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Studies of Organic Catalytic Reactions. V.[1)]
The Function of the Chelates formed in the Hydrolysis of 2-Cyanopyridine with Metal Oxide Catalysts

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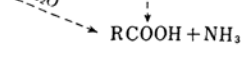
When 2-cyanopyridine is refluxed with water in the presence of nickel or copper oxide, it is easily hydrolyzed and affords a chelate compound of the acid with nickel or copper. On the other hand, 3- or 4-cyanopyridine affords only the corresponding free amide by the same reaction. The interfering effect of thiophene is not observed in the reaction of 2-cyanopyridine, but it is observed in the case of the 3- or 4-cyanopyridine. When 2-cyanopyridine is refluxed with an aqueous solution of nickel or cupric chloride, it is hydrated to form a chelate of the amide with nickel or copper. These chelates are hydrolyzed with the metal oxides in water to afford the chelates of the acid. Pyridine-2-carboxylic acid amide is also hydrolyzed to the chelate of the acid, but the hydrolysis of the 3- or 4-amide isomer does not occur under the same conditions. The four chelates of the acid and amide are excellent catalysts for the hydration of 2-cyanopyridine, giving the free amide in a high yield. From these facts, it may be presumed that: 1) The adsorption of 2-cyanopyridine or its amide on the catalysts is stereospecific and results in the formation of a kind of chelate. Upon forming the acid, the metal atom of the catalyst is drawn out of the catalyst to form the chelate. 2) The metal oxide is the most suitable catalyst for the chelate-type adsorption and for the chelate formation. 3) The chelate of the acid formed during the hydrolysis of 2-cyanopyridine acts as another catalyst in the formation of the free amide, then, the amide is further converted into the chelate of the acid by means of the metal oxide catalyst.

Nitriles are hydrated to the corresponding amides by refluxing them with nickel catalysts in water.[2)] The hydration mechanism of nitriles has previously been reported.[3)] In this reaction, a small quantity of the corresponding acid is obtained, but this side reaction is not remarkable, especially in the hydration of aromatic nitriles. It is notable, however, that in the hydration of 2-cyanopyridine a con-



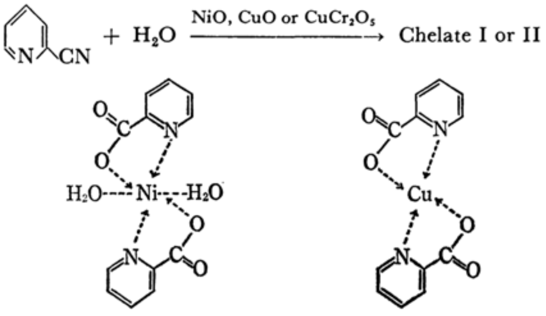
[1)] Paper IV: "A Redox Reaction between Unsaturated Organic Compounds and Primary Alcohols in the Presence of Nickel Catalysts," K. Sakai, T. Ito and K. Watanabe, This Bulletin, **39**, 2230 (1966).

[2)] K. Watanabe, *ibid.*, **37**, 1325 (1964).

[3)] K. Watanabe and K. Sakai, *ibid.*, **39**, 8 (1966).

siderable amount of the acid-nickel complex was obtained, along with the corresponding amide. In the hydration of 3-cyanopyridine, nicotinamide was obtained in a high yield (90%), while no formation of nickel complex was detected.

In this paper, first of all, it will be reported that the metal complex obtained in the hydration of 2-cyanopyridine has been proved to be a chelate compound of pyridine-2-carboxylic acid with the nickel atom of the catalysts (Chelate I). It has also been found that the ordinary metal oxide catalysts for hydrogenation mainly afford the corresponding chelates with 2-cyanopyridine. For example, chelate II is obtained with the copper oxide catalyst in the same manner. The chelates I and II were identical with those obtained by other workers.[4,5]

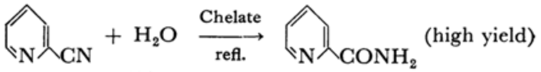


I (Blue Crystal) II (Violet Crystal)

Further, the correlation of the hydrolysis mechanism on the surface of catalysts with the formation of the chelates has been investigated, and some new facts will be presented and discussed.

