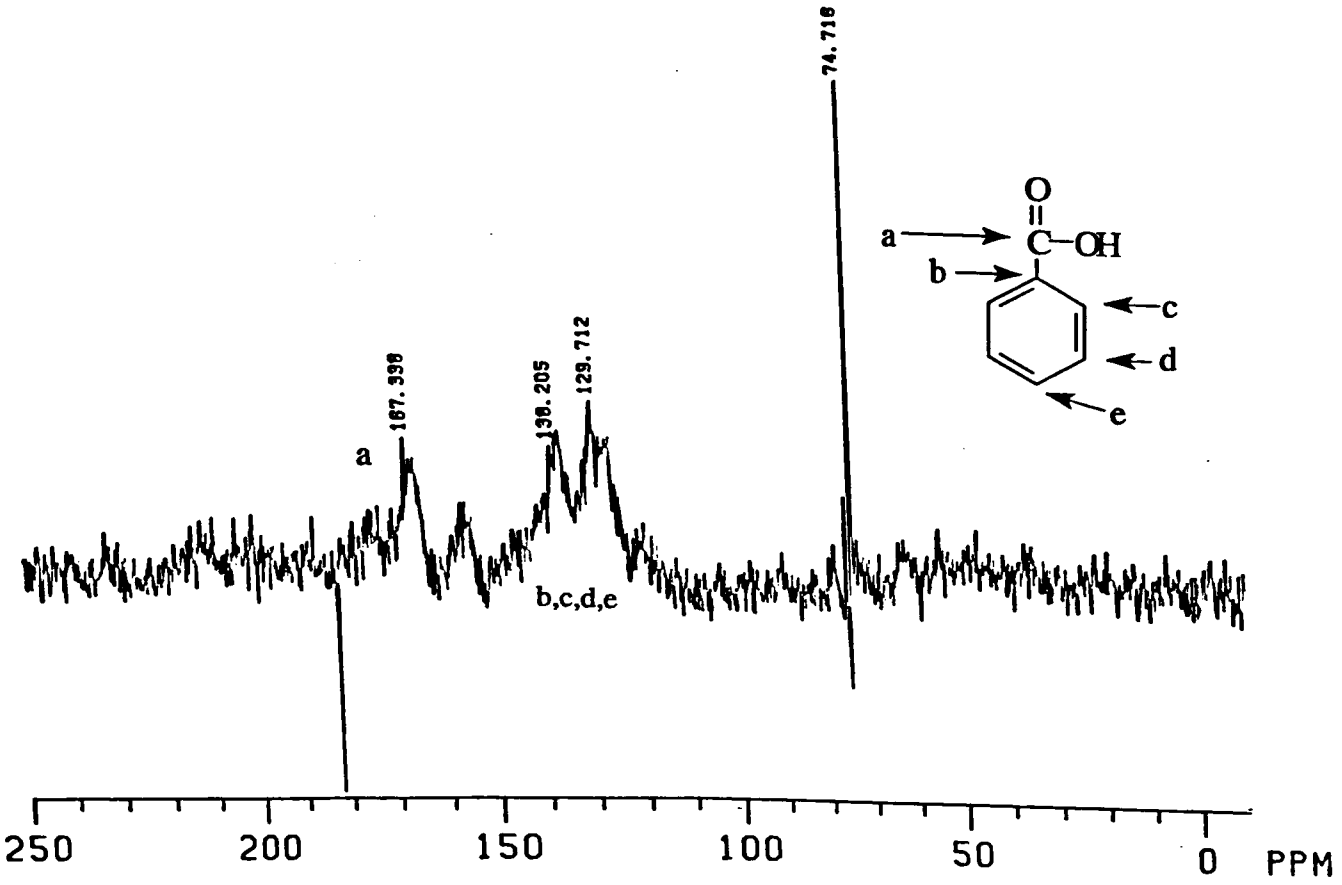


Figure 15

13-C SS NMR of Benzoic Acid Chemisorbed on the Surface of Alumina

a. Resonance peak (167.338 ppm) of carbonyl carbon of benzoic acid. **b, c, d, e.** Resonance peaks (138.205 ppm, 129.712 ppm) of aromatic ring carbons.

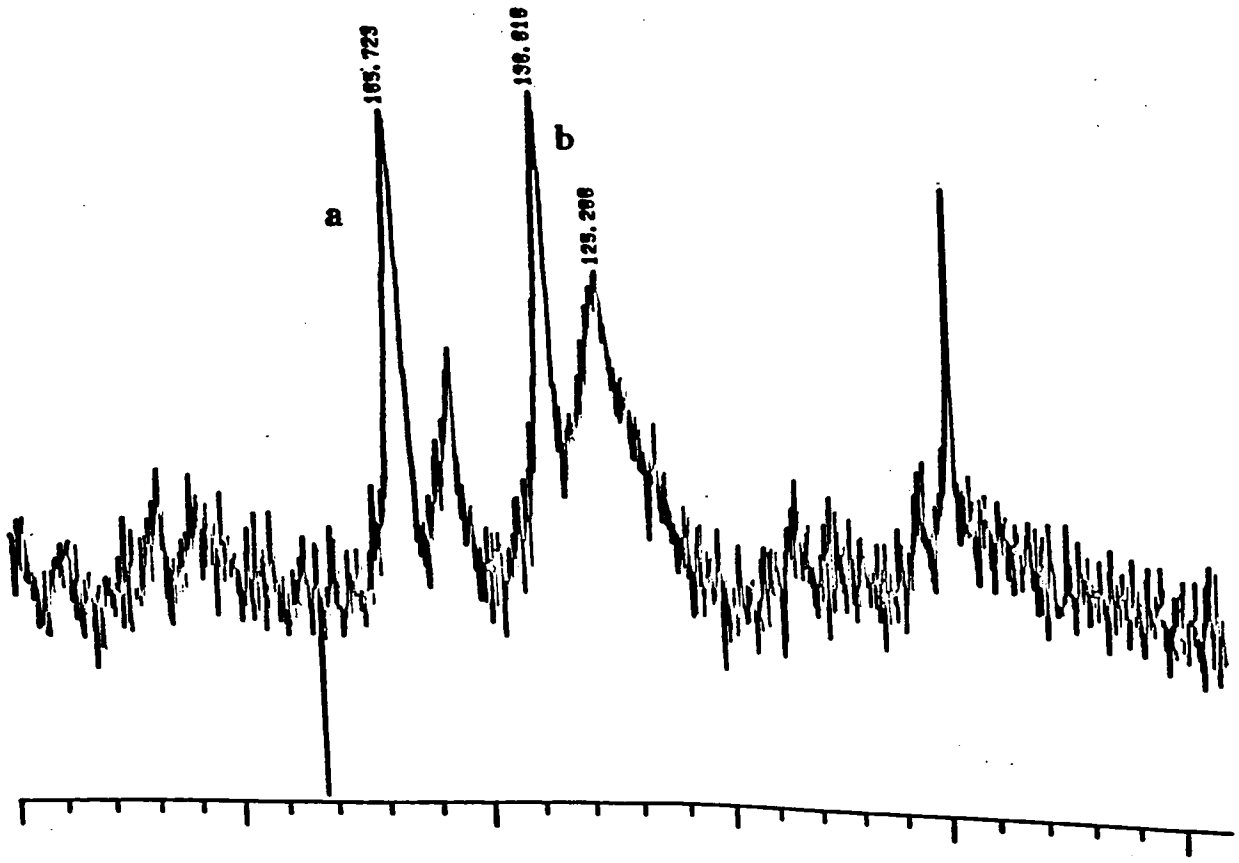


Figure 16
13-C SS NMR of Reaction *D* (Table 3)

$$C_6H_5CN + Al_2O_3 \xrightarrow[72\ hr./60\ ^\circ C]{CF_3SO_3H} C_6H_5C(O)NH_2$$

a. Resonance peak (165.723 ppm) of an aromatic carbonyl carbon. **b.** Resonance peaks (136.616 ppm, 125.268 ppm) of aromatic ring carbons.

