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# Chemial Evolution

## XVIII. Synthesis of Pyrimidines from Guanidine and Cyanoacetaldehyde*

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*Summary.* Cyanoacetaldehyde condenses with guanidine in dilute aqueous solution to form 2,4-diaminopyrimidine which in turn is hydrolyzed to cytosine and uracil. The concentration of reagents required for the synthesis of 2,4-diaminopyrimidine is quite low, and cyanoacetadehyde is expected to have been present on the primitive earth since it is formed by the hydrolysis of cyanoacetylene. The stability of cyanoacetaldehyde and its aldol dimer to hydrolysis is $10^3$ times that of cyanoacetylene. The half life for guanidine hydrolysis is $10^5$–$10^8$ years at pH 9. The prebiotic synthesis of pyrimidines from cyanoacetaldehyde and guanidine is preferred over the previously proposed route from cyanoacetylene and cyanate because of the greater stability of the reactants.

## 1. Introduction

In a previous paper we described a prebiotic synthesis of the pyrimidine cytosine starting from cyanoacetylene (*1*) and cyanate (Ferris, Sanchez and Orgel, 1968). The rapid hydrolysis of both cyanate and cyanoacetylene (a few years under prebiotic conditions) raised the question of the importance of this route for pyrimidine synthesis on the primitive earth. The triple bond of cyanoacetylene is especially susceptible to nucleophilic attack by ammonia, hydroxide ion, alkoxide ion (Ferris, Sanchez and Orgel, 1968), phosphate (Ferris, 1968; Ferris, Goldstein and Beaulieu, 1970) and cyanide (Sanchez, Ferris and Orgel, 1966). It is clear that, due to competition with other nucleophiles, only a small fraction of the cyanoacetylene that was present in the primitive ocean could have reacted with cyanate to give primidines.

One of the main reactions of cyanoacetylene in dilute aqueous base is hydrolysis to cyanoacetaldehyde (*2*) which in turn dimerizes (with elimination of water) to *3* [Eq. (1)] (Ferris, Sanchez and Orgel, 1968). It is apparent from studies of the hydrolysis of cyanovinyl phosphate that *2* and *3* will be the ultimate hydrolytic products of most compounds formed by the addition of nucleophiles and hydroxide to cyanoacetylene (Ferris, Gold-

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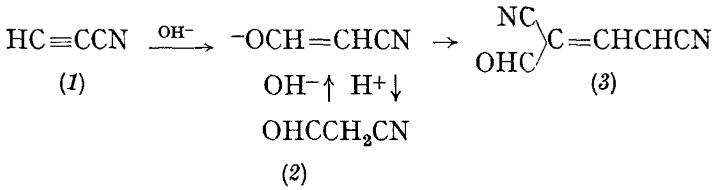
* For the previous paper in this series see Ferris *et al.* (1974).

stein and Beaulieu, 1970). Therefore a pyrimidine synthesis based on cyanoacetaldehyde would overcome some of the questions raised by the route from cyanoacetylene and cyanate. This is the subject of this paper.



$$\begin{array}{ccccc} HC\equiv CCN & \xrightarrow{OH^-} & {}^-OCH=CHCN & \rightarrow & \begin{matrix}NC\\OHC\end{matrix}\Big\rangle C=CHCHCN \\ (1) & & OH^-\uparrow\ H^+\downarrow & & (3) \\ & & OHCCH_2CN & & \\ & & (2) & & \end{array} \qquad (1)$$

## 2. Materials and Methods

### *a) General*

The uv spectra were measured on a Unicam SP 800 A spectrophotometer; the infrared spectra were measured on a Perkin Elmer 137 spectrophotometer; pH measurements were made on a Radiometer Model 26 pH meter equipped with a Corning 476050 electrode; electrophoreses were performed on a Savant FP-30 H instrument at 2000–4000 volts on WH 330-3MM paper using acetic acid—formic acid—water (45:15:240) and ascending paper chromatography was performed on Whatman 3MM paper using *n*-propanol-14.7 $M$ ammonia 3:1 (PA) and *n*-butanol saturated with water (BW). pHydroin buffers (Micro Essential Laboratory, Brooklyn 10, N.Y.) were used unless otherwise noted. Cyanoacetylene, cyanoacetaldehyde, the aldol dimer of cyanoacetaldehyde (Ferris, Sanchez and Orgel, 1968) and cyanovinyl phosphate (Ferris, Goldstein and Beaulieu, 1970) were prepared by literature procedures.

