Photochemical Reactions and the Chemical Evolution of Purines and Nicotinamide Derivatives

Abstract. The photochemical rearrangement of a tetramer of hydrogen cyanide to 4-aminoimidazole-5-carbonitrile, a critical step in the proposed prebiotic synthesis of purines, proceeds in high yield in the absence of oxygen without photodestruction of the reaction product. The mechanism of the rearrangement involves the conversion of the excited singlet of the hydrogen cyanide tetramer to 2-imino-3-cyano-4-aminoazetine, which then rearranges to the imidazole product. The photolysis of the vinylogous enaminonitrile 1,3-dicyano-4-amino-1,3-butadiene yields 6-aminonicotinonitrile. The latter reaction affords an efficient route to a nicotinamide derivative from cyanoacetylene.

A pathway has been proposed for the chemical evolution of purines which involves the oligomerization of dilute aqueous solutions of HCN (1-3). A crucial step in the proposed prebiotic synthesis is the photochemical isomerization of diaminomaleonitrile (HCN tetramer) (I) to 4-aminoimidazole-5-carbonitrile (III) (2, 3).



The rearrangement of compound I to compound III proceeds in high yield (80 to 85 percent); however, compound III undergoes a sensitized photodestruction at about half the rate at which it is synthesized photochemically from compound I (2, 4). This observation required the postulate that during the prebiotic synthesis of purines the conversion of compound I to compound III took place in the presence of ultraviolet light, while the subsequent conversion of compound III to purines proceeded in the absence of ultraviolet radiation (3). While one can envisage situations on the primitive earth where these conditions would be met, this restriction obviously diminished the attractiveness of the proposed scheme.

To learn more about this photosensitized decomposition of compound III, we investigated the minor products produced during the photolysis of HCN tetramer. With preparative paper chromatographic techniques, two compounds which sensitized the photodestruction of compound III were isolated (5). We discovered that if the reaction solutions are carefully degassed by five freeze-pumpthaw cycles (6) the rearrangement pro-

7 NOVEMBER 1969

ceeded in over 90 percent yield and that compound III was stable indefinitely to further irradiation. Furthermore, when the reaction mixture was chromatographed (Whatman 3MM paper, nbutanol saturated with water) and the reaction products were visualized with ultraviolet light, only compound III, together with a trace amount of fluorescence near the solvent front, was observed on the chromatograms of the degassed reaction mixtures. At least six spots were observed on the paper chromatogram of the reaction mixture which was not degassed. Finally, it was confirmed that the destruction of compound III was due to a photosensitized oxidation by irradiating a mixture of compound III and one of the photosensitizers, with and without degassing (7). After 3 hours of irradiation the absorption maximum of compound III at 245 nm decreased 2 percent in the degassed solution, but a 65 percent decrease was observed in the solution that was not degassed. Since it is generally agreed that there was no oxygen present in the atmosphere of the primitive earth, these experiments obviate the need of postulating that compound III was protected in some way from photodestruction. Furthermore, these results demonstrate the need for performing experiments which model primitive earth conditions in the absence of oxygen (8).

The nature of the excited state and the mechanism of the conversion of enaminonitriles to imidazoles has been investigated with, as typical examples, the photorearrangements of compound I to compound III and of β -aminocrotonitrile (IV) to 4-methylimidazole (V). The formation of compounds III and V is not sensitized by benzophenone or triphenylene, nor is it quenched by piperylene or cyclohexadiene. These data suggest that the rearrangement proceeds via a singlet excited state. However, the photochemical *cis-trans* isomerization of compound IV is sensitized by benzophenone and triphenylene and, therefore, proceeds by a triplet. The phosphorescence of blacetyl ($E_{\rm triplet} = 55$ kcal) (9) is quenched by compound I, a result which suggests that the triplet energy of compound I is less than 55 kcal.

Cleavage of the C–CN bond, but not the C–CNH₂ bond, takes place at some point during the rearrangement. This was shown by the detection of only 4methylimidazole but none of the 2methyl isomer when compound IV was irradiated. Furthermore, a ketimine intermediate (VI) was eliminated by the



observation that no 5-deutero-4-methylimidazole is produced when compound IV is irradiated in D_2O solution.

An iminoazetine (II) is proposed as the photochemical reaction intermediate from studies on the photochemistry of a vinylogous enaminonitrile, 1,3-dicyano-4-amino-1,3-butadiene (VIII). Compound VIII is produced, in equilibrium with the anion of compound VII, when compound VII is dissolved in aqueous ammonia (10). Irradiation of a $10^{-4}M$ solution of compound VII in 1M ammonia with lamps with principal emission at 350 nm resulted in a 10 percent yield (determined spectrophotometrically) of 6-aminonicotinonitrile (IX). The cyclization of compound VIII to compound IX is completely analogous to the cyclization of compound I to compound II, with the exception that compound IX is stable and does not undergo further rearrangement. In this way, the reaction intermediate has been trapped.



The photochemical synthesis of 6aminonicotinonitrile (IX) proceeds in much higher yield and with lower concentrations of compound VII than the corresponding thermal synthesis (10). Nitrile IX hydrolyzes readily to the corresponding nicotinamide derivative in aqueous base (10). Since cyanoacetylene and most of its adducts are hydrolyzed to cyanoacetaldehyde and that in turn condenses to compound VII in aqueous solution (1, 10), this photochemical reaction suggests an efficient pathway for the prebiotic synthesis of a potential nicotinamide-like hydrogen transfer system from cyanoacetylene (11).