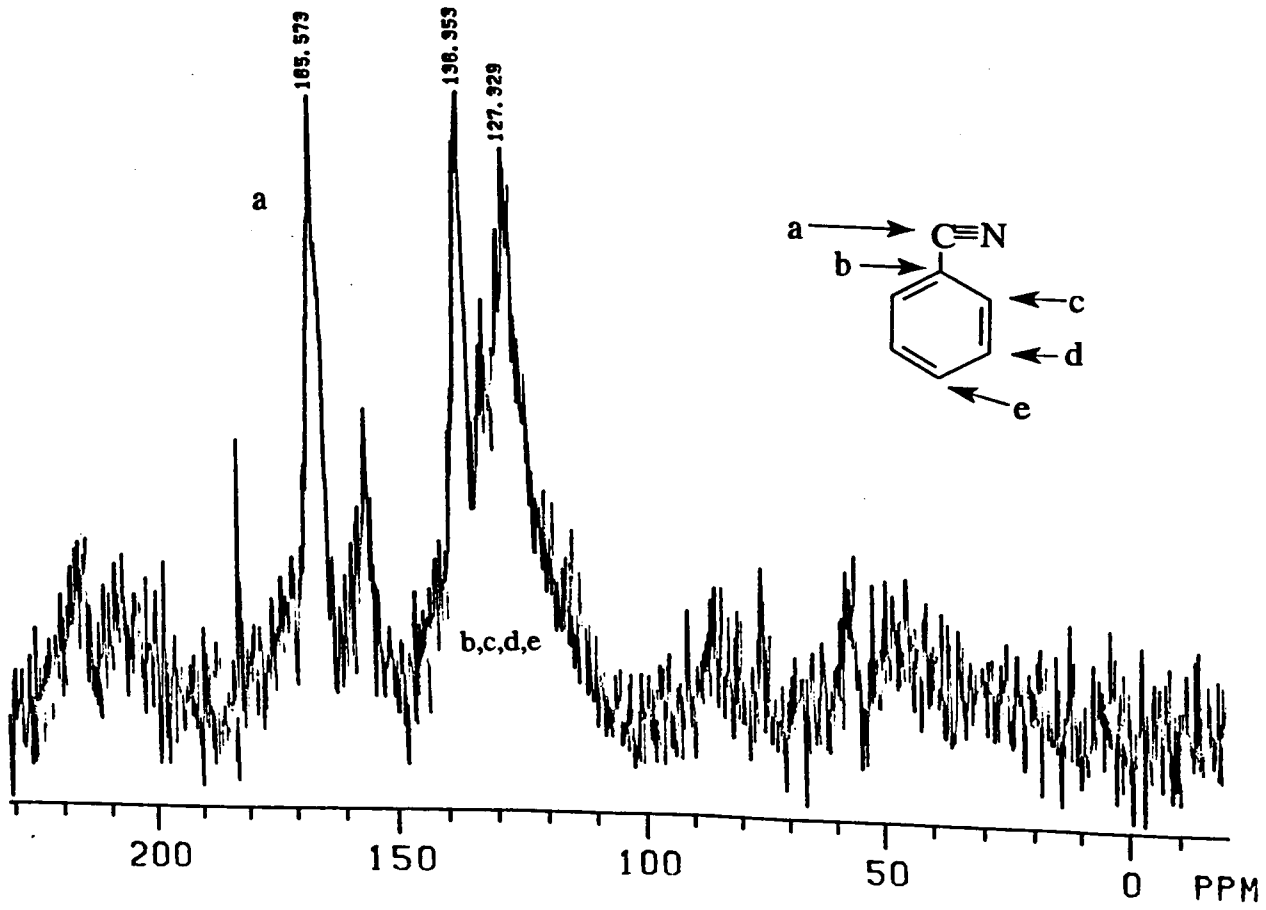


Figure 17
13-C SS NMR of Benzonitrile Chemisorbed on the Surface of Alumina

a. Resonance peak (165.455 ppm) of carbonyl carbon of benzamide. **b, c, d, e.** Resonance peaks (136.500 ppm, 127.188 ppm) of aromatic ring carbons.

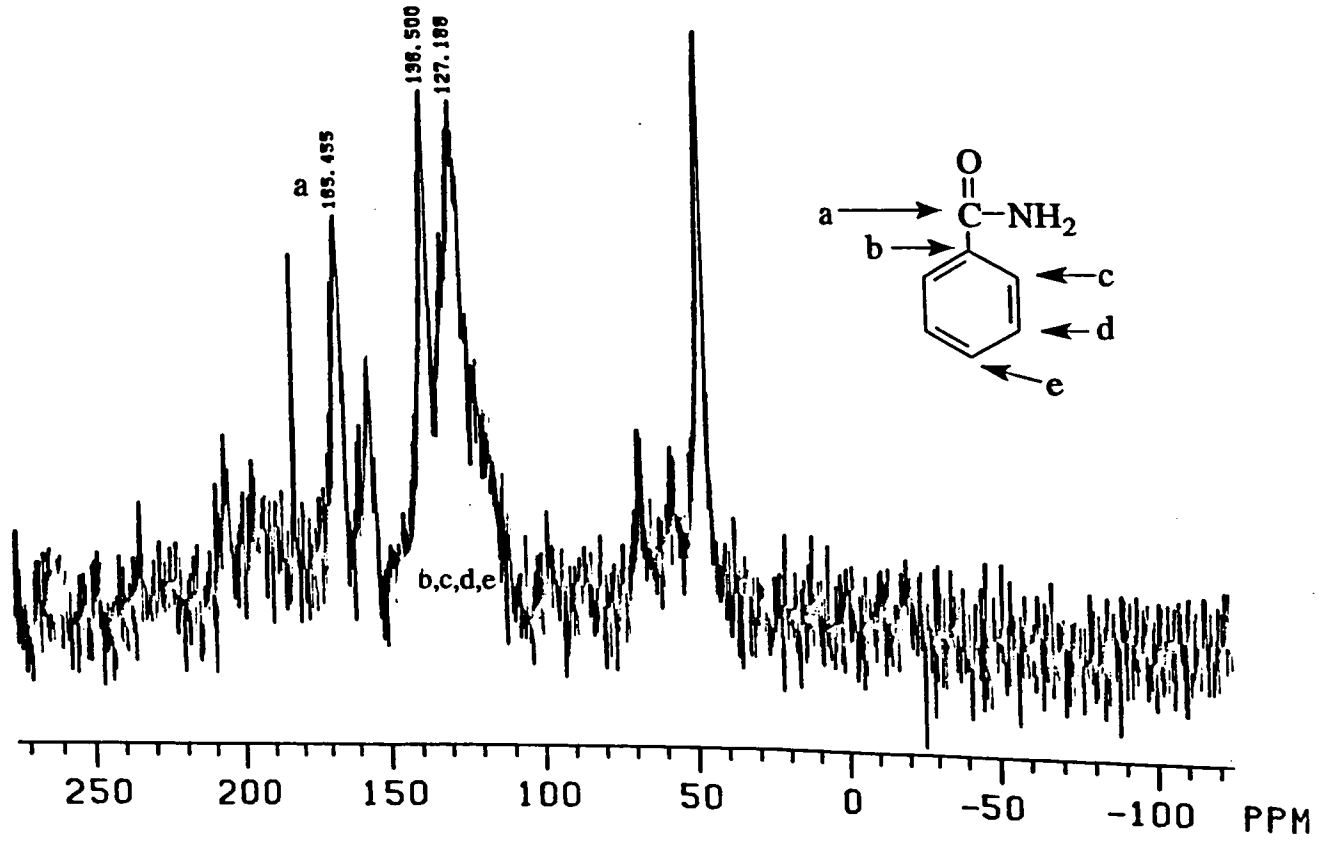


Figure 18

13-C SS NMR of Benzamide Chemisorbed on the Surface of Alumina

a. Resonance peak (165.573 ppm) of carbonyl carbon of benzonitrile. **b, c, d, e.** Resonance peaks (136.353 ppm, 127.329 ppm) of aromatic ring carbons.

similarity of the ^{13}C NMR resonances of benzamide and benzoic acid, the amide cannot be distinguished from the acid with SS NMR when both are present in the same product mixture. No unequivocal proof exists that the reason the benzamide yields are low is because of secondary hydrolysis to benzoic acid. The formation of carboxylic acids in the hydrolysis reactions can only be inferred from the relationship between the amount of recovered nitrile and the amount of amide produced.

Acetonitrile

On the basis of the work done by Deno[17] and coworkers, acetonitrile should be the most reactive of the nitriles studied. Therefore, it should require the least amount of activation to produce the corresponding amide. Based on the results of the benzonitrile reactions, the reactions were performed with 3.0 mmoles (0.12 g, 0.16 mL) of acetonitrile, 15 grams of alumina, and 0.10 mL of either CF_3SO_3H or CF_3CO_2H (eq. 12). A few acetonitrile reactions were also executed without catalyst. Sonication was also utilized for some of

$$CH_3-C\equiv N \xrightarrow[\text{or } CF_3CO_2H/Al_2O_3]{CF_3SO_3H/Al_2O_3} CH_3-\overset{\overset{O}{\|}}{C}-NH_2 \qquad \textbf{(12)}$$

the reactions. The results of the various acetonitrile reactions are shown in Table 11.