### *b) 2,4-Diaminopyrimidine*

To a stirred suspension of guanidine (3 g) in 75 ml of boiling $CH_3CN$ was added 1 ml of $ClCH=CHCN$ in 30 ml $CH_3CN$ over a 30 min period. The mixture was heated at reflux for 5 hrs cooled and the solution decanted and concentrated to dryness (Fanshawe, Bauer and Safir, 1965). The residue was extracted into 2–50 ml portions of $CHCl_3$ and the soluble material subjected to dry column chromatography (10 ml fractions) using *n*-butanol saturated with water. Fractions 4–10 were shown by paper chromatography (PA) to contain 2,4-diaminopyrimidine. These fractions were combined, concentrated to a gum which crystallized on trituration with acetone. Recrystallization from ethanol-ether gave needles, mp 187–188°; lit. mp 147–149° (Fanshawe, Bauer and Safir, 1965). Fractions 7–10 were combined and crystallized from ethanol-acetone; mp 146°, uv max, (pH 7) 281 nm ($\varepsilon$ 6500), 227 nm ($\varepsilon$ 9600); (pH 11) 281 nm ($\varepsilon$ 6900), 227 nm ($\varepsilon$ 9600); (pH 2) 265 nm ($\varepsilon$ 5000); lit. uv max, (pH 11) 282 nm ($\varepsilon$ 7100); (pH 2) 267 nm ($\varepsilon$ 5600) (Roth and Hitchings, 1961). The uv spectra and $R_f$ values (PA) of the samples melting at 187° and 146° were identical, the ir spectra exhibited similar absorption bands; however there were some differences in position and intensity; mixture melting point 143–176°.

### *c) Hydrolysis of 2,4-Diaminopyrimidine*

Aqueous solutions of 2,4-diaminopyrimidine ($10^{-2}\,M$) were buffered to pH 7, 9 and 11. These were sealed in ampuls after degassing by 3 freeze-pump-thaw cycles and heated at 100° in a steam bath. The reaction mixtures were chromatographed (PA) after heating for 12 and 48 days. The main components of the mixture after 12 days were shown by paper chromatography and the uv spectra of the eluted material from the paper chromatography to be uracil and 2,4-diaminopyrimidine, together with a trace amount of cytosine. The yields (Table 1) after 48 days were determined by measuring the absorbance of the compound after elution from the paper chromatogram.

Table 1. Yields of uracil and 2,4-diaminopyrimidine (%)

| | pH 7 | pH 9 | pH 11 |
|---|---|---|---|
| Uracil | 36 | 29 | 26 |
| Diaminopyrimidine | 41 | 47 | 52 |

### d) Synthesis of 2,4-Diaminopyrimidine from Prebiotic Precursors

*(i) Attempted Syntheses from a Variety of Precursors.* Solutions of 0.2 *M* cyanoacetylene, cyanoacetaldehyde anion ($K^+$ salt) cyanovinyl phosphate ($Ba^{++}$ salt) and the potassium salt of the aldol dimer of cyanoacetaldehyde in pH 9 buffer were mixed individually with 0.2 *M* solutions of cyanamide, urea, cyanoguanidine and guanidine in pH 9 buffer. The solutions (0.1 *M* in each reactant) were heated for 24 hrs in sealed ampuls. The reaction solutions were concentrated and chromatographed (BW) along with an authentic sample of 2,4-diaminopyrimidine. The area with the same $R_f$ as the 2,4-diaminopyrimidine was eluted and rechromatographed (PA). The identity of the product was established by comparison of the uv spectrum of the authentic 2,4-diaminopyrimidine in acid, base and neutral solution with the reaction product eluted from the second paper chromatogram. All the reaction mixtures containing guanidine yielded 2,4-diaminopyrimidine .The yields of 2,4-diaminopyrimidine were: from cyanoacetylene, 3.7 %; cyanoacetaldehyde, 3.5 %; cyanovinyl phosphate, 1.3 %.