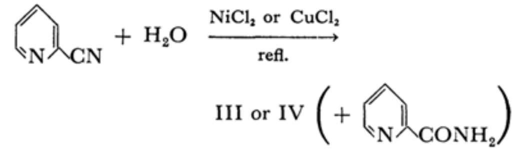
It is widely known that the metal chelates show catalytic activities in many organic and biological reactions. However, little attention has been paid to the catalytic function with regard to the reaction mechanism on the surface of catalysts from the point of view of chelate formation. In order to elucidate this problem, the hydration of 2-, 3- and 4-cyanopyridine was studied. In the hydration of 3- and 4-cyanopyridine with some catalysts, the corresponding amides were obtained in high yields, whereas 2-cyanopyridine was generally converted into the corresponding acid in the form of the nickel or copper chelate (I or II) with the same catalysts.

The catalysts used were Urushibara nickel-B (U-Ni-B),[*1] a stabilized nickel (S-Ni),[*2] nickel oxide, Raney copper (R-Cu), copper chromium oxide, copper oxide, and copper powder. On the other hand, it has been found that the chelates (I and II) have a high catalytic activity in the hydration of 2-cyanopyridine, affording the corresponding amide, but that they are not active in the further hydrolysis to the acid.



(Chelate: I, II, III or IV)

It has been also found that when 2-cyanopyridine is refluxed with an aqueous solution of nickel or cupric chloride, hydration takes place to form the chelate of the corresponding amide (pia H) with nickel or copper (III or IV), while no reaction occurs in the case of 3- or 4-cyanopyridine. Chelates III and IV were identical with those obtained by Yamasaki and Sekizaki.[6] The chelates III and IV show catalytic activities in the hydration of 2-cyanopyridine to amide as do I and II. The chelates I—IV are all so soluble in water that the hydration reactions with these chelates can be carried out as homogeneous catalytic reactions in aqueous solutions.



$[Ni(pia\ H)_2]Cl_2 \cdot 2H_2O$ III (Blue Crystal)

$[Cu(pia\ H)_2]Cl_2 \cdot 2H_2O$ IV (Violet Crystal)

The results of the hydrolysis of 2-cyanopyridine with various kinds of catalysts in water are shown in Table 1. Soon after the reaction was started, the originally colorless reaction mixture turned light purple. After thirty minutes, the color became deeper, and there was a vigorous generation of ammonia gas. The purple coloration indicates the formation of chelate I or II, while the generation of ammonia gas shows the occurrence of the hydrolysis of the nitrile group. It is assumed that the nitrile is first converted into the amide, and that then the amide is gradually converted into the chelate. Evidence for this is shown in Exp. 2, which presents a comparison with Exp. 3 (Table 1).[*3]

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4) R. W. Green, *J. Am. Chem. Soc.*, **79**, 5608 (1957).

5) M. Páris, G. Thomas and J.-C. Merlin, *Bull. Soc. Chim. France*, **28**, 715 (1961).

[*1] The nickel precipitated on the zinc dust from a nickel chloride solution, treated with a sodium hydroxide solution and water, is active as Raney nickel; K. Watanabe, This Bulletin, **37**, 1325 (1964).

[*2] Stabilized nickel S-10: Obtained from Nikko Scientific & Chemical Industry Co., Ltd., Tokyo. This is a kind of nickel kieselguhr catalyst (50%) prepared from nickel oxide and stabilized with inert gas and diluted oxygen. The catalyst was used directly for the reaction without any treatment.

6) K. Yamasaki and M. Sekizaki, This Bulletin, **38**, 2206 (1965); *Nippon Kagaku Zasshi*, (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **87**, 1053 (1966).

[*3] In the reaction with the copper oxide catalyst, a part of the reaction mixture was analyzed by visible and ultraviolet spectra after a fifty-minute reaction. The existence of both pyridine-2-carboxylic acid amide and the chelate II was observed. After a reaction of several hours, the reaction mixture consisted almost entirely of the chelate II. Free pyridine-2-carboxylic acid was not detected in any case. Therefore, it seems most reasonable that the pyridine-2-carboxylic acid is not formed, or that, as soon as it is formed, the formation of chelate II occurs extremely fast. When the pyridine-2-carboxylic acid was refluxed with nickel or copper oxide in water, the corresponding chelate, I or II, was easily obtained.