TABLE 11

REACTION CONDITIONS FOR THE HYDROLYSIS OF ACETONITRILE ON THE SURFACE OF ALUMINA[a]

	Catalyst	Time (hours)	Temp. (°C)	Acetamide (mmoles)	% Yield[b]
A[c]	CF_3SO_3H	15	25	2.4	80%
B[c]	CF_3CO_2H	20	60	0.17	5.7%
C	CF_3SO_3H	24	60	2.7	90%
D	None	24	60	1.7	57%
E	CF_3SO_3H	48	60	2.0	67%
F	None	48	60	1.0	33%
G[c]	CF_3CO_2H	70	60	1.2	40%
H	CF_3CO_2H	72	60	1.7	57%

[a]Reactions run with 15 g of alumina, 3 mmoles of acetonitrile, and 0.10 mL acid catalyst.

[b]Reactions analyzed by NMR; yields obtained by weight of products.

[c]Reactions performed under sonication.

In order to remove the amide from the alumina, the work-up for the surface reactions involved rinsing the alumina with large volumes of methanol. Any recovered acetonitrile (b.p. 81.6 °C), was unavoidably lost when the methanol (b.p. 65.0 °C) was evaporated. Therefore, the amount of recovered acetonitrile from the nitrile hydrolyses cannot be determined. A lower boiling solvent was not used because it did not remove amides from alumina.

Reaction *C*, which was run at 60 °C for 24 hours, produced the most acetamide of all the acetonitrile reactions. The results of this reaction show that a short and mild nitrile hydrolysis can be obtained on alumina. The acetonitrile reactions *E* and *H*, which were performed under the same conditions for longer than 24 hours, did not yield as much acetamide as reaction *C*. Since the amount of remaining acetonitrile from these reactions is unknown, an exact explanation for the lower yields cannot be made. However, based on the results of the benzonitrile reactions, some of the acetamide produced in these reactions was probably hydrolyzed to acetic acid during the longer reaction periods. Since benzoic acid could not be recovered from the alumina, acetic acid also would also have remained on the surface after the work-up; therefore, its presence would not have been detected in the product mixture analysis.

A comparison of reactions *G* and *H* shows that sonication does not enhance the production of acetamide. Reactions *G* and *H* only differed in the fact that *G* was performed under sonication. Reaction *H* yielded 17% more acetamide than reaction *G*.

Comparisons can also be made between the acid-catalyzed and uncatalyzed reactions. Both of the uncatalyzed acetonitrile reactions (*D* and *F*) produced significantly less acetamide than the acid-catalyzed reactions run under identical conditions (*C* and *E*). Thus, an acid catalyst is necessary for production of large amounts of acetamide. Since the amount of remaining acetonitrile is unknown, no explanation can be offered as to why the uncatalyzed reactions produced less acetamide.

The mechanism for the acid-catalyzed hydrolysis of acetonitrile on alumina is presumably the same as the mechanism depicted in Figure 9 on page 21 for the HBr-catalyzed benzonitrile reaction. This is the representative mechanism for all the acid-catalyzed hydration reactions. The mechanism for the base-catalyzed reaction is identical to the one in Figure 14.

The relative reactivity differences of aryl and aliphatic nitriles in the surface hydrations can be obtained by comparing the corresponding reactions of acetonitrile and benzonitrile (Table 12). Since corrected yields from the acetonitrile reactions cannot be calculated, the comparison of the acetonitrile and benzonitrile reactions can only be made between the differences in yield of amide. Acetonitrile yielded more amide than benzonitrile in all cases, except for the uncatalyzed reactions (*F* and *C*). As stated earlier, the rate of nitrile hydrolysis under acidic conditions is determined by two conflicting factors: the basicity of the nitrile and the intrinsic reactivity of the conjugate acid towards water. Actual pKb values for different nitriles have not been calculated. Benzonitrile is assumed to be more basic than acetonitrile because its protonated form receives resonance stabilization which is unavailable to the protonated form of acetonitrile. However, because acetonitrile was more reactive than benzonitrile, the greater intrinsic reactivity of the conjugate acid of acetonitrile towards water seems to have a bigger effect on the surface hydrolysis than the increased basicity of benzonitrile.

TABLE 12

A COMPARISON OF THE ACETONITRILE AND BENZONITRILE SURFACE HYDROLYSES[a]

	Nitrile	Time (hours)	Catalyst	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield	% Yield[b]
B[c] *Table 11*	CH_3CN	20	CF_3CO_2H	*	.17	5.7%	*
A[c] *Table 7*	C_6H_5CN	20	CF_3CO_2H	1.3	0.00	0.00%	0.00%
C *Table 11*	CH_3CN	24	CF_3SO_3H	*	2.7	90%	*
A *Table 3*	C_6H_5CN	24	CF_3SO_3H	0.60	0.33	11%	14%
D *Table 11*	CH_3CN	24	None	*	1.7	57%	*
A *Table 9*	C_6H_5CN	24	None	0.00	0.73	24%	24%
E *Table 11*	CH_3CN	48	CF_3SO_3H	*	2.0	67%	*
B *Table 3*	C_6H_5CN	48	CF_3SO_3H	0.028	0.63	21%	21%
F *Table 11*	CH_3CN	48	None	*	1.0	33%	*
C *Table 9*	C_6H_5CN	48	None	0.02	1.7	57%	57%
G[c] *Table 11*	CH_3CN	48	CF_3CO_2H	*	1.2	40%	*
B[c] *Table 7*	C_6H_5CN	48	CF_3CO_2H	0.52	1.0	33%	40%

*The recovered starting material from the acetonitrile reactions could not be collected; therefore, the yields cannot be corrected for recovered starting material.

[a]Reactions performed with 15 g of alumina, 3.0 mmoles of nitrile and 0.10 mL of acid catalyst (if listed) at 60 °C with unless noted otherwise.

[b]Yield corrected for remaining starting material.

[c]Reaction performed under sonication.

Propionitrile

Three reactions of propionitrile (3.0 mmoles, 0.17 g, 0.21 mL) were carried out using 15 grams of unactivated alumina in the presence of trifluoromethanesulfonic acid (0.10 mL)(eq.13). The

$$CH_3CH_2{-}C{\equiv}N \xrightarrow[CF_3SO_3H]{Al_2O_3} CH_3CH_2{-}\overset{\overset{O}{\|}}{C}{-}NH_2 \qquad \textbf{(13)}$$

reactions were run at various temperatures but all were performed for 24 hours. One reaction was also run under sonication.

As with the acetonitrile reactions, the work-up for the propionitrile reactions involved rinsing the alumina with large volumes of methanol. Even though the boiling point of propionitrile (b.p. 97.3 °C) is higher than that of acetonitrile, any remaining propionitrile was also unavoidably lost when the methanol (b.p. 65.0 °C) was evaporated. Therefore, the amount of recovered propionitrile from the nitrile hydrolyses cannot be determined.

The results of the propionitrile reactions (Table 13) are consistent with what was observed in both the acetonitrile and benzonitrile reactions. As the reaction temperature goes up, the yield of amide goes down. Reactions *A* and *B* are prime examples of the detrimental effect of a higher temperature on nitrile hydrolysis. Reaction *B*, which was run at 90 °C, produced 38% less propionamide than *A*, which was run at 60 °C. The most propionamide was obtained when the reaction was run at 60 °C; however, this gave only

TABLE 13

REACTION CONDITIONS FOR THE HYDROLYSIS OF PROPIONITRILE ON THE SURFACE OF ALUMINA[a]

	Temp. (°C)	Amide Produced (mmoles)	% Yield[b]
A	60	1.4	47%
B	90	0.25	8.3%
C[c]	60	0.00	0.00%

[a]Reactions performed for 24 hours with 15 g of alumina, 3.0 mmoles of propionitrile, and 0.10 mL trifluoromethanesulfonic acid.

[b]Reactions analyzed by GC/MS; yields calculated with a decane internal standard.

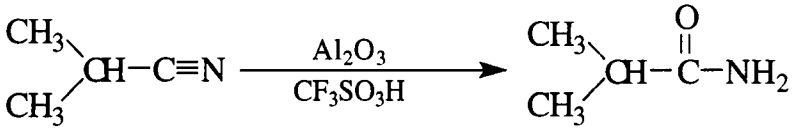
[c]Reaction performed under sonication.

a 46% yield.

