Studies on Organic Catalytic Reactions. II. The Hydration of Nitriles to Amides with Nickel Catalysts

By Ken-ichi WATANABE

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In a preliminary note,[1] it was reported that nitriles are hydrated to the corresponding amides by the catalytic action of nickel. It is notably important that the hydration of nitriles is effected in water without any acid, alkali or hydrogen peroxide and that it is generally stopped at the amide stage. This paper will describe and discuss the results of further investigation of the hydration of nitriles.

In general, aromatic nitriles are hydrated to the corresponding amides, the yields of amides range from 30 to 90 per cent of the nitriles used except in special cases. The reaction of aliphatic nitriles is somewhat complicated and is different from that of aromatic ones: the yield of the amides is comparatively lower than that from aromatic nitriles, and the hydration reaction is accompanied by side reactions forming some acidic compounds. The catalysts used are Urushibara nickel (U-Ni),[2] Raney nickel, "stabilized nickel"[3] and related substances. The general procedure for the hydration is completed by refluxing a nitrile for five to ten hours in water with a suitable amount of a nickel catalyst. During the reaction, a small quantity of ammonia is generated; this can be detected with litmus. After the reaction, the catalyst is filtered off, and the solution is evaporated to a solid mass which consists of a crude amide.

In a few cases, a very small quantity of the corresponding acid is obtained by hydrolysis. However, benzamide itself is hardly ever hydrolyzed to benzoic acid, even when it is refluxed for a long time with a newly-prepared nickel catalyst. Amines are obtained in some cases because of the hydrogenation of the nitrile with hydrogen adsorped on the nickel catalyst. The yield of amines increases largely when a solvent other than water, especially ethanol, is used. In some cases, the formation of a metal complex is observed by a presumable side reaction between the nitrile and the catalyst. In general, the hydration to an amide is predominant over the other side reactions mentioned above if the condition of the reactions is suitable: the features of this metal-catalyzed hydration are peculiar and are unlike those of acid- or base-catalyzed hydration.

The Effect of the Nature and the Position of the Substituents in Substituted Benzonitriles.— The results of experiments on the hydration of various nitriles with U-Ni-B in water are given in Table I. As is shown in the table, the hydration of substituted benzonitriles is governed largely by the nature and the position of the substituent in the benzene nucleus. It is rather remarkable that amides can not be obtained from *p*-hydroxybenzonitrile (Exp. 6), ethyl *o*- and *p*-cyanobenzoates (Exp. 13 and 14) or *p*-cyanobenzaldehyde (Exp. 16). On the other hand, a complex-formation between the nitrile (or intermediate) and the catalyst metal is observed with *p*-hydroxybenzonitrile (Exp. 6), *p*-nitrobenzonitrile (Exp. 7), *o*- and *p*-aminobenzonitriles (Exp. 9 and 10), mesitonitrile (Exp. 11), ethyl *o*- and *p*-cyanobenzoates (Exp. 13 and 14) and *p*-cyanobenzaldehyde (Exp. 16). The yield of the complexes varies with the kind of nitrile.

It has been found that there are two types of complexes, one containing zinc and the other containing nickel. Zinc complexes are obtained from *p*-cyanobenzoic acid, ethyl *o*- and *p*-cyanobenzoates and *p*-hydroxybenzonitrile. Nickel complexes are obtained from *p*-nitrobenzonitrile, *o*- and *p*-aminobenzonitriles and *p*-cyanobenzaldehyde. The former is easily decomposed to the corresponding carboxylic acids with acid or aqueous alkaliliberating ammonia. On the other hand, the latter is very stable to acid, alkali and oxidizing agents. As a whole, electron-releasing substituents retard the hydration reaction and electron-attracting substituents effect the formation of metal complexes. 3-Cyanopyridine gives rise to a very high yield of the amide, the nitrogen in the pyridine nucleus having an important electron-attracting effect on the cyano group.

A remarkable ortho effect is observed in this hydration reaction, which has been similarly recognized in the case of acid or alkaline hydration. The yield of amides is

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[1] K. Watanabe, This Bulletin, **32**, 1280 (1959).