TABLE 1. THE HYDRATION AND CHELATE-FORMATION WITH 2-CYANOPYRIDINE IN THE PRESENCE OF VARIOUS CATALYSTS

Exp. No.	Catalysts	Sample g	Sample g	Solvent (water) m*l*	Reaction time hr	Yield of amide %	Yield of chelate %
1	U-Ni-B	4	5	100	10	85	15[1]
2	NiO	2	0.5	20	0.5	60	10[1]
3	NiO	2	0.5	20	10	Trace	90[1]
4	S-Ni	4	5	100	10	10	70[1]
5	R-Cu	4	5	100	10	50	+[2]
6	Cu-powder	2	0.5	20	8	75	+[2]
7	$CuCr_2O_5$	4	5	100	10	—	90[2]
8	CuO	2	0.5	20	8	10	70[2]
9	Chelate I	0.5	0.5	15	7	95	+[3]
10	Chelate II	0.5	0.5	15	7	90	+[4]
11	$NiCl_2 \cdot 6H_2O$	0.3	0.5	15	7	20	65[5]
12	$NiCl_2 \cdot 6H_2O$	0.5	0.5	20[6]	5	—	55[7]

1) Chelate I 2) Chelate II 3) Recovered chelate I 4) Recovered chelate II 5) Chelate III
6) *n*-Heptane instead of water 7) Along with recovered nitrile, *ca.* 40%

TABLE 2. THE HYDRATION OF 2-, 3- AND 4-CYANOPYRIDINE WITH VARIOUS CATALYSTS
A half gram of cyanopyridine, 2 g of the catalyst and 20 m*l* of water were used in each run.

Expt.[1] No.	Cyanopyridine isomers[2]	Catalysts	Reaction time hr	Amide %	Chelate %	Recovered nitrile %
1	2-	NiO	10	Trace	90 (I)	—
2	2-	CuO	8	10	70 (II)	—
3	2-	Cu-powder	8	75	+	—
4	3-	NiO	7	90	—	—
5	3-	CuO	7	10	—	70
6	3-	Cu-powder	7	45	—	40
7	4-	NiO	7	90	—	—
8	4-	CuO	7	20	—	60
9	4-	Cu-powder	7	50	—	30
10	2-	NiO(+ )[3]	7	—	80 (I)	—
11	3-	NiO(+ )	7	60	—	20
12	4-	NiO(+ )	7	60	—	20
13	2-	Cu-powder(+ )	5	70	10 (II)	—

1) Exps. 1—3 are the same with that in Table 1 (Exps. 3, 8 and 6).
2) Cyanopyridine isomers: 2-, 3- and 4- mean 2-, 3- and 4-isomers.
3) Thiophene: 0.3 m*l* of thiophene was added in Exps. 10—13.

Four chelates (I—IV) were identified by a study of their infrared[5,6] and ultraviolet[4,6] absorption spectrum analyses, the chelates I and II were also identified by elementary analysis (see Experimental Section). These chelates were easily obtained, too, when pyridine-2-carboxylic acid or its amide was added to an aqueous solution of nickel (II) or cupric chloride (the ordinary method).[4-7] It is of interest to note that the chelate III is easily hydrolyzed to the chelate I by refluxing it with nickel oxide in water (the chlorine ion is not found in the chelate I).

As is shown in Exps. 3, 7, and 8 in Table 1, it is obvious that the metal oxide catalysts (MO) are remarkably excellent for the formation of the chelates. Since the surface of S-Ni was treated with diluted oxygen in inert gas to some extent, the catalyst may be regarded as a kind of MO (Exp. 4). On

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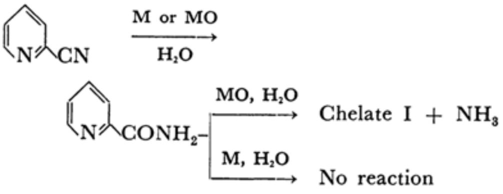
[7] "Organic Syntheses," Coll. Vol. III, p. 740 (1955).

the contrary, when U-Ni (Exp. 1), R-Cu (Exp. 5), and copper powder (Exp. 6) were used, the main product was the free amide. It may be presumed that the function of metal oxide catalysts (MO) is different from that of metal catalysts (M) in the hydrolysis of cyanopyridines. Actually, MO is less active than M for the ordinary catalytic hydration and hydrolysis of nitriles.[2)] It may be assumed that the surface of MO affords a suitable structure for the formation of chelate-type adsorption with 2-cyanopyridine, and that the metal atom (such as the ion) of the catalyst may be drawn out easily from the surface of the catalyst to form the chelate by the polarization of M-O.