The fact that no propionamide was collected from reaction *C* indicates that sonication was not beneficial in the synthesis of the amide.

Isobutyronitrile

Several reactions were performed using isobutyronitrile (3.0 mmoles, 0.21 g, 0.27 mL) on alumina (15 g) in the presence of CF_3SO_3H (0.10 mL) (eq. 14). The reactions were performed at either 60 or 100 °C, with reaction periods ranging from 24 to 168 hours.



(14)

One reaction was also run under sonication.

The results of the isobutyronitrile reactions (Table 14) demonstrate the same trend observed with the other surface hydrolyses: when the temperature or reaction period increased, the yield of amide decreased. Two of the 24 hour reactions (*A* and *B*) were the only isobutyronitrile reactions to produce any isobutyramide; the yields for these reactions are negligible. Unfortunately, as was observed for both the acetonitrile and propionitrile reactions, none of the starting material was quantitated because it couldn't be separated from the extraction solvent. Therefore, an accurate explanation for the behavior of isobutyronitrile cannot be made.

The fact that no isobutyramide was collected from reaction *C* indicates that sonication was not beneficial for the synthesis of the amide. These results are consistent with those of the sonicated propionitrile reactions.

Hexanenitrile

Several reactions were performed with 3.0 mmoles (0.29 g, 0.36 mL) of hexanenitrile, on 15 grams of alumina, catalyzed with 0.10 mL CF_3SO_3H (eq. 15). The reactions were run at either 60 or 95

TABLE 14

REACTION CONDITIONS FOR THE HYDROLYSIS OF ISOBUTYRONITRILE ON ALUMINA[a]

	Time (hours)	Temp. °C	Amide Produced (mmoles)	% Yield[b]
A	24	60	0.54	18%
B	24	100	0.34	11%
C[c]	24	60	0.00	0.00%
D	48	100	0.00	0.00%
E	72	100	0.00	0.00%
F	168	100	0.00	0.00%

[a]Reactions performed with 15 g of alumina, 3.0 mmoles of isobutyronitrile, and 0.10 mL trifluoromethanesulfonic acid.

[b]Reactions analyzed by GC/MS; yields calculated with a decane internal standard.

[c]Reaction performed under sonication.

$$CH_3(CH_2)_4-C\equiv N \xrightarrow[CF_3SO_3H]{Al_2O_3} CH_3(CH_2)_4-\overset{\overset{O}{\|}}{C}-NH_2 \qquad \textbf{(15)}$$

°C with reaction periods ranging from 24 to 168 hours. One reaction was run under sonication and catalyzed with CF_3CO_2H.

The results of the hexanenitrile reactions (Table 15) indicate that when the reaction temperature or time was increased, the yield of amide decreased. This trend was observed in all the previously discussed surface nitrile hydrolyses. Unlike the previously mentioned aliphatic nitriles, the lack of hexanenitrile in the product mixture is not due to evaporation during work-up because it has a much higher boiling point (162 °C). Also, for reaction *E*, some hexanenitrile was recovered. Therefore, no hexanenitrile remained after the reactions *A, B, C, D,* and *F* were quenched. The low yields of hexanoamide and the absence of hexanenitrile indicate that the amide was hydrolyzed to the corresponding carboxylic acid which remained on the alumina.

The sonicated reaction of hexanenitrile (*E*) did produce more hexanoamide than the unsonicated reaction run under similar conditions (*D*). Reaction *E* was catalyzed with CF_3CO_2H, while *D,* like the other hexanenitrile reactions, was catalyzed with the stronger acid, CF_3SO_3H. Since two variables were different for reaction *E*, it is unclear which affects the reaction's outcome. Hexanenitrile was recovered only from reaction *E,* so for some reason the hydrolysis of hexanenitrile and the subsequent hydrolysis of hexaneamide was

TABLE 15

REACTION CONDITIONS FOR THE HYDROLYSIS OF HEXANENITRILE ON THE SURFACE OF ALUMNA[a]

	Time (hours)	Temp. (°C)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A	24	60	0.00	0.77	26%	26%
B	24	95	0.00	0.54	18%	18%
C	48	95	0.00	0.090	3.1%	3.1%
D	72	95	0.00	0.030	0.90%	0.90%
E[d]	72	60	0.67	0.15	5.0%	6.4%
F	168	95	0.00	0.00	0.00%	0.00%

[a]Reactions performed with 3.0 mmoles of hexanenitrile, 15 g of alumina, and 0.10 mL trifluoromethanesulfonic acid, unless otherwise noted.

[b]Reactions analyzed by GC/MS; yields calculated with a tetradecane internal standard.

[c]Yields corrected for remaining starting material.

[d]Reaction performed under sonication and catalyzed with trifluoroacetic acid.

slowed. Either the weaker acid or sonication retards the hydrolyses in reaction *E*.

The results of the hexanenitrile reactions can be compared to the results of all of the previously studied nitrile reactions. Table 16 lists the data for the reactions performed at 60 °C for 24 hours. Hexanenitrile did produce more amide than isobutyronitrile and benzonitrile but less amide than acetonitrile and propionitrile. Since the amount of remaining starting material for all the aliphatic nitriles

TABLE 16

COMPARISON OF THE RESULTS OF VARIOUS NITRILE HYDRATIONS ON ALUMINA[a]

	Nitrile (mmoles)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield	% Yield[b]
A	$CH_3(CH_2)_4CN$	0.00	0.77	26%	26%
B	$(CH_3)_2CHCN$	*	0.54	18%	*
C	CH_3CH_2CN	*	1.4	47%	*
D	CH_3CN	*	2.7	90%	*
E	C_6H_5CN	0.60	0.33	11%	14%

*The recovered starting material from the reactions of acetonitrile, propionitrile, and isobutyronitrile could not be collected; hence, a corrected yield could not be calculated.

[a]Reactions performed for 24 hours at 60°C with 15 g of alumina, 3.0 mmoles of nitrile, and 0.10 mL trifluoromethanesulfonic acid.

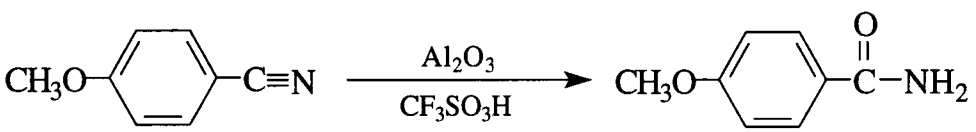
[b]Yield corrected for remaining starting material

except hexanenitrile is unknown, it is difficult to rationalize the results of these reactions. The comparison of the benzonitrile reaction (*A*) with the hexanenitrile reaction (*E*) is not limited because starting material was recovered from the reactions of both of these nitriles. Because no hexanenitrile was recovered from reaction *E*, but 0.60 mmoles of benzonitrile was recovered from reaction *A*, it is obvious that the hydrolysis of hexanenitrile was faster than the hydrolysis of benzonitrile. Since there are no recorded pKb values for these various nitriles it is difficult to reason why the

hexanenitrile reaction was faster.

4- Methoxybenzonitrile

Several reactions were performed with 4-methoxybenzonitrile (3.0 mmoles, 0.40 g) on alumina (15 g), in the presence of CF_3SO_3H (0.10 mL) (eq. 16). One reaction was also



(16)

performed under sonication in the presence of CF_3CO_2H (0.10 mL).

The results of the 4-methoxybenzonitrile reactions, shown in Table 17, are for the most part consistent with those from the benzonitrile reactions. Again, the length of the reaction period has a significant effect on the amount of amide which is isolated.

Reactions *A* and *B* differ in the fact that *A* was run for a shorter time period than *B*. In *A*, slightly more than half of the 4-methoxybenzonitrile has been hydrolyzed to 4-methoxybenzamide, which is why 0.47 mmoles of starting material of reaction *A* was not accounted for. It is logical to assume that because benzoic acid could not be extracted from alumina, 4-methoxybenzoic acid would also remain on the surface. Therefore, any 4-methoxybenzoic acid which was generated would remain undetected. In reaction *B*, more of the

TABLE 17

REACTION CONDITIONS FOR THE HYDROLYSIS OF 4-METHOXYBENZONITRILE ON ALUMINA[a]

	Time (hours)	Temp. (°C)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A	24	60	1.3	1.3	43%	76%
B	48	60	0.98	1.5	50%	74%
C[c]	72	60	2.0	0.53	18%	53%
D[d]	168	50	0.36	0.066	2.2%	2.5%
E	216	100	0.52	0.20	6.7%	8.1%

[a]Reactions performed with 15 g of alumina, 3 mmoles of nitrile, and 0.10 mL trifluoromethanesulfonic acid, unless noted otherwise.