*(ii) Limiting Reagent Concentrations for Synthesis.* The lower limit of reagent concentration where 2,4-diaminopyrimidine was still observed was determined by mixing varying amounts of guanidine with the cyanocarbon compounds. The yield was determined from the uv spectrum of the product with the correct $R_f$ value after chromatography (PA), elution, electrophoresis and elution of the substance which migrated to the same position as authenic 2,4-diaminopyrimidine. In the experiments with $HC{\equiv}CCN$ a second chromatogram in butanol-acetic acid-water (4:1:5) was used in place of electrophoresis. The results are tabulated in Table 2.

### e) Kinetic Measurements

Kinetic runs were carried out at 100° in a steam bath or at lower temperatures (±0.1°) in a Haake Model FS constant temperature bath. Some measurements were also carried out in a thermostated uv cell with circulating water from the Haake constant temperature bath for temperature control. The temperature in the cell was measured with an iron-constantan thermocouple.

The kinetics were measured spectrophotometrically. Pseudo-first-order rate constants were obtained from the plot of $\log(\mathrm{OD}\text{-}\mathrm{OD}_\infty/\mathrm{OD}_i\text{-}\mathrm{OD}_\infty)$ *vs* time. Average values of the pseudo-first-order rate constants were used in subsequent calculations.

The kinetics of the hydrolysis of the anion of cyanoacetaldehyde were measured in $10^{-4}$ *M* solution by following the decrease in uv absorption at 249 nm. The kinetics of the hydrolysis of the anion of the aldol dimer of cyanoacetaldehyde were measured in $10^{-4}$–$10^{-5}$ *M* solution by following the decrease in uv absorption at 310 nm. The results are given in Tables 3 and 4.

The kinetics for the hydrolysis of cyanoacetaldehyde were found to be consistent with the following rate expression:

$$\text{rate} = k_2\,[\text{cyanoacetaldehyde}]\,[\text{OH}^-] + k_2'\,[\text{cyanoacetaldehyde}]\,[\text{phosphate}].$$

Table 2. Variation in yield of diaminopyrimidine with concentration

| Reactant concentrations (*M*) | | | | |
|---|---|---|---|---|
| $OHCCH_2CN$ | Aldol dimer | HC≡CCN | Guanidine | 2,4-Diamino-pyrimidine (%) |
| 0.1 | | | 0.1 | 1.2 |
| | 0.1 | | 0.1 | 1.0 |
| 0.01 | | | 0.01 | 1.1 |
| | 0.01 | | 0.01 | 1.0 |
| | | 0.01 | 0.01 | 0.1 |
| 0.005 | | | 0.005 | 1.0 |
| | 0.005 | | 0.005 | 0.7 |
| | | 0.005 | 0.005 | 1.7 |
| 0.001 | | | 0.001 | — |
| | 0.001 | | 0.001 | — |
| | | 0.001 | 0.001 | — |
| 0.01 | | | 0.005 | 1.0 |
| 0.01 | | | 0.001 | — |
| | 0.01 | | 0.005 | 0.8 |
| | 0.01 | | 0.001 | — |
| 0.005 | | | 0.01 | 1.0 |
| 0.001 | | | 0.01 | — |
| | 0.005 | | 0.01 | 0.7 |
| | 0.001 | | 0.01 | — |