To elucidate this difference further, pyridine-2-carboxylic acid amide was hydrolyzed with M and with MO. In the reaction with MO, the chelate I was easily obtained in a high yield, with a simultaneous generation of ammonia gas, while no reaction occurred with M.[*4] When 3- and 4-amide (isomers) were hydrolyzed with M or MO in the same manner, the reaction did not proceed. 3- and 4-Cyanopyridine were also hydrated in almost the same way as in the reaction of 2-cyanopyridine, using nickel oxide, copper oxide, and copper powder. The results of representative experiments are shown in Table 2. In Exps. 1—9 in Table 2, the chelate I or II was obtained in a high yield only in the reaction of the 2-isomer, while the reaction of 3- or 4-isomer was generally stopped at the amide stage. It has been reported[8)] that not so great a difference could be observed between the reactivity and activation energies of the 2- and 4-amide isomers in ordinary hydrolysis. Consequently, it is conceivable that the catalytic function of MO in the hydrolysis of 2-cyanopyridine reveals a specific factor of behavior in the steric and electronic interaction between the surface of the catalyst and the 2-cyanopyridine (or its acid amide) adsorbed on it.



It is interesting to note that, when a large quantity of thiophene was added to the catalysts before the cyanopyridines were added, the hydration reaction was interfered with in the cases of the 3- and 4-isomers (Exps. 11 and 12 in Table 2), while no effect of thiophene was observed on the hydrolysis of the 2-isomer (chelate formation) and the yield of the chelate was high (Exp. 10). When the copper catalyst was employed for the reaction of the 2-isomer, the addition of thiophene promoted the formation of the chelate II (Exp. 13) more than when no thiophene was used (Exp. 3). An adsorption model of 2-cyanopyridine is shown in Fig. 1. It seems reasonable that the nitrogen atom of the pyridine nucleus and the nitrile group of the 2-isomer are adsorbed simultaneously on the surface of the catalysts from one side as a result of their geminate positions. In this case, the molecule might not be adsorbed in a flat and uniform manner on the surface of catalysts. Accordingly, if the adsorption of the nitrogen atom of the pyridine nucleus is stronger than that of the sulfur atom of thiophene, the interfering effect of thiophene in the adsorption and hydrolysis of the nitrile group in the 2-isomer would not occur. An assumed adsorption model of 3- or 4-cyanopyridine on the catalysts is also shown in Fig. 1. The nitrogen atom of the pyridine nucleus also interacts with the catalysts, while the nitrile group is adsorbed on the catalysts in another way. When thiophene is added to the catalysts, it may be adsorbed on the catalysts, thus suppressing the interaction of the nitrile group with the catalysts as in the case of the hydration of ordinary nitriles.[8)] In this case, the adsorption of the nitrogen atom of the pyridine nucleus is not essentially concerned with the interfering effect of thiophene.

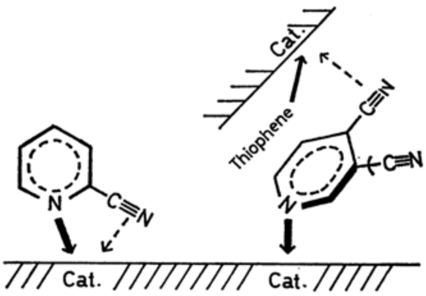


Fig. 1. Stereospecific adsorption of cyanopyridines.
⟶ Strong interaction
- - → Weak interaction