[2] Y. Urushibara and S. Nishimura, ibid., **27**, 480 (1954); **28**, 446 (1955).

[3] T. Yamanaka and Y. Takagi, *J. Sci. Res. Inst.*, **51**, 168 (1957); **52**, 143, 224 (1958).

TABLE I. THE HYDRATION OF NITRILES TO AMIDES WITH U-Ni-B IN WATER
(4 g. of U-Ni-B was used in each run)

Exp. No.	Nitriles	Water (solvent) g.	Water (solvent) cc.	Reaction time hr.	Yield[1] of amides %	Recovered nitrile %	Other products
1	Benzonitrile	5	80	8	78	−	
2	*o*-Tolunitrile	5.5	80	12	49	−	Unidentified oil
3	*p*-Tolunitrile	7	100	8	63	−	
4	*o*-Methoxy-benzonitrile	10	100	10	33	32	Phenolic substance, amine
5	*p*-Methoxy-benzonitrile	10	100	10	65	+	Amine
6	*p*-Hydroxy-benzonitrile	4.5	100	5	—	−	Metal complex (3.5 g.), tarry matter
7	*o*-Nitrobenzo-nitrile	5	150	10	54	−	*o*-Aminobenzamide (43%), tarry matter
8	*p*-Nitrobenzo-nitrile	5	200	10	50	−	*p*-Aminobenzonitrile, metal complex (2 g.)
9	*o*-Aminobenzo-nitrile	5	100	5	ca. 45	20	Metal complex (0.5 g.) (purple)
10	*p*-Aminobenzo-nitrile	5	100	5	65	+	Metal complex (0.9%.) (yellow)
11	Mesitonitrile	7	100	10	?	The most part	Metal complex (0.6 g.), amine
12	Benzyl cyanide	10	150	10	52	30	Amine
13	Ethyl *p*-cyano-benzoate	5	150	8	—	>40	Metal complex (2 g.)
14[2]	Ethyl *p*-cyano-benzoate	5	150	10	—	+	Metal complex (2 g.), unidentified oil
15	*p*-Cyano-benzoic acid	5	100	12	—	−	Metal complex
16	*p*-Cyano-benzaldehyde	5	150	8	—	−	Metal complex (5 g.)
17	α-Naphthonitrile	7	100	8	19	35.7	Amine
18	Acetonitrile	7	100	5	47	−	Acids
19[3]	Enanthonitrile	3.6	50	5	38	+	
20	Adiponitrile	10	100	10	14	−	Unidentified oil, acidic substance
21	3-Cyanopyridine	7	100	10	89	−	

1) Yield of amides was calculated from the weight of amides obtained.
2) It was almost the same with a reaction on *p*-cyanobenzoic acid.
3) Two grams of the catalyst was used.

more or less diminished with ortho-substituted benzonitriles, such as *o*-tolunitrile (Exp. 2), *o*-methoxybenzonitrile (Exp. 4), *o*-nitrobenzonitrile (Exp. 7), *o*-aminobenzonitrile (Exp. 9), mesitonitrile (Exp. II), ethyl *o*-cyanobenzoate (Exp. 13) and α-naphthonitrile (Exp. 17), the largest effect being observed with mesitonitrile. The reaction velocity becomes slower, and often a considerable quantity of the starting materials is recovered unchanged. In some cases, unfavorable side reactions are alternated.

The Effect of the Nature of the Catalyst.—When *o*-nitrobenzonitrile was hydrogenated with a nickel catalyst in either the liquid[4] or the vapor phase, it was reported that a considerable quantity of *o*-aminobenzamide was formed by the hydration of the nitrile group.[5] It has been presumed that the hydrogenating activity of the nickel catalyst is largely depressed by poisoning with the amino group produced by the reduction of the nitro group,[6] and that the nitrile group is hydrated with water produced by the hydrogenolysis of the nitoro group or originally present in the solvent. The present investigation shows that such is the case, since the ability of nickel catalysts to effect the hydration of nitrile group has been proved. Ordinary nickel catalysts for

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[4] H. Rupe, *Helv. Chim. Acta*, **8**, 832 (1925).

[5] K. Watanabe, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **76**, 398 (1955); *Chem. Abstr.*, **51**, 17815 (1957).