Table 3. Kinetics of cyanoacetaldehyde (2) decomposition

| Run | pH | Buffer | Temp. °C | $k \times 10^2$ (hr$^{-1}$) |
|---|---|---|---|---|
| 1 | 12.0 | 0.1 *M* phosphate | 100 | 112 |
| 2 | 12.0 | 0.1 *M* phosphate | 100 | 111 |
| 3 | 11.0 | 0.1 *M* phosphate | 100 | 18.1 |
| 4 | 11.0 | 0.1 *M* phosphate | 100 | 17.6 |
| 5 | 12.3 | 0.1 *M* hydroxide | 80.6 | 45.1 |
| 6 | 12.3 | 0.1 *M* hydroxide | 80.6 | 44.6 |
| 7 | 12.0 | 0.1 *M* phosphate | 79.3 | 27.4 |
| 8 | 12.0 | 0.1 *M* phosphate | 79.3 | 28.1 |
| 9 | 11.7 | 0.01 *M* hydroxide | 80.6 | 2.78 |
| 10 | 11.7 | 0.01 *M* hydroxide | 80.6 | 2.25 |
| 11 | 11.0 | 0.1 *M* phosphate | 79.3 | 3.69 |
| 12 | 11.0 | 0.1 *M* phosphate | 79.3 | 3.36 |
| 13 | 11.0 | pHydrion[a] | 79.3 | 3.58 |
| 14 | 11.0 | pHydrion[a] | 79.3 | 4.99 |

[a] Carbonate-borax mixture.

Values of $k_2 = 104$ l mol$^{-1}$hr$^{-1}$ and $k_2' = 0.75$ l mol$^{-1}$hr$^{-1}$ were calculated at 100° from pseudo first order rate constants at pH 11 and 12 (runs 1–4). Values of $k_2 = 27$ l mol$^{-1}$hr$^{-1}$ and $k_2' = 0.080$ l mol$^{-1}$hr$^{-1}$ were calculated at 79.6° (runs 7, 8, 11, 12). The value of $k_2 = 20.4$ l mol$^{-1}$hr$^{-1}$ found at pH 12.3 (runs 5,6) is in fair agreement with the value of $k_2$ calculated above while that of $k_2 = 4.8$ l mol$^{-1}$hr$^{-1}$ at pH 11.7

Table 4. Kinetics of cyanoacetaldehyde dimer (*3*) decomposition

| Run | pH | Buffer | Temp. °C | $k \times 10^2$ ($hr^{-1}$) |
|---|---|---|---|---|
| 1 | — | none ($H_2O$) | 100 | 2.16 |
| 2 | — | none ($H_2O$) | 100 | 2.32 |
| 3 | — | none ($H_2O$) | 100 | 1.69 |
| 4 | 7.0 | phosphate 0.015 *M* | 100 | 1.73 |
| 5 | 7.0 | phosphate 0.015 *M* | 100 | 1.92 |
| 6 | 9.0 | borate ~0.05 *M* | 100 | 1.78 |
| 7 | 9.0 | borate ~0.05 *M* | 100 | 1.78 |
| 8 | 9.0 | borate 0.02 *M* | 100 | 2.17 |
| 9 | 9.0 | borate 0.02 *M* | 100 | 2.2 |
| 10 | 9.0 | borate 0.02 *M* | 100 | 2.32 |
| 11 | 9.0 | pHydrion[a] | 100 | 3.09 |
| 12 | 11.8 | hydroxide 0.01 *M* | 100 | 2.4 |
| 13 | 12.0 | hydroxide 0.01 *M* | 100 | 3.59 |
| 14 | 12.0 | hydroxide 0.01 *M* | 100 | 2.81 |
| 15 | 12.0 | phosphate 0.1 *M* | 100 | 7.73 |
| 16 | 12.0 | phosphate 0.1 *M* | 100 | 7.85 |
| 17 | 12.0 | phosphate 0.01 *M* | 100 | 3.59 |
| 18 | 12.0 | phosphate 0.01 *M* | 100 | 3.54 |
| 19 | — | none ($H_2O$) | 80.6 | 0.354 |
| 20 | — | none ($H_2O$) | 80.6 | 0.275 |
| 21 | — | none ($H_2O$) | 80.6 | 0.226 |
| 22 | — | none ($H_2O$) | 80.6 | 0.223 |

[a] Borax-phosphate mixture.

