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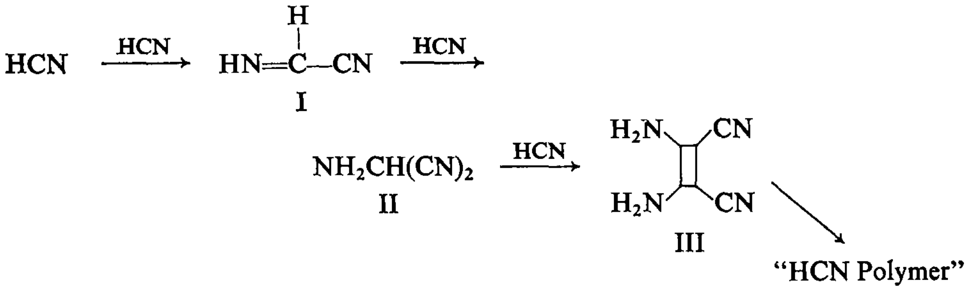
Communication

The Possible Role of HCN in the Origins of Life. The Oligomerization of HCN and the Reaction of HCN with N-Alkyliminoacetonitriles[1,2]

Hydrogen cyanide is believed to have had a central role in the chemical processes leading to the origins of life (*2*). For example, pathways leading from HCN to both amino acids and purines have been discovered (*2–4*). The mechanism of formation of these important biomonomers is not well understood and we have undertaken an investigation of the chemistry of HCN with the goal of understanding more precisely its possible role in chemical evolution.

Two mechanistic pathways have been postulated for the condensation of hydrogen cyanide. In one proposal it was suggested that HCN oligomers were built up in stepwise fashion from HCN (Scheme I) (*2*).



Scheme I

It was shown that the chemistry of HCN and compounds II and III is consistent with the above scheme (*2*, *3*). The synthesis and characterization of the dimeric species I was not attempted in that study.

In an alternative proposal (Scheme II) it was suggested that the dimeric species I has the properties of a carbene (IV). It was postulated that this carbene would undergo dimerization to III and polymerization to the "HCN polymer" (V) (*4*). It was proposed that mild hydrolysis of V yields peptides (*4*). The reactions leading to the alkyl substituent of V were not discussed in detail.

We felt that several of the proposals in Scheme II were questionable and merited further investigation. For example, the evidence for structure V is that amino acids are

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[1] Chemical Evolution VIII. For previous papers in this series, see Ref. 1.

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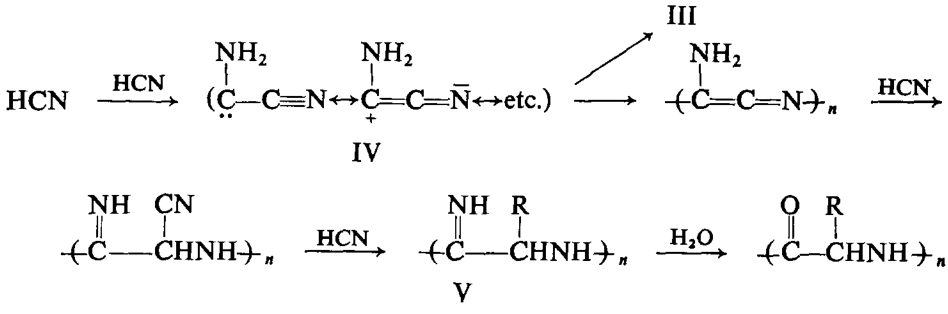
released on acid or base hydrolysis. However, glycine is formed on hydrolysis of III, yet the latter does not contain an amide linkage (*2*). Hydrolytic release of amino acids from a compound does not constitute evidence for peptide linkages.

A second aspect of Scheme II that we felt warranted further investigation is the claim that HCN dimer is a carbene (*4*). In considering the methods that have been used for the generation of carbenes it seemed highly improbable that such a reactive intermediate would be formed in the condensation of cyanide in aqueous medium (*5*).



Scheme II

We were unable to find evidence for the peptide link in the HCN polymer. No amino acids were released from this material on incubation with the proteolytic enzymes pronase and carboxypeptidase. These results suggest that the latter stages of Scheme II are not correct. We then directed our attention to the proposal in Scheme II that dimeric HCN is a carbene.