[6] K. Watanabe, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **77**, 225 (1956); *Chem. Abstr.*, **51**, 17816 (1957).

hydrogenation are generally available for the hydration of nitriles.

In this connection, precipitated nickel, precipitated copper, nickel oxide, cupric oxide and Urushibara copper (U-Cu) were also tested with relation to the hydration of benzonitrile. The results of representative experiments are shown in Table II. The highest yield of benzamide was given with U-Ni-B, followed by those with U-Ni-A, Raney nickel and stabilized

TABLE II. THE HYDRATION OF BENZONITRILE TO BENZAMIDE WITH VARIOUS CATALYSTS

Exp. No.	Catalysts	g.	Weight of benzonitrile g.	Solvent	cc.	Reaction time hr.	Yield of benzamide %	Recovered benzonitrile g.	Other products
1*	U-Ni-B	4	5	Water	80	8	78	–	
2	U-Ni-A	3	5	Ethanol	60	8	5	1.6	Amine
3	U-Ni-A	3	3	Water	80	8	71.5	–	
4	U-Ni-BA	4	5	Ethanol	80	9	5	1.7	Amine
5	U-Ni-BA	4	5	Water	80	9	34.5	1.4	Amine
6	U-Cu-A	4	5	Ethanol	60	8	+	0.8	Amine
7	U-Cu-A	4	5	Water	100	8	24	–	
8	U-Cu-B	4	5	Ethanol	60	8	7	–	Amine, unidentified oil and crystals
9	ppt. Ni (Zn)	4	10	Ethanol	100	13	–	–	Complex of amine and nickel (6.8 g.), amine-HCl (3 g.), unidentified oil
10	ppt. Ni (Zn)	4	10	Water	150	10	–	–	Complex of amine and zinc, unidentified crystals
11	ppt. Cu (Zn)	4	5	Ethanol	80	8	7	–	Amine-HCl (1.7 g.), unidentified oil
12	Reduced Ni	4	5	Water	80	16	10.7	>0.8	
13	Raney Ni (W-4)	4	10	Ethanol	100	8	+	>5	
14	Raney Ni (W-4)	4	10	Water	100	8	65	–	
15	Stabilized Ni	10	2	Water	50	6	70	–	
16	NiO+CuO	5	5	Ethanol	80	10	5	2.5	

* Same as Exp. I, Table I
U-Ni-B in ethanol: see Table III

TABLE III. THE HYDRATION OF BENZONITRILE TO BENZAMIDE IN VARIOUS SOLVENTS
(Catalyst: U-Ni-B)

Exp. No.	Weight of benzonitrile g.	Weight of catalyst g.	Solvent	cc.	Reaction time hr.	Yield of benzamide %	Recovered benzonitrile g.	Other products
1	5	2	Water	80	9	57	+	
2	5	4	Water	80	11	73	–	
3	5	4	Water	80	8	78	–	
4	15	8	Water	150	10	74	–	
5	5	4	Ethanol	60	9	11	–	Amine-HCl (4 g.), tarry matter
6	5	8	Ethanol	100	2.5	19	0.6	Amine-HCl (2 g.), tarry matter
7	10	8	Ethanol	100	8	19	1	Amine-HCl (3.6 g.), tarry matter
8	10	4	Methanol	100	10	12	ca. 4	Amine
9	5	4	1-Butanol	80	4	7	–	Amine-HCl (3.4 g.), unidentified oil
10	10	8	Dioxane	100	12	34	+	Amine-HCl (1.5 g.), unidentified crystal; m. p. 220°C

* Sample as Exp. I, Table I

nickel. The other substances mentioned above gave poor results as catalysts for the hydration, and they sometimes caused unexpected side reactions.

It should be noted that the procedure for the preparation of U-Ni may be simpler for the hydration than for hydrogenation. Common city water serves well enough for preparing the catalyst, and it does not matter if the catalyst is exposed to air during the preparation. To prepare Raney nickel (W-4) for the hydration, caution is unnecessary with regard to the temperature, air and water. The stabilized nickel and the reduced nickel catalysts are less active than the U-Ni's and Raney nickel. It was found that the precipitated nickel or copper is of no use at all for the hydration of nitriles to amides, a large amount of complexes of corresponding amines and zinc being formed.