As has been mentioned above, 2-cyanopyridine is hydrated to the corresponding amide chelate (III or IV) by refluxing it with a nickel or cupric chloride solution. When a large excess of the nickel or cupric chloride was employed in this reaction, 2-cyanopyridine was completely converted into the amide chelate.[*5] However, when a small quantity of the nickel chloride was employed, the nickel chloride was first consumed to form the chelate III, and then the chelate formed worked as a catalyst in the hydration of unreacted nitrile to form the corresponding free amide (Exp. 11 in Table 1). No

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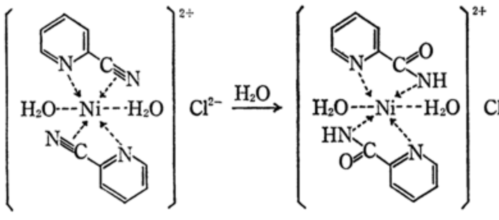
[*4] When benzamide was hydrolyzed with a freshly-prepared nickel catalyst, the reaction did not take place.

8) H. H. Jellink and J. R. Urevin, *J. Phys. Chem.*, **57**, 900 (1953).

[*5] During the reaction of 2-cyanopyridine with a large excess of cupric chloride,the reaction mixture was analyzed by means of a study of its ultraviolet absorption sectra. Only the corresponding amide chelate was detected.

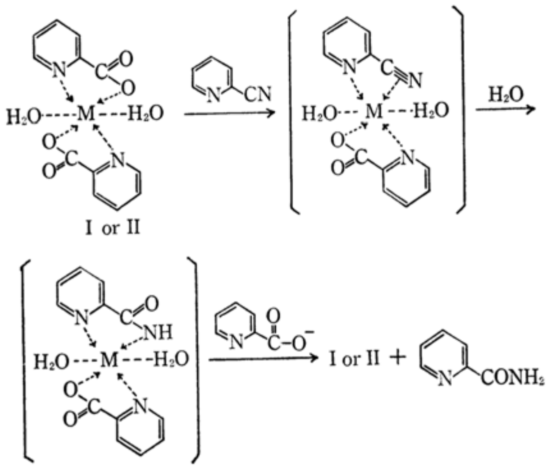
reaction of 3- or 4-cyanopyridine occurred with a metal chloride solution, and the unreacted nitrile was recovered. In these homogeneous catalytic reactions, the catalysts should be the metal ions. The fact that the reaction proceeded only with 2-cyanopyridine suggests that the interaction of the 2-isomer with the metal ion is stereospecific, and that the hydration may occur to form the chelate III.



III

Ion-catalyzed hydration of 2-cyanopyridine.

The fact that all of the four chelates (I—IV) work as specific catalysts only for the hydration of the 2-isomer to give the free amide suggests that the reaction occurs through the exchange of the ligand of the chelate of the 2-isomer.



Chelate-catalyzed hydration of 2-cyanopyridine (Same in III or IV).

Chelate I is more stable than chelate III. Therefore, it is apparent that 2-cyanopyridine or its acid amide is not further hydrolyzed to the acid (acid chelate) by any of the four chelates.[*6]

It may be concluded that the hydrolysis (or hydration) of 2-cyanopyridine with MO is stereospecific and has an essential correlation to the formation of the chelates. The chelate (I or II) produced during the hydrolysis may act as another catalyst in the formation of the free amide, which is then further converted into the chelate (I or II) by means of MO. After all, as long as any chelate (I—IV) exists or is formed in this hydrolysis (or hydration) of 2-cyanopyridine, the nitrile may be converted to the free amide.

Experimental

Catalysts. The copper chromium oxide catalyst was prepared by the Adkins method. Commercial copper powder, obtained from the KOSO Scientific & Chemical Industry Co., Ltd., Tokyo, was used as the catalyst without any treatment. Commercial copper oxide, obtained from Merck's Reagenzien, was ground into a powder and thus used as a catalyst. The nickel oxide catalyst was prepared by the careful decomposition of nickel carbonate at *ca.* 250—300°C.