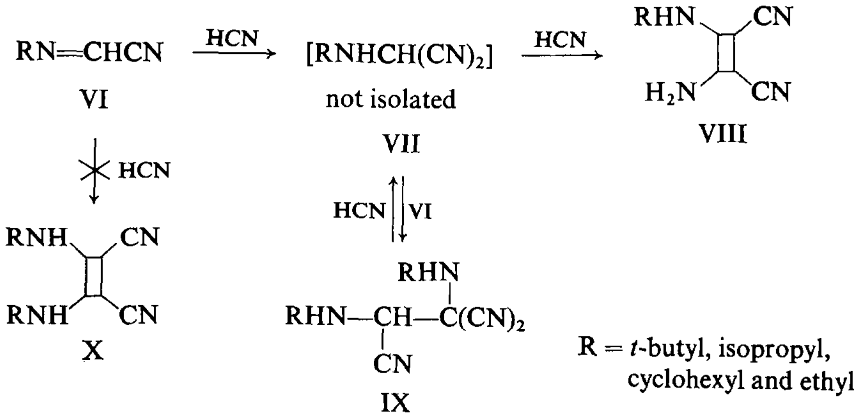
A series of compounds of structure VI (R = *t*-butyl, isopropyl, cyclohexyl, ethyl) were prepared [when R = isopropyl: bp 38°C/10 Torr; uv max (CH_3CN) 288.5 nm (ϵ 90); ir (neat) 2250 cm^{-1} ($C{\equiv}N$), 1620 cm^{-1} ($C{=}N$)] as analogs of dimeric HCN by the procedure of Boyer and Dabek (*6*). None of the *N*-alkylated forms of dimeric HCN (VI) exhibited the chemical behaviour of a carbene. For example, the compounds were sufficiently stable so that complete characterization was possible. Furthermore, all the compounds of structure VI are colorless and do not exhibit the uv-visible spectral properties reported for structure I (or IV) (*4*).

The reaction of VI with one equivalent of HCN, in both water and acetonitrile, (Scheme III) resulted in the formation of VIII [when R = isopropyl: 20% yield, mp 86.5–87.5°C; uv max (CH_3CN) 310.5 nm (ϵ 1.31 × 10^4); ir (KBr) 2250, intense, (conjugated $C{\equiv}N$) 1650 cm^{-1} ($C{=}C$)] and IX [when R = isopropyl: 27% yield, mp 50°C; uv max (CH_3CN) 228 nm (ϵ 240); ir (KBr) 2250 cm^{-1}, weak, ($C{\equiv}N$)].

The chemistry outlined in Scheme III is completely in accord with the formation of cyanide oligomers by the stepwise addition of HCN postulated in Scheme I and exhibits no similarity to the carbene mechanism proposed in Scheme II. Of particular significance is the formation of the monoalkylated diaminomaleonitrile (VIII) instead of the dialkylaminonitrile (X) in the presence of cyanide. If the dialkylaminonitrile X were formed it would have been readily detected by an ultraviolet maximum at 325 nm (ϵ 1.12 × 10^4)

in the reaction mixture. (The synthesis of X with R = isopropyl and cyclohexyl will be described separately.) This observation clearly shows that nucleophilic addition of cyanide to VI takes place rather than the proposed dimerization of I to X. Consequently we have found no experimental basis for the proposal (*4*) that oligomerization of cyanide proceeds via a carbenoid mechanism.

Superficially the formation of IX appeared to be inconsistent with Scheme I. However, the formation of IX in significant amounts is due to the use of equimolar amounts of HCN and VI in the reaction mixture. The conversion of IX to VIII with excess cyanide demonstrates that if VI were added to excess cyanide then VIII would be the predominant product. Furthermore, it has been calculated that the steady state concentration of II in 1 *M* HCN (pH 9.3) is 10^{-5}–10^{-6} *M* (*2*). The observed reactivity of VI demonstrates that the concentration of hydrogen analog (I) would be equally as low or lower. Therefore the bimolecular reaction of I and II to form IX (R = H) is not likely to be observed in aqueous cyanide.



R = *t*-butyl, isopropyl, cyclohexyl and ethyl

Scheme III

One can conclude from the stepwise reactions outlined in Scheme I that the so called "HCN polymer" is a mixture of low molecular weight compounds. Cyanide polymerizations occur only under mildly alkaline conditions where the concentrations of initiator (CN^-) and monomer (HCN) are similar (*2*). It is difficult to imagine the formation of high molecular weight polymers under these conditions (*7*). This conclusion is in agreement with preliminary molecular weight measurements. Also smaller molecules such as urea and oxalic acid account for a significant proportion of the products of the cyanide oligomerization.

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