[b]Reactions analyzed by HPLC; yields obtained by weight.

[c]Reaction performed under sonication with 0.10 mL trifluoroacetic acid.

[d]Reaction catalyzed with 0.10 mL trifluoroacetic acid.

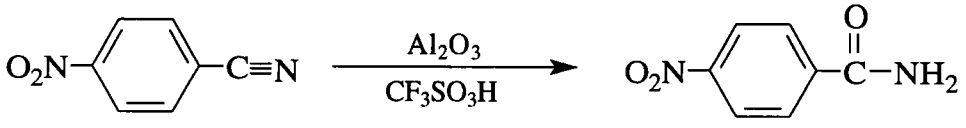
nitrile has been hydrolyzed, but approximately the same amount(0.50 mmoles) of nitrile as in *A* is unaccounted for. More amide was collected from *B* as well. Therefore, the hydrolysis of 4-methoxybenzamide is probably slower than the hydrolysis of 4-methoxybenzonitrile. If amide hydrolysis were faster than nitrile hydrolysis, less amide would have been collected from *B* because more of it would have been hydrolyzed. However, this is not what was observed; *B* produced more amide than *A*, while the same amount of nitrile was unaccounted for in *A* and in *B*. Over time,

more of the 4-methoxybenzamide is converted to 4-methoxybenzoic acid. Reaction *E*, which was performed for 216 hours, produced less amide than reactions *A* and *B* which were performed for 24 and 48 hours, respectively. Therefore, in order to obtain a significant amount of 4-methoxybenzamide, the reaction cannot be run over extendend periods of time.

Since the sonicated reaction, *C*, differed in several ways from the other reactions, an exact explanation for its behavior cannot be made.

4-Nitrobenzonitrile

Two reactions were performed at 100 °C with 4-nitrobenzonitrile (3.0 mmoles, 0.44g) on alumina (15 g) in the presence of CF_3SO_3H (0.10 mL) (eq. 17). One additional reaction was also performed under sonication with the same quantities of nitrile and alumina, and catalyed with CF_3CO_2H (0.10 mL).



(17)

The results of the 4-nitrobenzonitrile reactions (Table 18) show that a extended reaction period is necessary for the production of 4-nitrobenzamide. Reaction *A*, which ran for 72 hours, did not produce

TABLE 18

REACTION CONDITIONS FOR THE HYDRATION OF 4-NITROBENZONITRILE ON ALUMINA[a]

	Time (hours)	Temp. (°C)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A[c]	72	60	2.9	0.00	0.00%	0.00%
B	168	100	0.90	1.9	60%	90%
C	216	100	1.7	0.78	26%	60%

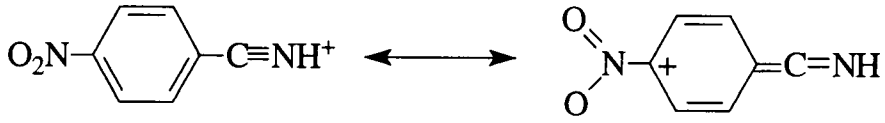
[a]Reactions performed with 15 g of alumina, 3 mmoles of nitrile, and 0.10 mL trifluoromethanesulfonic acid, unless noted otherwise.

[b]Reactions analyzed by HPLC; yields obtained by weight.

[c]Reaction performed under sonication with 0.10 mL trifluoroacetic acid.

4-nitrobenzamide, but 97% 4-nitrobenzonitrile was recovered. Therefore, the other two reactions were allowed to run for 168 hours and 216 hours, respectively.

The major reason for the low reactivity of 4-nitrobenzonitrile on the surface hydrolysis has to do with the presence of the para-nitro substituent. As previously mentioned, one of the effects which influences nitrile reactivity in acidic conditions is the basicity of the nitrile. Since actual measurements of the basicity of various nitriles have not been made, the basicity of the nitriles in this study was inferred. When the intermediate of a reaction is stabilized, the energy of the transition state is lowered and the reaction proceeds with less input of energy. The intermediate is commonly stabilized

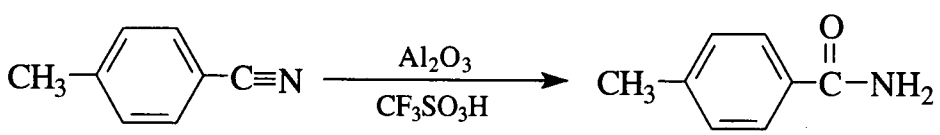


by means of resonance and/or inductive effects. Conversely, when the intermediate is destabilized, the energy of the transition state is raised, and the reaction requires more energy to form the products. The presence of the *p*-nitro substituent, an electron withdrawing group, destabilizes the intermediate of the 4-nitrobenzonitrile reactions. For this reason, the hydrolysis of 4-nitrobenzonitrile requires a lengthy reaction period and a higher temperature to generate 4-nitrobenzamide.

P-Tolunitrile

Three reactions were performed with *p*-tolunitrile (3.0 mmoles, 0.35 g, 0.36 mL) on alumina (15 g) in the presence of CF_3SO_3H (0.10 mL) (eq. 18). One other reaction of *p*-tolunitrile was performed with identical quantities of nitrile, alumina, and CF_3CO_2H catalyst. This reaction was run under sonication.

The results of the *p*-tolunitrile reactions (Table 19) show, as with all of the other nitriles studied, that the yield of amide



(18)

TABLE 19

REACTION CONDITIONS FOR THE HYDROLYSIS OF *p*-TOLUNITIRILE ON ALUMINA[a]

	Time (hours)	Temp. °C	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A	24	60	0.58	0.60	20%	25%
B	48	60	0.55	0.21	6.9%	8.6%
C[d]	72	60	1.9	0.00	0.00%	0.00%
D	168	90	0.84	0.33	11%	15%

[a]Reactions performed with 15 g of alumina, 3.0 mmoles of nitrile, and 0.10 mL trifluoromethanesulfonic acid, unless otherwise noted.

[b]Reactions analyzed by GC/MS; yields calculated with a tetradecane internal standard.

[c]Yields corrected for remaining starting material.

[d]Reaction performed under sonication and catalyzed with trifluoroacetic acid.

decreases when the reaction period increases. Reactions *A* and *B* were run under identical conditions except for reaction time; *A* was run for 24 hours, while *B* was run for 48 hours. Approximately the same amount of nitrile was recovered (0.50 mmoles) from both reactions, but significantly less amide was collected from the longer reaction, *B*. When the reaction was allowed to run over a longer time period, more of the *p*-toluamide was hydrolyzed to *p*-toluic acid. As with benzoic acid, *p*-toluic acid is expected to remain on the alumina (even after numerous attempts had been taken to remove it); therefore, it would not be detected in the product analysis.

Since the sonicated reaction, *C*, differed from the other reactions in several aspects, an exact explanation for its behavior cannot be made.

Conclusions

The goal of this research was to develop a mild and simple method for converting nitriles to amides. For the most part, this goal was accomplished; the surface reactions occur under mild conditions. However, the synthetic utility of this method is questionable. Table 20 lists the yields from the CF_3SO_3H-catalyzed hydrations performed for 24 hours at 60 °C. All of the reactions were run with 3.0 mmoles of nitrile, 15 g of alumina, and 0.10 mL of CF_3SO_3H. A large yield of acetamide was obtained from the 24-hour reaction of acetonitrile (*B*), but the 24-hour reactions of the other nitriles were not as successful. 4-nitrobenzonitrile reacted for 168 hours before a significant yield of 4-nitrobenzamide was obtained (82%*). The question remains as to why some of the nitrile hydrolyses generated lower yields of amide.

The main reason for lack of amide is the fact that the amide is subsequently hydrolyzed to the corresponding carboxylic acid. It is known that amides are easily hydrolyzed to carboxylic acids, which is the reason the conversion of nitriles to amides is so difficult. Previous work has documented that it is difficult to stop a nitrile hydrolysis at the amide stage.[5, 13, 14] Nitrile hydrolysis was

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* Yield corrected for remaining starting material.