The results of the experiments indicate that the hydrating activity of the nickel catalysts depends on the size of the crystallites of the catalysts. It is known that the approximate sizes of the crystallites of U-Ni-A, U-Ni-B, U-Ni-BA, U-Cu and reduced nickel are 40 Å 40 Å, 120 Å, 260 Å and 350 Å respectively. The yields of benzamide obtained with these catalysts follows the above-mentioned order. If too small a quantity of a catalyst is used, or if the reaction time is insufficient for the hydration, the nitrile is sometimes recovered unchanged in a considerable quantity. Gas chromatographic research shows that about 90 per cent of benzonitrile is changed after five hours with a U-Ni-B catalyst. When the catalyst is not so active, a large quantity is necessary for a satisfactory hydration, as is shown by Exp. 15 and 16 in Table II.

In the previous experiments, any specific behavior of thiophene or pyridine as a promoter of the catalyst was examined, and it was shown shat a small quantity of thiophene or pyridine exhibited no promoter action in an ethanolic solution but, rather, had an unfavorable effect. In the present investigation, however, some different information was put forward on this subject. It is noteworthy in Table I that nitriles of basic character, such as 3-cyanopyridine and *p*-aminobenzonitrile, give good yields of amides, whereas those of an acidic character, such as *p*-hydroxybenzonitrile and *p*-cyanobenzoic acid, give no hydration products. The aliphatic nitriles, some of which are hydrolyzed to acids during the reaction, also give unfavorable results, as in the normal hydration. From these results, it may be inferred that the hydration of nitriles is due to the catalytic action of the basic contact sites (active center) of the nickel catalysts.

It is assumed that a nickel catalyst acts in two different ways, exhibiting acidic and basic functions. It has been suggested that the catalytic hydrogenation of nitriles and nitro groups is due to the acidic contact sites of the catalyst,[7] as is the reductive dehydroxymethylation of primary alcohols.[8] On the other hand, the catalytic hydrogenation of carbonyl groups[9] and the dehydroxylation of alcohols are attributed to basic sites.[8] In the hydration of nitriles, acidic substances or acidic parts of the nitrile molecules may cover the basic sites of the catalyst, resulting in the depression of the hydration reaction. Ammonia, generated by the hydrogenolysis of nitriles during the reaction, and basic parts of the nitrile molecules may cover the acidic sites of the catalyst and accentuate the catalytic activity of the basic sites to realize a favorable hydration. According to the studies of the reaction mechanism of the hydrolysis of nitriles with acid or alkali, the hydration has been assumed to be initiated at the carbon atom of a nitrile group, endowed with a carbonium character. In the catalytic hydration of nitriles, the reaction may be similarly initiated at the carbon atom attached to the basic sites of the catalyst. Our preliminary test for the effects of pyridine and thiophene on the hydration of benzyl cyanide proved that the former increases the yield of the amide, while the latter decreases it. This will be discussed in a subsequent report of this series.

The Effect of Solvents.—Methanol, ethanol, 1-butanol, dioxane and water were examined for as possible solvents for the catalytic hydration of benzonitrile. Water was proved to be the most excellent of all. When any other solvent than water is used, the nitrile group is hydrogenated more or less by hydrogen adsorped on the catalyst; sometimes undesirable side reactions are caused. The reactions in water generally give good yields of amides. The results of the experiments are listed in Table III, while the results of the hydration in water and ethanol are compared in Table II. It is noteworthy that water suppresses the catalytic activity for hydrogenation and emphasizes the catalytic activity for hydration.

Experimental

The Preparation of Catalysts for the Hydration of Nitriles.—*U-Ni-A.*—To 40 g. of commercial zinc

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[7] K. Watanabe, *J. Chem. Soc. Japan, Pure, Chem. Sec.* (*Nippon Kagaku Zassi*), **78**, 1478 (1958); *Chem. Abstr.*, **54**, 1370 (1960).

[8] H. Pines, M. Shamaienger and W. S. Postal, *J. Am. Chem. Soc.*, **77**, 5099 (1955).

