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THE TRANSFORMATION OF NITRILES INTO AMIDES BY THE USE OF $TiCl_4$

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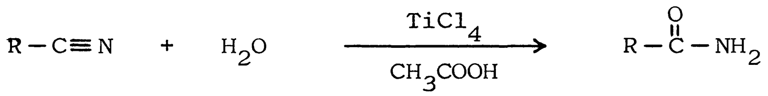
It was found that various carboxamides were prepared in good yields without accompanying the formation of acids by the hydrolysis of nitriles by using $TiCl_4$ in acetic acid.

In general, it is difficult to stop the hydrolysis of a nitrile at an amide stage under basic or acidic condition,$^{1)}$ which is often accompanied with the formation of a carboxylic acid except for the basic condition in the presence of hydrogen peroxide.$^{2)}$

In the present investigation, it was established that nitriles are hydrolyzed to the corresponding amides in good yields by using $TiCl_4$. For example, when phenylacetonitrile (0.585 g, 0.005 mol) was treated with a mixture of $TiCl_4$ (1.90 g, 0.01 mol) and water (0.36 ml, 0.02 mol) in 30 ml of acetic acid, phenylacetamide was obtained in 90% yield, and phenylacetic acid could not be detected. Contrary to the present result, it is known that in the case of the hydrolysis of phenylacetonitrile by using sulfuric acid, phenylacetic acid resulted by further hydrolysis of initially formed phenylacetamide. In a similar manner, various nitriles were hydrolyzed to the corresponding amides. These results are listed in the following table.



$$R-C\equiv N \quad + \quad H_2O \quad \xrightarrow[CH_3COOH]{TiCl_4} \quad R-\overset{\overset{O}{\|}}{C}-NH_2$$

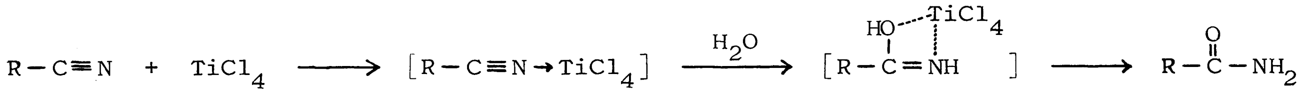
	Yield (%)
$C_6H_5CH_2$	$90^{a)}$
$n\text{-}C_3H_7$	$88^{b)}$
$(CH_3)_2CH$	$65^{b)}$
$(CH_3)_3C$	$48^{b)}$
C_6H_5	20

a) When the reaction was carried out in methylene chloride or benzene, phenylacetamide was obtained only in 7% or 4% yield, respectively.

b) 3 molar amounts of water was added.

As shown in the table, benzonitrile was hydrolyzed to benzamide only in 20% yield under the above mentioned condition. Then, hydrolysis of benzonitrile was further examined varying the relative amount of solvent, water and $TiCl_4$. After a number of experiments, it was found that the hydrolysis reaction proceeds smoothly in highly concentrated solution and the increase of the yield was achieved. For example, when benzonitrile (0.52 g, 0.005 mol) was treated with a mixture of $TiCl_4$ (3.80 g, 0.02 mol) and 5 ml of acetic acid, followed by the addition of 1.44 ml of water, and after being stirred at room temperature for 24 hr, benzamide was isolated in 64% yield. In a similar manner, pivalonitrile was hydrolyzed to pivalamide in 87% yield.

This $TiCl_4$-promoted hydrolysis reaction would proceed through the initial formation of $TiCl_4$-nitrile complex, 1, followed by the hydration to result amide.



$$R-C\equiv N + TiCl_4 \longrightarrow [R-C\equiv N\rightarrow TiCl_4] \xrightarrow{H_2O} [R-\overset{HO\cdots TiCl_4}{C=NH}] \longrightarrow R-\overset{O}{\overset{\|}{C}}-NH_2$$

1 2

The fact that this hydrolysis reaction stops at the amide stage may be probably due to the formation of the stable amide-Ti^{IV} complex, 2.

In conclusion, it is noted that various carboxamides were prepared in good yields without accompanying the formation of acids by the hydrolysis of nitriles in acetic acid with $TiCl_4$.

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