(runs 9, 10) is in poor agreement with the values calculated above using phosphate buffers. However since no buffer was used in runs 5, 6, 9, 10 these values of $k$ are not considered to be as reliable as those where phosphate buffers were used. The pseudo first order rate constants in runs 13 and 14 using pHydrion buffers are difficult to interpret in detail because the exact composition of the buffer is not known; however the rate constants are similar in magnitude to those where phosphate buffer was used (runs 11, 12). The values of $k_2$ at 30° and 0° were estimated to be 0.252 l mol$^{-1}$hr$^{-1}$ and $7.76 \times 10^{-3}$ l mol$^{-1}$hr$^{-1}$ from an extrapolation of the Arrhenius plot.

The kinetics for the hydrolysis of aldol dimer (*3*) were found to be consistent with the following rate expression:

$$\text{rate} = k_1\,[\text{dimer}] + k_2\,[\text{dimer}]\,[\text{OH}^-] + k_2'\,[\text{dimer}]\,[\text{phosphate}].$$

The value of $k_1$ was evaluated from the first order rates observed in the pH 7–9 range (runs 1–11) and an average value of 0.021 hr$^{-1}$ was obtained. A value of 1.1 l mol$^{-1}$hr$^{-1}$ was calculated for $k_2$ from the average pseudo first order rate constant at pH 12 of 0.032 (runs 13 and 14) and $k_1$. A value of 0.46 l mol$^{-1}$hr$^{-1}$ was calculated for $k_2'$ from the values of $k_1$, $k_2$ and 0.078, the observed pseudo first order rate at pH 12 with 0.1 *M* phosphate (runs 15, 16). This value of $k_2'$ agrees well with the value 0.40 l mol$^{-1}$hr$^{-1}$ calculated using 0.036 hr$^{-1}$, the observed first order rate at pH 12 and 0.01 *M* phosphate (runs 17, 18). The values of $k_1$ at 30° and 0° were estimated to be $5 \times 10^{-6}$ hr$^{-1}$ and $5 \times 10^{-8}$ hr$^{-1}$, respectively from an extrapolation of the Arrhenius plot of the average values of $k_1$ at 100° (0.021 hr$^{-1}$) and 80.6° (0.0027 hr$^{-1}$) (runs 19–22).

The equilibration of cyanoacetaldehyde anion with its aldol dimer was apparent in the kinetic runs by the development of the uv spectrum of aldol dimer at 310 nm when the rate of hydrolysis of cyanoacetaldehyde anion was investigated and the development of the uv spectrum of cyanoacetaldehyde at 249 nm when rate of hydrolysis of the aldol dimer was investigated. Approximately a 1:1 ratio of monomer and dimer was noted at pH 9. Less monomer was noted in more basic solution.

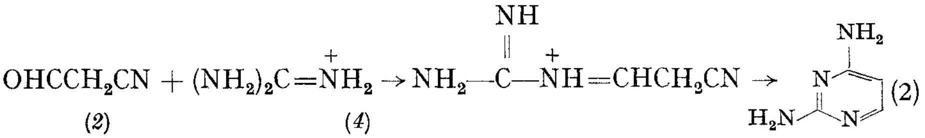
### *f) pKa of Cyanoacetaldehyde*

A $10^{-4}$ *M* solution of the anion of cyanoacetaldehyde was prepared in 0.1 *M* NaOH. This solution was titrated with 1 *M* HCl and the pH and uv absorption of the mixture was measured. It was found in two determinations that the half neutralization of cyanoacetaldehyde occurred at pH 8.05. Therefore a *pKa* of 8.1 has been adopted in preference to the value of 8.4 determined previously (Ferris, Sanchez and Orgel, 1968).

## 3. Results

The reaction of guanidine (*4*)[1] with cyanoacetaldehyde (*2*), aldol dimer (*3*), cyanovinyl phosphate and cyanoacetylene (*1*) resulted in the formation of 2,4-diaminopyrimidine (*5*). No pyrimidines were detected when urea, cyanamide or cyanoguanidine were substituted for guanidine. We established previously that pyrimidines are not formed by heating a mixture of cyanate and *2* or *3* (Ferris, Sanchez and Orgel, 1968).