TABLE 20

A COMPARISON OF THE RESULTS OF NITRILE HYDRATIONS OF VARIOUS ALIPHATIC AND AROMATIC NITRILES ON ALUMINA[a]

	Nitrile (mmoles)	Recovered Nitrile (mmoles)	Amide Produced (mmoles)	% Yield[b]	% Yield[c]
A	C_6H_5CN	0.60	0.33	11%	14%
B	CH_3CN	*	2.7	90%	*
C	CH_3CH_2CN	*	1.4	47%	*
D	$(CH_3)_2CHCN$	*	0.54	18%	*
E	$CH_3(CH_2)_4CN$	0.0	0.77	26%	26%
F	4-$CH_3OC_6H_4CN$	1.3	1.3	43%	76%
G	*p*-$CH_3C_6H_4CN$	0.58	0.60	20%	25%

*The recovered starting material from the reactions of acetonitrile, propionitrile, and isobutyronitrile could not be collected; hence, a corrected yield could not be calculated.

[a]Reactions performed for 24 hours at 60°C with 15 g of alumina, 3.0 mmoles of nitrile, and 0.10 mL trifluoromethanesulfonic acid.

[b]Yield corrected for remaining starting material

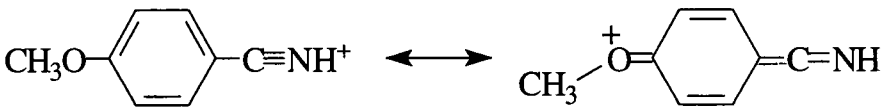
attempted on alumina with the hope that the surface of alumina would favor the production of amides more than carboxylic acids. It was found that under specific conditions, it was possible to obtain a significant yield of amide from the surface reactions. Since each nitrile is different, the conditions for maximum production of amides will also be different. The "perfect" balance of reaction time, temperature, catalyst, and ratio of alumina to nitrile has to be determined in order to obtain amides and not carboxylic acids.

The length of the reaction time was found to be the key factor for obtaining more amide than carboxylic acid in the alumina reactions. Obviously, the longer the reaction is allowed to run, the more chance for amide hydrolysis. A difficulty with the surface reactions arose from the fact that carboxylic acids could not be extracted from the alumina. Therefore, the exact amount of carboxylic acid produced from amide hydrolysis could only be inferred from the difference in recovered nitrile and amide product. For the acetonitrile, propionitrile, and isobutyronitrile reactions the recovered starting material could not be quantified. Hence, accurate estimates of the amount of carboxylic acid produced from the reactions of these nitriles could not be made. For the other nitriles, an accurate estimation of amount of carboxylic acid could be determined; consequently the ideal reaction time could also be ascertained.

The rate of the hydrolysis of the nitrile and the successive hydrolysis of the amide depends upon the basicity of the nitrile and

the intrinsic reactivity of its conjugate acid with water. Since these two factors are in opposition to one another, it was unclear which would have the greatest effect on the surface hydrolyses. Measurements of the basicity of various nitriles in solution have not been recorded, so the basicity of the various nitriles in this study were inferred based on possible resonance and inductive effects. The ideal reaction time for the surface hydrolyses is related to both the basicity of the nitrile and the reactivity of its conjugate acid with water. The results of the surface hydration reactions indicate that the intrinsic reactivity of the protonated nitrile toward water dominates the nitrile hydrolysis. However, the basicity of the nitrile also plays an important role.

As mentioned previously, 4-nitrobenzonitrile was less reactive in the surface hydrolyses than the other nitriles because its intermediate was destabilized by the presence of the *p*-nitro substituent. The reactions of 4-nitrobenzonitrile were predicted to require a longer reaction period than the other nitriles; the results of the 4-nitrobenzonitrile reactions validated this prediction. Furthermore, the reactions of 4-methoxybenzonitrile were predicted to require a short reaction period because of the stabilizing resonance effects of the *p*-methoxy substituent. The *p*-methoxy group will stabilize the positive charge of the conjugate acid of 4-methoxybenzonitrile. Therefore, 4-methoxybenzonitrile is more basic than the other nitriles involved in this study. The reactions of 4-methoxybenzonitrile should have produced more amide and



carboxylic acid in less time than those of benzonitrile and *p*-tolunitrile; however, the results of the 24-hour reactions do not reflect this. Less nitrile was recovered from both the benzonitrile and the *p*-tolunitrile reactions than was recovered from the 4-methoxybenzonitrile reaction. The reactivity of the conjugate acids of benzonitrile and *p*-tolunitrile toward water must have a greater effect on the surface hydrolysis since the reactions of benzonitrile and *p*-tolunitrile were faster than the reaction of the more basic 4-methoxybenzonitrile.

Deno and coworkers showed that under acidic conditions, solution reactions of acetonitrile and propionitrile were faster than those of benzonitrile, even though benzonitrile is a stronger base.[17] They proposed that the faster rates of the aliphatic nitrile reactions were due to the fact that the conjugate acids of the aliphatic nitriles were innately more reactive towards water than the conjugate acid of benzonitrile. The absolute percent yields for the 24-hour surface hydrolysis reactions show that the aliphatic nitriles were also more reactive than aryl nitriles on alumina. For the aliphatic nitriles, the intrinsic reactivity of their conjugate acids towards water has the greatest effect on the rate of reaction. The conjugate acids of benzonitrile and *p*-tolunitrile are inherently more reactive with

water than the conjugate acid of 4-methoxybenzonitrile, which is why more amide is produced from the 24-hour reactions of the two former nitriles than from the 24-hour reaction of the latter.

In summary, for surface nitrile hydrolyses, the intrinsic reactivity of the protonated nitrile towards water has a greater effect on the rate of the reaction than the basicity of the nitrile. The length of time needed for production of amides from nitriles on alumina can be correlated with the fundamental strength of the conjugate acid of the nitrile. Before performing the hydrolysis, the reactivity of the protonated nitrile must be estimated in order to determine the optimum reaction period. If the reaction is run for too long, the amide will be hydrolyzed to the corresponding carboxylic acid. The basicity of the nitrile must also be taken into account, as shown by the results obtained with 4-nitrobenzonitrile. If the individual characteristics of the nitrile are studied before the reaction is run, nitrile hydrolysis on alumina should be a useful method for obtaining amides.

CHAPTER III

EXPERIMENTAL

Materials

Solvents: The following solvents were used without purification.

Acetone, Mallinckrodt, ACS grade

Anhydrous Diethyl Ether, Mallinckrodt, ACS grade

Benzene, Fisher Scientific, ACS grade

Chloroform, Mallinckrodt, ACS grade

Distilled Water, Departmental distilled water

Hexanes, Mallinckrodt, ACS grade

Methanol, Mallinckrodt, ACS grade

Methylene Chloride, Mallinckrodt, ACS grade

Xylenes, Mallinckrodt

Gases:

Argon, Ar. MG Industries, prepurified Argon was used as purchased.

Reagents: The following reagents were used as purchased.

Acetonitrile, Mallinckrodt

Alumina, Brockman Activity Grade 1 (neutral), Aldrich Chemical Company

Benzonitrile, Eastman Organic Chemicals

Boron Tribromide, 99.99%, Aldrich Chemical Company

Bromine, 99.5%, ACS grade, Aldrich Chemical Company

Hexanenitrile, 98%, Aldrich Chemical Company

Isobutyronitrile, 99%, Aldrich Chemical Company

4-Methoxybenzonitrile, 99%, Aldrich Chemical Company

4-Nitrobenzonitrile, 97%, Aldrich Chemical Company

Propionitrile, 99%, Aldrich Chemical Company

p-Tolunitrile, 98%, Aldrich Chemical Company

Trifluoacetic acid, 99%, Aldrich Chemical Company

Trifluoromethanesulfonic acid, 98%, Fluka Chemical Company

Experimental Methods

Physical Properties and Analytical Methods

Gas chromatography was performed on a Hewlett-Packard 5890 series gas chromatographer/mass spectrometer equipped with a 30 m x .25 mm column packed with 100% dimethyl polysiloxane.

High performance liquid chromatography was performed on a Varian 5000 liquid chromatograph equipped with a semi prep scale reverse phase column. A Varian 2050 variable wavelength detector was used to detect the presence of selective amides. The quantitations of these amides were obtained using a Varian 4400 integrator.

Fourier transform infrared spectrometry was performed on a BIO-RAD FTS-60A fourier transform infrared spectrophotomer with a SPC 3200 data system and a model 896 interferometer infrared spectrometer.

Mass spectra were obtained via the mass selective detector of the Hewlett-Packard 5970 series gas chromatographer/mass spectrometer.