J. P. FERRIS J. E. KUDER

A. W. CATALANO

Department of Chemistry, Rensselaer Polytechnic Institute,

Troy, New York 12181

References and Notes

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- paper are essentially those described in (2) and (3).12. Sponsored by NIH grant GM 15915. J.P.F.
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Phenylalanine and Tyrosine

Synthesis under Primitive Earth Conditions

Abstract. Phenylacetylene can be synthesized in substantial yields from various hydrocarbons by high temperatures, electric discharges, and ultraviolet light. Phenylacetylene is hydrated to phenylacetaldehyde by way of both nucleophilic and radical additions of H_2S followed by hydrolysis of the thioaldehyde. The addition of NH_3 and HCN to phenylacetaldehyde yields phenylalanine nitrile which is hydrolyzed to phenylalanine. A small yield of tyrosine is obtained from the radical addition of H_2S to phenylacetylene. This sequence of reactions is a possible mechanism for the synthesis of these amino acids on the primitive earth.

A wide variety of processes have been used for synthesizing amino acids under primitive earth conditions (1), but the synthesis of the aromatic amino acids phenylalanine and tyrosine has not been demonstrated (2). The lack of phenylalanine and tyrosine in such experiments combined with the apparent difficulty of synthesizing them results in their absence from some lists of "primitive" amino acids (3).

We propose that phenylalanine was synthesized on the primitive earth from phenylacetylene, followed by hydration to phenylacetaldehyde and a Strecker synthesis with the HCN and NH_3 , which are generally assumed to have been present in the primitive oceans.



Phenylacetylene can be synthesized from a variety of mixtures of simple hydrocarbons by high temperatures, electric discharges, and ultraviolet light (4) (Table 1). Phenylacetylene was identified by its gas chromatography retention time (5) and by ultraviolet and infrared spectra. Benzene, styrene, and naphthalene are also synthesized in most of these experiments. Success in these experiments is dependent on removing the products from the region of the hot wire or electric discharge by cooling the walls of the flask to approximately -20° C (6). This is analogous to reactions in the atmosphere where the phenylacetylene would have time to diffuse to the ocean before being broken up by various energy sources in the atmosphere. The yields of phenylacetylene in these experiments are 0.001 to 5 percent. The rate of production of phenylacetylene in the primitive atmosphere is difficult to estimate, but the phenylacetylene vields in these experiments suggest that the rate could be substantial.

The hydration of phenylacetylene is difficult to achieve under primitive earth conditions. The hydration can take place in two ways, electrophilic (acid catalyzed) to give acetophenone

(7) and nucleophilic (base catalyzed) to give phenylacetaldehyde (8). A Strecker synthesis with acetophenone gives α -amino- α -phenylpropionic acid, a compound which is presumed to have played no role in the origin of life. Heating phenylacetylene in aqueous solutions buffered between pH 7 and 10 results in very small yields of phenylacetaldehyde and acetophenone (9). The hydration products were detected by converting them to the amino acids with NH3 and HCN, followed by hydrolysis. The mixture was desalted, and the amino acids were analyzed on the Beckman-Spinco amino acid analyzer (10) and by paper chromatography. Heating aqueous ammonia solutions buffered between pH 7 and 10 also gives only small yields of phenylacetaldehyde (half life, approximately 500 years at 100°C and pH 8). Increasing the pH to 14 does not increase the yield because of decomposition of the phenylacetaldehyde produced. At lower temperatures, the rate of addition of OH- or NH₃ to phenylacetylene would probably be too slow to have been effective in the primitive ocean.

The nucleophilic addition of HCN to phenylacetylene gives cinnamonitrile, which upon addition of NH₃ and hydrolysis, yields β -aminohydrocinnamic acid rather than phenylalanine. The addition of NH₃ to cinnamic acid gives exclusively β -aminohydrocinnamic acid at *p*H values between

Table 1. Formation of phenylacetylene from simple hydrocarbons. The hot wire source was a tungsten wire at approximately 1300° C in a 1-liter flask. The spark source was a Corona-type discharge from a Tesla coil in a 3-liter flask. The ultraviolet source was a Hanovia medium-pressure Hg ultraviolet lamp at 22°C.

Gas	Energy source	Time (hr)	Yield of $C_{\theta}H_{5}$ - $C \equiv$ CH (%)
CH ₄ (450 mm)	Hot wire	3	0.05
	Spark	12	.001
$C_{2}H_{6}$ (450 mm)	Hot wire	1.5	4.7*
	Spark	12	0.00 3
$C_{2}H_{4}$ (50 mm) +	Hot wire	2	1.5†
CH ₄ (400 mm)	Spark	12	0.04†
$C_{2}H_{2}$ (5 mm) +	Hot wire	3	.40†
CH ₄ (445 mm)	Spark	12	.02†
$C_{2}H_{2}$ (10 mm) + CH ₄ (360 mm)	Ultraviolet	0. 7	.12†

* The yield is not affected substantially on the addition of 200 mm of nitrogen or 50 mm of ammonia to the reaction flask. † Yield based on either C₂H₄ or C₂H₂.