

ALCOHOLYSIS OF PYRIDINECARBONITRILES WITH METAL CHELATES

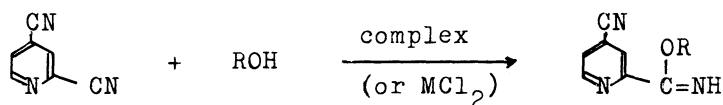
Ken-ichi WATANABE and Koji KIDOKORO

Department of Chemistry, Faculty of Science, Tokyo

Metropolitan University, Setagayaku, Tokyo 158

Metal chelate catalyzed alcoholysis of pyridinecarbonitriles revealed that the reaction products are alkyl pyridinecarboximidates. The use of copper(II) complexes containing one molecular amine gave good results. The reactivities of alcohols were in the order: methanol > ethanol > butanol > isopropyl alcohol. Cu(II), Ni(II), and Co(II) salts were also effective for the reactions.


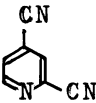
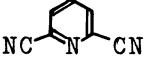
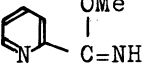
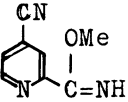
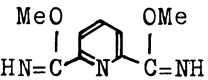
It has been known that alkyl carboximidates are formed by the addition of alcohols to nitriles in the presence of strong acid or base such as HCl or Na(CH₃ONa).¹⁾ We have studied the alcoholysis of pyridinecarbonitriles in the presence of transition metal complexes or metal salts, and have found that the nitrile group in α -position undergoes alcoholysis catalytically. By means of the complex catalyzed reaction, no drastic reagent such as acid or base is necessary, and a selective reaction of dinitrile is realized as follows:



The nitrile group in α -position is presumed to have a particular interaction with metal ions coordinated to the ring nitrogen atom and the activated nitrile group undergoes alcoholysis to afford the imidate through ligand exchange. We have also found that metal oxides such as nickel oxide (black) are effective catalysts for this reaction but they do not show the selectivity.

Many metal complexes have been examined for the reaction and it has been found that copper(II) complexes containing one molecular amine are preferable. The catalysts²⁾ and pyridinecarbonitriles³⁾ employed for the methanolysis are listed in Table 1, along with the reaction conditions, products, and yields.

Table 1. Methanolysis of Pyridinecarbonitriles -yield of imidates (%)-
 sample: 1.92×10^{-2} mol, catalyst: 0.24×10^{-2} mol, methanol: 60 ml
 reaction temp.: 60°C , reaction time: 5 hr

catalyst*	sample			
	$[\text{CuCl}(\text{PhCH}_2\text{NH}_2)(\text{MeOpy})] \text{Cl}$	53	39	9
	$[\text{CuCl}(\text{piperidine})(\text{MeOpy})] \text{Cl}$	54	-	-
	$[\text{CuCl}(\text{Me}_2\text{NH})(\text{MeOpy})] \text{Cl}$	42	-	-
	$[\text{CuCl}_2(\text{MeOpy})]$	24	21	≈ 0
	$[\text{Cu}(\text{MeOpy})_2] \text{Cl}_2$	3	3	≈ 0
	$[\text{CoCl}_2(\text{MeOpy})] \text{H}_2\text{O}$	28	-	-
	CuCl_2	34	34	12
	product (bp $^\circ\text{C}$) [mp $^\circ\text{C}$] IR(cm^{-1}) NMR(δ)**	 (66-67) 4 mmHg 3290, 1650, 1365 (3H, -OMe) 4.01(s) (1H, =NH) 9.28(br)	 [73] $\sqrt{\text{C}=\text{N}}$: 2240 4.02(s) 9.22(br)	 [100-103] 3270, 1655, 1360 4.03(s) 9.25(br)