Materials. 2-Cyanopyridine (mp 29°C) and 3-cyanopyridine (mp 49—50°C) were obtained from the Aldrich Chemical Co., Inc., U.S.A. They were almost entirely pure without any purification. 4-Cyanopyridine[9] was prepared by the dehydration of the corresponding amide with phosphorus pentachloride, (mp 79°C). α-Picoline was oxidized to pyridine-2-carboxylic acid with potassium permanganate, and the corresponding amide (mp 107°C) was prepared through esterification.[10]

The Hydration of 2-Cyanopyridine with the Nickel Oxide Catalyst (Exp. 3 in Table 1). A half gram of 2-cyanopyridine and 20 m*l* of water were refluxed vigorously in the presence of 2 g of a nickel oxide catalyst for ten hours. After a thirty-minute reaction, a small quantity of ammonia gas was generated, as detected with litmus paper. During the reaction, the colorless contents turned blue. After the reaction was over, the catalyst was separated by filtration while hot and washed with hot water. When the filtrate, combined with the washings, was evaporated carefully on a water bath, blue crystals were obtained. The product was dissolved in hot methanol and then separated by column chromatography using active alumina (*ca.* 100—200 mesh), developed with methanol. After the elution of the methanol fraction (light brown) had been obtained, the elution of the water fraction (blue) was obtained. The methanol elution was then evaporated carefully on a water bath. A small quantity of blue crystals was thus obtained; they were washed with ether, and pyridine-2-carboxylic acid amide was obtained from the ether solution, mp 108—109°C. When the amide was heated with concentrated hydrochloric acid, pyridine-2-carboxylic acid hydrochloride was obtained, mp 229.8—232°C. When the blue solution (water fraction) was evaporated carefully on a water bath, 0.67 g of a blue solid was obtained, mp>250°C. When this solid was heated on a gas burner, black ashes were obtained. The nickel ion was identified by means of the dimethyl glyoxime reaction. When it was heated with concentrated hydrochloric acid, pyridine-2-carboxylic acid hydrochloride was obtained. Elementary analysis (samples were dried at 56°C in reduced pressure

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[*6] This means that the exchange of the ligand of I or II (acid chelate) for the free amide does not occur because of the stability of I; namely, the reverse reaction does not proceed. In the case of III or IV (amide chelate), there is no change in the results, although the exchange of the ligand may occur for the free amide.

9) C. R. Hauser and G. A. Reynolds, *J. Org. Chem.*, **15**, 1224 (1950).

10) O. Engler, *Ber.*, **27**, 1784 (1894).

for one hour.): Found: C, 41.14; H, 3.84; N, 8.10%. Calcd for $C_{12}H_8N_2O_4Ni \cdot 2H_2O$: C, 42.5; H, 3.55; N, 8.25%. It was also identified by infrared,[5] ultraviolet,[4] and visible absorption spectrum analyses, and found to be the nickel chelate of pyridine-2-carboxylic acid. IR: ν_{max}^{KBr} 1630, 1595, 1570, 865 cm^{-1}. UV: $\lambda_{max}^{H_2O}$ 610, 274, 267, 260 mμ. The yield of nickel chelate was *ca.* 90%. Its paramagnetic character[11] was also observed. It was soluble in water, methanol, ethanol, and dilute hydrochloric acid, and slightly soluble in a dilute solution of sodium hydroxide; a part of the chelate was decomposed.

The Hydration of 2-Cyanopyridine with the Copper Oxide Catalyst (Exp. 8 in Table 1). A half gram of 2-cyanopyridine, 20 m*l* of water, and 2 g of the copper oxide catalyst were refluxed as in Exp. 3 in Table 1. After a thirty-minute reaction, the generation of a small quantity of ammonia was observed and the colorless contents turned greenish blue. After an eight-hour reaction, the catalyst was separated by filtration while hot and washed with hot water. Then the filtrate was evaporated carefully on a water bath; the violet solid thus obtained was washed with ether. The white solid of pyridine-2-carboxylic acid amide was obtained from the ether washings. The yield of amide was *ca.* 10%. Almost all of the violet solid was insoluble in ether and was obtained as violet crystals, 0.45 g, mp> 250°C. When it was heated on a gas burner, black ashes were obtained. When this compound was recrystallized with hot water, bluish-violet needle crystals were obtained. Elementary analysis (samples were dried at 56°C under reduced pressure for one hour.): Found: C, 43.21; H, 3.49; N, 8.61%. Calcd for $C_{12}H_8N_2O_4Cu$: C, 43.80; H, 3.66; N, 8.55%. It was also identified by infrared,[5] ultraviolet,[4] and visible absorption spectrum analyses, and found to be the copper chelate of pyridine-2-carboxylic acid. IR: ν_{max}^{KBr} 1635, 1608, 1595, 1570, 865 cm^{-1}. UV: $\lambda_{max}^{H_2O}$ 630, 274, 267, 260 mμ. The yield of copper chelate was *ca.* 70%. Its paramagnetic character was also observed.[12] It was soluble in water, hot methanol, ethanol, dilute hydrochloric acid, and a dilute solution of sodium hydroxide. A dilute hydrochloric acid solution of the chelate was greenish yellow, while a dilute sodium hydroxide solution of it was blue-violet.