Both proton and carbon nuclear magnetic resonance spectra were recorded on a Bruker 250 MHz spectrometer. The samples were run in $CDCl_3$ with 1% tetramethylsilane (TMS) as the internal standard. The chemical shift for TMS resonance was set at 0 parts per million. Chemical shifts are reported in parts per million (ppm) downfield from TMS.

Solid state nuclear magnetic resonance spectrometry was performed on a Nicolet 200 MHz spectrometer. A Doty probe and a zirconium rotor were used to obtain the solid state spectra. Hexamethylbenzene was used as an external reference. The chemical shift for the methyl group of hexamethylbenzene was reported to be 17.36 ppm and the chemical shift for the aromatic carbons was reported to be 132.30 ppm.

Sonication was performed with a 50/60 Hz, 117 volts, 1.0 amp B-22-4 Branson ultrasonic cleaner.

Apparatus

All glassware, stirbars, syringes, and needles were washed thoroughly, rinsed with acetone, and oven dried before use.

The reactions involving boron tribromide and hexanes were performed under a slight positive pressure of argon using a pressure-regulated argon source and a mercury bubbler.

The reactions involving hydrogen bromide gas were pressure-regulated using a mineral oil bubbler.

Preparation of Al_2O_3/BBr_3

Bromoboronated alumina was prepared using 1.00 mmole (0.251g) of boron tribromide per gram of alumina. A 250-mL round-bottomed flask equipped with a side arm, magnetic stir bar, and three-arm adapter with a stopcock was flame dried under argon. To the flask, 21 grams of alumina were added in an argon atmosphere. Using a cannula, 21 mL of hexane were added to the alumina in the flask under a slight positive pressure of argon. Using a cannula, 21 mL (21 mmoles) of 1.0 molar BBr_3 were next added to the alumina under a slight positive pressure of argon. The flask was placed on a magnetic stir plate and the slurry was allowed to stir in an ice bath. After 35 minutes the flask was removed from the ice bath and stirred for 30 minutes at room temperature. The hexane was removed from the alumina *in vacuo* to leave Al_2O_3/BBr_3.

Production of the Hydrogen Bromide Gas

A still was constructed in order to generate hydrogen bromide gas from the reaction of bromine and xylene. Approximately 200 mL of xylene were placed in a 500-mL round-bottomed flask which contained a magnetic stirbar. The flask was placed on a magnetic stir plate and the xylene was stirred slowly. An adapter with a side arm was inserted into the 500-mL round-bottomed flask. A 50 cm length of tygon tubing was attached to the side arm of the adapter. A needle was inserted into the other end of the tygon tubing. A pressure equalizing drop addition funnel was fitted into the other end of the side arm adapter. Bromine (10 mL) was added to the funnel. A glass stopper closed the top of the funnel. Three drops of bromine were added from the funnel to the stirring xylene. The color of the xylene immediately changed from colorless to the dark orange color characteristic of bromine. Once the xylene solution was again colorless, seven drops of bromine were added to the xylene from the funnel. The addition of bromine was continued as long as hydrogen bromide gas was needed to catalyze the reaction in process.

Manipulation of Trifluoromethanesulfonic acid

Due to the extreme reactivity of trifluoromethanesulfonic acid, it had to be added to the reaction vessels using special precautions. The flask containing the trifluoromethanesulfonic acid was enclosed in a plastic glove equipped with a septum. Argon was flushed

through the glove before the flask was opened. Trifluoromethanesulfonic acid was drawn from the flask using an argon-flushed syringe and then added to the reaction vessel.

Experimental Procedures

Hydrolysis of Benzonitrile on Al_2O_3/BBr_3

The conversion of benzonitrile to benzamide on alumina was first attempted on Al_2O_3/BBr_3.

Benzonitrile

Unactivated alumina (40 g) was added to a 250-mL round-bottomed flask. BBr_3 (1.0 M in hexanes) was added to the flask using the method described for the preparation of Al_2O_3/BBr_3. The hexanes were removed from the alumina *in vacuo* to leave bromoboronated alumina. Benzonitrile (40 mmoles, 4.9 g, 4.1 mL) of was added to the flask through the side arm. The flask was placed on a magnetic stir plate and its contents were allowed to stir in an ice bath. After 36 hours the flask was removed from the ice bath and methanol (150 mL) was added to the flask. The methanol slurry was stirred for thirty minutes at room temperature. The methanol solution was then filtered from the alumina. The alumina was rinsed with an additional 500 mL of methanol. The methanol was evaporated from the crude product. Analysis of the residue showed no benzamide was produced from this reaction. Table 1 lists the

various conditions used for the attempted hydrolysis reactions of benzonitrile on Al_2O_3/BBr_3.

HBr-Catalyzed Hydration of Nitriles on Alumina

Several HBr-catalyzed benzonitrile-to-benzamide conversions were attempted on alumina.

Benzonitrile

Unactivated alumina (5.0 g) was added to a 250-mL round-bottomed flask equipped with a side arm and magnetic stir bar. The flask was placed in an oil bath heated to 60 °C on a magnetic stir/heat plate and the alumina was stirred via the magnetic stir bar. The flask was attached to a mineral oil bubbler and benzonitrile (5.0 mmoles, 0.51 g, 0.50 mL) was added to the flask. The flask was also attached to the hydrogen bromide still which was described previously. HBr gas was generated from the still and allowed to flow into the reaction flask. After 15 minutes of exposure to the HBr gas the connection to the mineral oil bubbler was removed from the flask. Gas continued to flow into the flask until a pressure increase became noticeable due to the swelling of the rubber septum. At this time the flask was detached from the still. The alumina was allowed to stir for 120 hours in a closed atmosphere, after which time the reaction was quenched with the addition of 150 milliters of methanol. The resulting mixture was stirred for 30 minutes. Once stirring was completed, the entire mixture was filtered over Celite 521. The alumina was rinsed with an additional 500 mL of

methanol. After the methanol was removed *in vacuo*, a white crystalline mixture of benzonitrile and benzamide remained. Flash chromatography was used to separate the benzamide from the benzonitrile. The product mixture was analyzed by GC/MS; the yield was obtained by means of a tetradecane internal standard. Table 2 lists the various conditions used for running the HBr-catalyzed benzonitrile reactions.

CF_3SO_3H-Catalyzed Hydration of Nitriles on Alumina

A variety of nitriles were converted to their corresponding amides on alumina using trifluoromethanesulfonic acid as a catalyst.

Benzonitrile

Unactivated alumina (15 g) was added to a 250-mL round-bottomed flask equipped with a magnetic stir bar and a glass stopper. The flask was placed on a magnetic stir/heat plate in an oil bath which had been heated to 60 °C. The alumina was stirred as of CF_3SO_3H (0.10 mL) was added to the flask. The flask was stoppered and stirred for approximately 5 minutes in order to ensure that the acid was chemisorbed on the alumina. After 5 minutes of stirring, benzonitrile (3.0 mmoles, 0.31 g, 0.30 mL) was added by means of a 1-mL syringe to the flask. After the addition of the benzonitrile was complete, the flask was restoppered and allowed to stir while the oil bath temperature was maintained. After the reaction was stirred for the designated amount of time, the flask was removed from the oil bath and allowed to cool to room temperature. The resulting reaction

was quenched with 150 mL of methanol and the mixture was stirred for 30 minutes. The entire mixture was then filtered over Celite 521, and, the alumina was rinsed with an additional 500 mL of methanol. The methanol was evaporated and a white crystalline mixture of benzonitrile and benzamide remained. Benzamide was separated from benzonitrile using acetone. (Benzonitrile dissolves readily in acetone while benzamide does not dissolve.) The nitrile solution was filtered through a fine frit while the benzamide solid remained on top of the frit. Methanol, which dissolves benzamide, was filtered through the frit and the benzamide solution was collected in a separate flask. The product mixture was analyzed by GC/MS; the yield was obtained using a tetradecane internal standard. TLC, ^{13}C and ^{1}H NMR, S.S. NMR, and FT-IR were also used to verify the presence of benzamide. Table 3 lists the conditions and yields of the CF_3SO_3H-catalyzed benzonitrile surface hydrolyses.

A few reactions were performed using 1.0 mL of CF_3SO_3H. All of the other conditions were the same as those described for the reactions involving 0.10 mL of the acid.