The reaction of cyanoacetaldehyde (*2*) with guanidine (*4*) is probably initiated by the addition of *4* to the aldehyde function of *2* followed by intramolecular attack of the guanidine group on the nitrile function to give *5* [Eq. (2)]. The synthesis of *5* from *3* and cyanovinyl phosphate probably involves the initial conversion of these compounds to cyanoacetaldehyde. The conversion of *3* to *2* will be discussed later and the conversion of cyanovinyl phosphate to *2* has been observed previously (Ferris, Goldstein and Beaulieu, 1970).



(*5*)

The yield of *5* was in the 1–3% range depending on the concentration of starting materials. Diaminopyrimidine was detectable as a reaction product when the concentration of reactants was as low as 0.005 *M*, however *5* could not be detected when a 0.001 *M* concentration of reactants was used (Table 2).

Uracil (*7*) was detected as the main product resulting from the hydrolysis of *5* (Table 1). Small amounts of cytosine (*6*) were also detected. Cytosine

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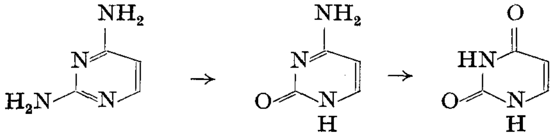
[1] Since the *pKa* of guanidinium ion is 13.65 (Hall and Sprinkle, 1932), guanidine is present as the guanidinium ion in all the experiments carried out in this work.

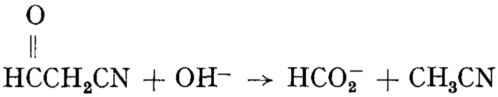
is undoubtedly an intermediate in the conversion of *5* to *7* [Eq. (3)] (Ferris, Sanchez and Orgel, 1968).



*5* *6* *7* (3)

The stability of *2* and *3* was estimated from the rates of decomposition of these compounds in aqueous solution. The rate of hydrolysis of cyanoacetaldehyde was determined spectrophotometrically from the rate of loss of the anion absorption at 249 nm. Pseudo first order kinetics were observed, however the second order nature of the reaction was demonstrated by an increase in the hydrolysis rate with increasing hydroxide ion concentration (Table 3). The rate of decomposition is also dependent on the phosphate concentration when phosphate buffers are used. We assumed that phosphate is serving as a general base, however this point has not been established.

It is assumed that formate and acetonitrile are the hydrolysis products of *2* [Eq. (4)]. These products are consistent with 1. the observed molecularity of the reaction, 2. the absence of significant uv absorption after the hydrolysis is complete and 3. the observation of similar base cleavage reactions with *β*-ketoesters (Royals, 1954).



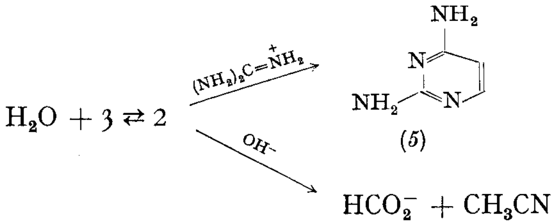
$$\mathrm{H\overset{\overset{O}{\|}}{C}CH_2CN + OH^- \rightarrow HCO_2^- + CH_3CN} \qquad (4)$$

(*2*)

The hydrolysis of the aldol dimer (*3*) exhibited first order kinetics in the pH 7–9 range. In addition to a specific phosphate effect there appears to be a specific hydroxide effect in the pH 12 range.

The conversion of *3* to *2* was observed in the hydrolysis of *3* at pH 9. This observation is consistent with the observed kinetic data. At 80° the second order rate constant for the hydrolysis of *2* is 27.0 $\mathrm{l\ mol^{-1}hr^{-1}}$ which is equivalent to a pseudo first order rate constant at pH 9 of $2.7 \times 10^{-4}$ $\mathrm{hr^{-1}}$. The first order rate constant for the hydrolysis of *3* is $2.7 \times 10^{-3}$ $\mathrm{hr^{-1}}$; a factor of ten faster. As the pH increases the pseudo first order rate for the hydrolysis of *2* increases and its steady state concentration decreases.