The Hydration of 2-Cyanopyridine with Nickel Chelate of Pyridine-2-Carboxylic Acid, Chelate I (Exp. 9 in Table 1). A half gram of 2-cyanopyridine and 20 m*l* of water were refluxed with 0.5 g of nickel chelate of pyridine-2-carboxylic acid for seven hours. The blue contents were almost homogeneous. After the reaction, the contents were carefully evaporated on a water bath; a blue solid was thus obtained. The separation of the products was almost the same as in the case of Exp. 3 in Table 1. The colorless elution of the methanol fraction gave white crystals, pyridine-2-carboxylic acid amide, mp 108—109°C (95% yield). The blue elution of the water fraction gave the nickel chelate of pyridine-2-carboxylic acid, which was used as the catalyst. The experiments with other chelates (II—IV) were almost the same.

The Hydration of 2-Cyanopyridine with Nickel Chloride (Exp. 11 in Table 1). A half gram of 2-cyanopyridine and 15 m*l* of water were refluxed with 0.3 g of nickel chloride for seven hours. During the reaction, the greenish contents turned into a blue solution, and ammonia gas was not generated. After the reaction was over, the contents were evaporated carefully on a water bath; a blue solid was thus obtained. The solid was then washed with ether, and pyridine-2-carboxylic acid amide was obtained from the ether washings, mp 103—105°C. The yield of amide was 20%. Almost all the blue solids were insoluble in ether. When this compound was recrystallized with hot water, greenish-blue needle crystals were obtained. They were identified by infrared absorption spectrum analysis, and found to be the nickel chelate of pyridine-2-carboxylic acid amide.[6] IR: ν_{max}^{KBr} 3290, 3090, 1650, 1430 cm^{-1}. The yield of nickel chelate was 0.5 g (65%).

The copper chelate of pyridine-2-carboxylic acid amide was obtained with cupric chloride in the same manner. IR: ν_{max}^{KBr} 3250, 3090, 1650, 1450 cm^{-1}. UV: $\lambda_{max}^{H_2O}$ 690, 273, 266, 260 mμ.

The Hydration of 3- or 4-Cyanopyridine with the Nickel Oxide Catalyst (Exp.4 or 7 in Table 2). A half gram of 3 (or 4)-cyanopyridine and 20 m*l* of water was refluxed with 2 g of nickel oxide catalyst for seven hours. During the reaction, no coloration or generation of ammonia was observed. After the reaction, the catalyst was separated by filtration while hot and washed with hot water. Then the filtrate was evaporated; white crystals were thus obtained. In the hydration of 3-cyanopyridine, the white crystal was nicotinamide,[13] 0.52 g (*ca.* 90%), mp 123—126°C (lit. 128—131°C). In the hydration of 4-cyanopyridine, the white crystal was pyridine-4-carboxylic acid amide, 0.5 g (*ca.* 90%), mp 153—154°C (lit. 152—154°C).[9]

The authors wish to express their thanks to Professor Kazuo Hata for his kind advice.

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[11] W. D. Luz and S. Fallab, *Helv. Chim. Acta*, **39**, 1163 (1956).

[12] G. Anderegg, *ibid.*, **43**, 414 (1960); Priyaclaranjan Ray and Dwijenclar Nath Sen, *J. Indian Chem. Soc.*, **25**, 473 (1948).

[13] S. Yoshida, *Chem.* & *Pharm. Bull.* (*Japan*), **11**, 628 (1963).