Other Nitriles

Most of the procedures used for the conversion of the other nitriles into their corresponding amides were the same as that described for the benzonitrile reactions. All of the reactions performed with nitriles other than benzonitrile were run with 15 grams of unactivated alumina, 3.0 mmoles of nitrile, and 0.10 mL of CF_3SO_3H. The reactions of isobutyronitrile, hexanenitrile,

propionitrile, and *p*-tolunitrile were analyzed by GC/MS. The yields were obtained using either decane (isobutryonitrile, propionitrile) or tetradecane (hexanenitrile, *p*-tolunitrile) internal standard. The reactions of 4-methoxybenzonitrile and 4-nitrobenzonitrile were analyzed by HPLC and TLC. The yields were determined in these instances by weight of products. The yields of the acetonitrile reactions were also obtained by weighing the products. ^{13}C and ^{1}H NMR were also used to verify the structures of the products. Tables 11, 13, 15, 16, 17, 18, and 19 show the conditions and yields of the reactions of acetonitrile, propionitrile, isobuyronitrile, hexanenitrile, 4-methoxybenzonitrile, 4-nitrobenzonitrile, and *p*-toulunitrile; respectively.

The procedures used with 4-methoxybenzonitrile and 4-nitrobenzonitrile differed from that used with benzonitrile because these nitriles are solids at room temperature. Therefore, these nitriles were dissolved in a small amount (3.0 mL) of a volatile solvent before addition to the alumina. Diethyl ether was used to dissolve 4-methoxybenzonitrile; methylene chloride was used to dissolve 4-nitrobenzonitrile. After the nitriles were dissolved, they were added to the alumina in the reaction flask in the same manner as benzonitrile.

The work-up for 4-methoxybenzonitrile and 4-nitrobenzonitrile also differed from that used with the other nitriles. Methanol was used to remove the other amides from the alumina when the reaction was completed, but 4-methoxybenzamide is not soluble in methanol so a mixture of methanol and diethyl ether was

used in its work-up. 4-Nitrobenzonitrile is also insoluble in methanol so a mixture of methanol and chloroform was used to quench its reactions.

CF_3CO_2H-Catalyzed Hydration of Nitriles on Alumina

Reactions of benzonitrile, acetonitrile, and 4-methoxybenzonitrile were performed on alumina using CF_3CO_2H as the catalyst.

Benzonitrile

The procedure involving CF_3CO_2H was identical to the procedure involving CF_3SO_3H except for the catalyst applied to the alumina. Before the addition of benzonitrile, trifluoroacetic acid (0.10 mL) was added to the alumina. A few reactions were also run using 1.0 mL of trifluoroacetic acid. Table 7 lists the conditions and yields of the CF_3CO_2H-catalyzed reactions.

Other Nitriles

Reactions involving acetonitrile and 4-methoxybenzonitrile were also catalyzed with CF_3CO_2H. The procedure used with the CF_3CO_2H catalyst is the same as that used for the CF_3SO_3H-catalyzed reactions All of the reactions were run with 15 grams of unactivated alumina, 3.0 mmoles of either acetonitrile or 4-methoxybenzonitrile, and 0.10 mL of trifluoroacetic acid. The procedure used with 4-methoxybenzonitrile differed in the same aspects which were described for the CF_3SO_3H-catalyzed reactions.

Tables 11 and 17 list the conditions and yields of the CF_3CO_2H-catalyzed reactions of acetonitrile and 4-methoxybenzonitrile, respectively.

Hydrolysis of Nitriles on Alumina Under Sonication

Several nitrile to amide conversions were also performed under sonication.

Benzonitrile

The procedure for the benzonitrile surface hydrolyses run under sonication was identical to that described for the reactions catalyzed with CF_3SO_3H except for the use of a sonicator. The reaction flask was placed on a magnetic stir plate and the alumina (15 g) was stirred when the CF_3CO_2H (0.10 mL) and benzonitrile (0.31 g, 0.30 mL) were added subsequently to the flask. The flask was placed in the sonicator after the addition of the benzonitrile. The sonicator was filled with water and the temperature of the water was monitored during the sonication; the average temperature was 60 °C. Unactivated alumina (15 g), benzonitrile (3.0 mmoles,0.31 g, 0.3 mL), and trifluoroacetic acid (0.1 mL) were sonicated for 72 hours. Following this sonication period, the flask was removed from the sonicator and placed on a magnetic stir plate. The glass stopper was removed from the flask and the reaction mixture was allowed to stir for approximately 24 hours. The reaction was quenched with 150 mL of methanol and worked up in the same manner as described for the CF_3SO_3H-catalyzed reactions. The conditions and

results of the reactions performed under sonication are found on Table 7.

Other Nitriles

Seven other nitrile to amide conversions were run under sonication. The procedure involving these nitriles was the same as that used with benzonitrile. As previously described, the procedures used with 4-methoxybenzonitrile and 4-nitrobenzonitrile were slightly different from the other procedures. All the reactions were run using 15 grams of unactivated alumina and 3.0 mmoles of nitrile. The reactions of propionitrile and isobutryonitrile were catalyzed with CF_3SO_3H (0.10 mL). The reactions of the other nitriles were catalyzed with CF_3CO_2H (0.10 mL). The conditions and results of the sonicated reactions of acetonitrile, propionitrile, isobutyronitrile, hexanenitrile, 4-methoxybenzonitrile, 4-nitrobenzonitrile, and *p*-tolunitrile are found on Tables 11, 13, 15, 16, 17, 18, and 19; respectively.

Uncatalyzed Hydration of Nitriles on Alumina

A few nitrile hydrolyses were run on alumina without the addition of a catalyst.

Benzonitrile

An uncatalyzed reaction using 3.0 mmoles (0.31 g, 0.3.0 mL) of benzonitrile and 15 grams of unactivated alumina was run at 60 °C for 24 hours. The procedure was the same as that described for

the CF_3SO_3H-catalyzed reactions except the acid catalyst was omitted. Table 9 contains the conditions and yields of the uncatalyzed benzonitrile reactions.

Acetonitrile

An uncatalyzed reaction using acetonitrile (3.0 mmoles, 0.12 g, 0.16 mL) and unactivated alumina (15 g) was run at 60 °C for 24 hours. The procedure was identical to the procedure described for the CF_3SO_3H-catalyzed reaction of benzonitrile on alumina except the acid catalyst was omitted. Table 11 contains the conditions and yields of the uncatalyzed acetonitrile reactions.

Sample "Reaction" Run with Benzoic Acid

A sample reaction was performed with benzoic acid (3.0 mmoles, 0.37 g) dissolved in diethyl ether (3.0 mL), unactivated alumina (15 g), and trifluoroacetic acid (0.10 mL). The procedure used for this "reaction" was identical to that described for the CF_3SO_3H-catalyzed reactions of benzonitrile. The benzoic acid "reaction" was sonicated for 72 hours. It was then quenched with 150 mL of methanol and allowed to stir for 30 minutes. The methanol solution was next filtered from the alumina; the alumina was rinsed twice with 250 mL of methanol per rinse. No solid was present after evaporation of the methanol was completed. The alumina was analyzed by means of S.S. NMR and FT-IR.

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APPENDIX

APPENDIX

DERIVATION OF THE RATE EQUATION FOR NITRILE HYDRATION

$$RCN + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RCNH^+$$

$$RCNH^+ \xrightarrow[\text{slow}]{k_2} RCONH_2$$

$$\frac{d[RCN]}{dt} = -k_1[RCN][H^+] + k_{-1}[RCNH^+]$$

$$\frac{d[RCNH^+]}{dt} = k_1[RCN][H^+] - (k_{-1} + k_2[H_20])[RCNH^+] = 0,$$

by the steady state assumption

$$[RCNH^+] = \frac{k_1}{k_{-1} + k_2[H_2O]}[RCN][H^+]$$

$$\frac{d[RCN]}{dt} = \left(-k_{-1} + \frac{k_1}{k_{-1} + k_2[H_2O]}\right)[RCN][H^+]$$

$$\frac{d[RCN]}{dt} = \left[\frac{-k_1k_{-1} - k_1k_2[H_2O] + k_{-1}k_1}{k_{-1} + k_2[H_2O]}\right][RCN][H^+]$$

$$\frac{d[RCN]}{dt} = \frac{k_1}{k_{-1} + k_2[H_2O]} k_2[RCN][H^+][H_2O]$$

$$k_{-1} >> k_2[H_2O]$$

assuming equlibrium is reached before

the rate determing step

$$\frac{d[RCN]}{dt} = \frac{k_1}{k_{-1}} k_2[RCN][H^+][H_2O]$$

$$\frac{d[RCN]}{dt} = -K_{eq} k_2[RCN][H^+][H_2O]$$

where: $K_{eq} = \frac{k_1}{k_{-1}}$

VITA

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