Reactions of Aminomalononitrile with Electrophiles

JOHN W. THANASSI
The Salk Institute for Biological Studies, San Diego

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Summary. Aminomalononitrile (HCN trimer) reacts with electrophiles such as aldehydes and acrylonitrile under very mild conditions of temperature and pH to produce intermediates which, after acid hydrolysis, yield amino acids. The following amino acids have been identified and quantitated: glycine, D, L-erythro- and D, L-threo-β-hydroxyaspartic acids, D, L glutamic acid, and D, L-threonine and allo-threonine. The mechanism of their formation and the possible significance of these reactions in prebiotic syntheses are discussed.

Key words: Aminomalononitrile - Amino Acids - Chemical Evolution

INTRODUCTION

A number of experiments have been reported describing the syntheses of amino acids under simulated prebiotic conditions.¹ These schemes involve a variety of experimental approaches and generally utilize simple, small molecules believed to have been present on the primitive earth. The reaction pathways are made possible by employing energy sources and creating reaction conditions considered plausible under prebiotic conditions. For example, the classical experiments of Miller (1955) utilized methane, ammonia, hydrogen, water, and an electric spark, and yielded a variety of biologically important molecules, including amino acids.

A key starting material in many prebiotic syntheses is believed to be hydrogen cyanide (Ferris et al., 1973a,b; Sanchez et al., 1967, and references therein). Under moder-

¹ For reviews and references to original literature, see Lemmon (1970), and Miller & Orgel (1974).
ately alkaline conditions, HCN oligomerizes to a tetramer, diaminomaleonitrile, which is valuable as a synthetic intermediate in both prebiotic experiments (Sanchez et al., 1967) and in conventional preparative chemistry (Begland et al., 1974). Acid hydrolysis of the material obtained from alkaline solutions of HCN results in the production of a number of naturally-occurring amino acids, particularly, glycine, alanine, and glutamic and aspartic acids (Ferris et al., 1974, and references therein). Although the mechanism of production of amino acids from polymerizing cyanide solutions is in dispute (Ferris et al., 1973a,b; Matthews, 1975), there is no doubt that the products of hydrogen cyanide kept under basic conditions can yield a number of amino acids.

One of the intermediates in the oligomerization of HCN to diaminomaleonitrile is a trimer of HCN, aminomalononitrile, $\text{NH}_2\text{CH(CN)}_2$ (Sanchez et al., 1967). This report deals with the reactions of aminomalononitrile and electrophilic reagents. Under very mild conditions of temperature and pH, aminomalononitrile reacts with several aldehydes and acrylonitrile to form amino acids. The possible relevance of these reactions in prebiotic chemistry is discussed.

**EXPERIMENTAL**

A. Reaction of Aminomalononitrile with Glyoxylic Acid

(i) Without Added Cyanide Ion. Glyoxylic acid hydrate (368 mg, 4 mmoles) and aminomalononitrile p-toluene-sulfonate (506 mg, 2 mmoles) (Ferris & Sanchez, 1970) were dissolved in 100 ml ice-cold pH 6.8 phosphate buffer (0.125M each in $\text{Na}_2\text{HPO}_4$ and $\text{NaH}_2\text{PO}_4$). After 20 hrs in a cold room at approximately $4^\circ$, 100 ml of concentrated hydrochloric acid were added to the slightly cloudy, light-orange solution. The acidified reaction mixture was kept at $110^\circ$ for 26 hrs. A small amount of black precipitate was filtered from the amber-colored solution which was then concentrated at $40^\circ$ on a rotary evaporator. The tan residue was concentrated several times from water and ethanol to remove excess HCl, and then dissolved in 75 ml of water. The positively charged amino acids were absorbed onto a 2.5×20 cm column of Dowex 50 H⁺ (200-400 mesh) and the anions and neutral compounds were washed through with 500 ml of water. Amino acids were then eluted by a frontal displacement with 350 ml of 3N $\text{NH}_4\text{OH}$. The ammonia eluate was concentrated to dryness. Thin-layer chromatography of the residue was carried out on Eastman