The first order nature of the hydrolysis and the observation of cyanoacetaldehyde as an intermediate is consistent with the attack of a water molecule on *3* in its conversion to *2*. Eq. (5) is also consistent with the kinetic data and the products observed in the hydrolysis and reactions of *2* and *3*.



(5)

## 4. Discussion

The formation of cyanoacetylene in an electric discharge and its conversion to cyanoacetaldehyde (*2*) have been discussed previously (Sanchez, Ferris and Orgel, 1966). Cyanoacetylene has recently been detected in interstellar space (Turner, 1971) — a result which suggests that it is formed under other reaction conditions. Guanidine (*4*) has been reported as a product of the oligomerization and photolysis of HCN (Lowe, Rees and Markham, 1963; Labadie, Jensen and Neuzil, 1968; Lohrmann, 1972). It is also formed by the reaction of ammonia with cyanamide (Blair and Braham, 1924) and the hydrolysis of cyanamide with hydroxide (Eloranta, 1960). Thus it seems likely that the requisite starting materials for the pyrimidine synthesis were present on the primitive earth. The yield of pyrimidines that could have been formed by this route and the limiting concentrations of *2* and *4* needed for synthesis are comparable in magnitude to the route to pyrimidines from cyanoacetylene and cyanate (Ferris, Sanchez and Orgel, 1967). The hydrolytic reactions leading to uracil are also comparable in both pathways.

Prebiotic pyrimidine synthesis from cyanoacetaldehyde and guanidine [Eq. (2)] appears to have been the more likely route because the stability of these starting materials is greater than that of cyanoacetylene and cyanate. Cyanoacetaldehyde and the aldol dimer of cyanoacetaldehyde are $10^3$ times more stable than cyanoacetylene (Table 5). The cyanoacetylene formed on the primitive earth would have been converted to an equilibrium mixture of *2* and *3* in lakes and oceans. Very high concentrations of guanidine could have been present in the primitive oceans because of its very slow rate of decomposition (Table 5). Its half life for hydrolysis of $10^5$–$10^8$ years is much greater than the 10–100 years estimated for cyanate (Ferris, Sanchez and Orgel, 1966). Higher concentrations of both reactants would have formed thus making the biomolecular reaction of cyanoacetaldehyde and guanidine to form 2,4-diaminopyrimidine (*5*) a more likely event.

Table 5. Extrapolated rate constants and half lifes at pH 9

| Compound | $k_2(30°)$ $l$ mol$^{-1}$hr$^{-1}$ | $k_2(0°)$ $l$ mol$^{-1}$hr$^{-1}$ | $t_{\frac{1}{2}}{}^{a}(30°)$ yr | $t_{\frac{1}{2}}{}^{a}(0°)$ yr |
|---|---|---|---|---|
| $HC{\equiv}CCN$ [b] | 300 | 8.4 | 0.03 | 1 |
| $OHCCH_2CN$ (*2*) | $2.5 \times 10^{-1}$ | $7.8 \times 10^{-3}$ | 31 | 1015 |
| Dimer (*3*) | $5 \times 10^{-6}$ [c] | $5 \times 10^{-8}$ [c] | 16 | 1600 |
| $(NH_2)_2C{=}\overset{+}{N}H_2$ [d] (*4*) | $1.4 \times 10^{-5}$ | $2.9 \times 10^{-8}$ | $0.5 \times 10^{6}$ | $0.27 \times 10^{9}$ |

[a] $t_{\frac{1}{2}}$ calculated from pseudo first order rate constant ($k_1 = k_2[OH^-]$) at pH 9 except for (*3*) where the first order rate constant was used.

[b] Rate constants obtained by extrapolation of the data of Ferris, Sanchez and Orgel (1968).

[c] A first order rate constant.

[d] Rate constants obtained by extrapolation of the Arrhenius plot of Eloranta (1961).

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