[9] D. R. Levering, F. L. Morritz and E. Lieber, ibid., **72**, 1190 (1950).

dust in a 1000 ml. Erlenmeyer flask, a small quantity of was added, and the mixture was heated to boil. In another vessel, 40 ml. of a nickel chloride solution containing 16 g. of $NiCl_2\cdot 6H_2O$ was heated to 60°C and then added to the zinc dust with vigorous shaking. A violent exchange reaction took place, depositing nickel on the surface of the zinc. When the generation of hydrogen had ceased, about 640 ml. of 13% acetic acid, prepared from 83 ml. of CH_3COOH and 560 ml. of water and heated to about 70°C in advance, was added gradually while the mixture was shaken well, lest the contents should overflow as a results of the vigorous generation of hydrogen. The whole was occasionally shaken for about twenty minutes, until the liquid turned slightly green; then the mixture was diluted with cold water. The acid solution was decanted off, and the residue was washed with water several times by decantation until the washing became neutral to litmus. The catalyst thus prepared was used directly for the reaction in water. For use in other solvents, it was collected by filtration and pressed between filter paper before adding it to the solvents. The catalyst thus obtained contains about 3 g. of nickel.

U-Ni-B.—For the preparation of U-Ni-B, 640 g. of a sodium hydroxide solution (70 g. of sodium hydroxide and 570 ml. of water) were used to digest the precipitated nickel. The procedure was the same as for U-Ni-A in other respects. The finished catalyst was repeatedly washed with water until the washing became neutral to phenolphthalein paper. The U-Ni-B thus obtained contains 4 g. of nickel and is more voluminous than U-Ni-A.

U-Ni-BA.—To 20 g. of aluminum grains of 40∼80 mesh in a 1000 ml. Erlenmeyer flask, a small quantity of hot water was added, and then 40 ml. of a hot nickel chloride solution containing 16 g. of $NiCl_2\cdot 6H_2O$ was added. The whole was occasionally shaken until the reaction mixture became slushy. The exchange reaction was controlled by either cooling with cold water or heating with hot water. The precipitate was washed with cold water by decantation, and 500 g. of a 20% sodium hydroxide solution (100 g. of sodium hydroxide and 400 ml. of water), heated to about 60°C in advance, was gradually added. Because of the vigorous exothermic reaction, the contents were shaken well. The aluminum dissolved completely in a short time. The solution was decanted off, and the residue was washed three or four times with cold water by decantation until the washings became neutral to phenolphthalein. The catalyst thus obtained contains about 4 g. of nickel.

U-Cu.—U-Cu was prepared by almost the same procedure as that used for U-Ni, cupric chloride being used instead of nickel chloride. The precipitated copper could not be digested well with aqueous alkali, but it was digested well with aqueous acetic acid.

Precipitate Nickel (or Copper).—The precipitated nickel (or copper), prepared from nickel (or copper) chloride and zinc dust, was used directly after being washed with only water. The catalyst is very voluminous and contains much more adsorbed hydrogen.

Stabilized Nickel. — This is a kind of reduced nickel supported on kieselguhr and stabilized by treatment with carbon dioxed. The KSY-6 FC type (Nikko Shokai, Tokyo) was used for the hydration of benzonitrile.

The Hydration of Nitriles.—The procedure for the hydration of benzonitrile to benzamide with U-Ni-B (Exp. I, Table I) is shown as an example. The nickel catalyst (containing 4 g. of nickel) in 80 ml. of water was placed in a 200 ml. round flask, and 5 g. of benzonitrile was added. The flask was fitted with an Allihn condenser. The mixture was refluxed vigorously for about eight hours until the oil drops of benzonitrile on the water disappeared. The catalyst was separated by filtration while hot and washed with hot water and ethanol. The filtrate, admixed with the washings, was evaporated on a water bath. Benzamide was obtained in white crystals. The yield was 4.5 g. (78%). The crude amide, although it was fairly pure, was recrystallized from hot water with a small quantity of active charcoal. M. p. 127∼128°C. It was identified by hydrolyzing to benzoic acid with alkali.

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Department of Chemistry
Faculty of Science
Tokyo Metropolitan University
Setagaya-ku Tokyo