* MeOpy: methyl pyridine-2-carboximidate

** NMR: reference TMS, solvent CDCl_3 , 60 Mc/s (HITACHI PERKIN ELMER R-20B)
 pyridine ring(H), covered 7.3-8.9 ppm (m)

A typical experiment was carried out as follows. A methanol solution of pyridinecarbonitriles and catalysts was kept at 60°C for 5 hr, and then the reaction mixture was distilled under reduced pressure to remove the methanol unreacted. The residue was extracted with ether several times and the catalyst deposited was filtered out. Then, ether was removed from the extract and the residue was dried in vacuo to be weighed. It was a mixture of the reaction product and pyridinecarbonitriles unreacted. An aliquot quantity of the residue was dissolved in CDCl_3 for the NMR analysis. Thus, the ratio of quantity of the imidate formed was obtained. The NMR signals of O-methyl hydrogen are shown in Table 1. When the reaction product was distilled under reduced pressure, almost pure imidate was obtained.

Generally, the metal complex catalysts* containing one molecule each of amine and imidate (MeOpy) gave good results (Table 1), but amine complex such as $[\text{Cu}(\text{en})_2]\text{Cl}_2 \cdot 2\text{H}_2\text{O}$ showed low activity (10 %). In the reaction of 2-pyridinecarbonitrile with NiCl_2 or CoCl_2 , the yield of the imidate was 38 or 43 % respectively. In the reaction with MCl_2 (M: metal), $[\text{MCl}_2(\text{MeOpy})]$ is first formed to show catalytic activity, but it turns into $[\text{M}(\text{MeOpy})_2]\text{Cl}_2$ gradually.

In the case of 2,4-pyridinecarbonitrile, the nitrile group only in α -position underwent alcoholysis selectively (Table 1). Therefore, the reactions of 3- and 4-pyridinecarbonitriles were examined in the presence of CuCl_2 catalyst. They afforded only their copper(II) complexes by the coordination of pyridine nitrogen atom and no alcoholysis of the nitrile group took place. But, it has been found that they undergo alcoholysis by use of nickel oxide catalyst (black), and both nitrile groups in 2,4-dinitrile, too. The yields of imidates were as follows (reflux, 5 hr):

position of -CN	2-	3-	4-	2,4-
methanolysis (%)	67	46	55	57
ethanolysis (%)	34	16	20	24

Thus, the selective reaction of α -nitrile group in 2,4-dinitrile is apparently attributed to the coordination of pyridine nitrogen atom to metal complexes (or salts). The reactivity of 2,6-dinitrile was extremely low with any catalyst. This may be attributed to steric hindrance in the coordination to the catalysts.

In Table 2, the results of reactions with methanol, ethanol, butanol, and isopropyl alcohol are summarized. The reactivities of bulky alcohols such as n-BuOH and i-PrOH were very low presumably due to the steric hindrance of the alkyl groups. Therefore, the reactions were then carried out at the refluxing temperature, but the mode of the reactions did not change very much. In the reactions of 2-pyridinecarbonitrile with nickel oxide catalyst, the reactivities of n-BuOH and i-PrOH were also low, yields of imidates: 20 and 0 % (reflux, 5 hr).


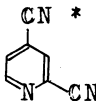
* We already reported²⁾ that these complexes were easily obtained from a methanol solution of copper(II) complex of 2-pyridinecarbonitrile and amine (1:1) at 0°C. The complexes used for the alcoholysis were recovered without any change.

Table 2. Alcoholysis of Pyridinecarbonitriles with CuCl_2

- yield of imidates (%) -

sample: 1.92×10^{-2} mol catalyst: 0.24×10^{-2} mol

alcohol: 60 ml reaction time: 5 hr

alcohol (bp °C)	sample				
		60 °C	reflux	60 °C	reflux
MeOH (64)		34	49	34	38
EtOH (78)		13	14	0	8
n-BuOH (117.5)		0	18	-	-
i-PrOH (82)		0	0	-	-

* selective alcoholysis in α -positionNMR(δ): reference TMS, solvent CDCl_3

-OEt 1.48(t), 4.43(q) ppm

-OBu 1.0(d), 1.2-2.1(m), 4.83(t) ppm

References

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