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HYDROLYSIS OF VARIOUS NITRILE COMPOUNDS TO THE AMIDES BY CATALYSIS OF 2-MERCAPTOETHANOL IN A PHOSPHATE BUFFER

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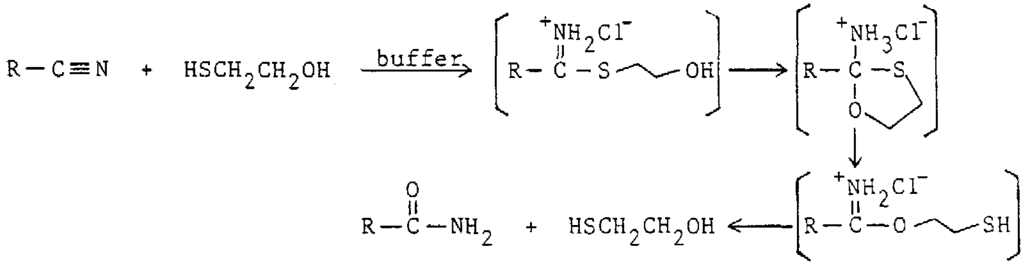
Abstract: α-Aminonitriles, 4-nitrobenzonitrile and 3,5-dinitrobenzonitrile were hydrolyzed exclusively to amides efficiently when they were stirred with 2-mercaptoethanol in a phosphate buffer (pH 7.0), 50 mM).

The active sites of the nitrile group-hydrolyzing enzymes are assumed to be composed of two functional groups[1,2]. Among many bifunctional compounds examined for the ability of hydrolyzing a nitrile group to the corresponding amide, 2-mercaptoethanol showed the highest catalytic activity on the hydrolysis of α-aminophenylacetonitrile to phenylglycinamide[3]. Thus, we have investigated further the catalytic activities of 2-mercaptoethanol on the hydrolysis of other nitrile compounds in a phosphate buffer and want to report the scope and limitation in this communication.

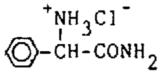
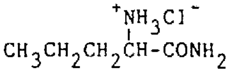
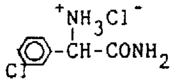
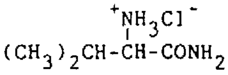
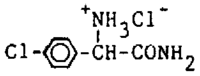
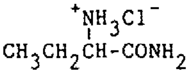
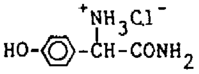
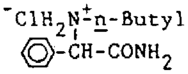
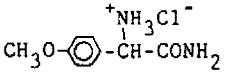
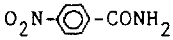
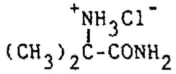
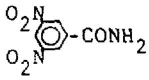
Stirring of nitrile compounds[4] with 2-mercaptoethanol in a phosphate buffer (50 mM, pH 7.0) at 20°C for 15 h and workup gave amides in good yields as summarized in Table 1[5]. Among nitrile compounds examined by us, benzyl cyanide, benzonitrile, *p*-hydroxybenzonitrile, *p*-cyanoaniline, 2-nitrobenzonitrile and *m*-cyanoaniline were not converted to the corresponding amide or to the acid analog. It seemed that the nitrile group having an α-amino group or those attached to the aromatic ring having an electron withdrawing group were easily hydrolyzed to the amides. 2-Mercaptoethanol seemed to react with nitrile compounds to produce bifunctional group-participated tetrahedral intermediates, decomposition of which might give the imidate analogs which should hydrolyzed to the amides (Scheme 1).

Scheme 1



Our early proposal[2] about the active sites of nitrile group-hydrolyzing enzymes seemes to have some meaning. We are currently investigating the detailed mechanism of the mercaptoethanol-catalyzed hydrolysis of nitrile compounds to amides.

Table 1. The amide analogs formed from the corresponding nitriles by shaking with 2-mercaptoethanol in a phosphate buffer (50 mM, pH 7.0)[5]

Amide	Yield(%)	mp(°C)	Amide	Yield(%)	mp(°C)
	70.0	210(dec)	 $CH_3CH_2CH_2\overset{^{+}NH_3Cl^{-}}{CH}-CONH_2$	61.3	231-233(dec)
	85.3	224-226(dec)	 $(CH_3)_2CH-\overset{^{+}NH_3Cl^{-}}{CH}-CONH_2$	56.1	231-234(dec)
	58.4	214-215(dec)	 $CH_3CH_2\overset{^{+}NH_3Cl^{-}}{CH}-CONH_2$	67.7	178-181(dec)
	65.4	215-218(dec)		27.4	212(dec)
	52.4	225-229(dec)		78.5	197
 $(CH_3)_2\overset{^{+}NH_3Cl^{-}}{C}-CONH_2$	58.8	254-256(dec)		86.5	179-181

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References and Notes

1. Y.B. Lee, M.S. Thesis, Seoul National University, 1986.
2. Y.M. Goo and Y.B. Lee, *J. Chem. Soc., Chem. Commun.*, 1247 (1986).
3. Y.B. Lee, Y.M. Goo and J.K. Lee, *Archi. Pharm. Res.*, 11, 285 (1988).
4. α-Aminonitriles were prepared by the procedures given in the following references. R.E. Steiger, *Org. Synth.*, 1955, Coll. Vol. III, 84; W.L. Matier, D.A. Owens, W.T. Comer, D. Deitchman, H.C. Ferguson, R.J. Seidehamel and J.R. Young, *J. Med. Chem.*, 16, 901 (1973).
5. Satisfactory analytical data were obtained.

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