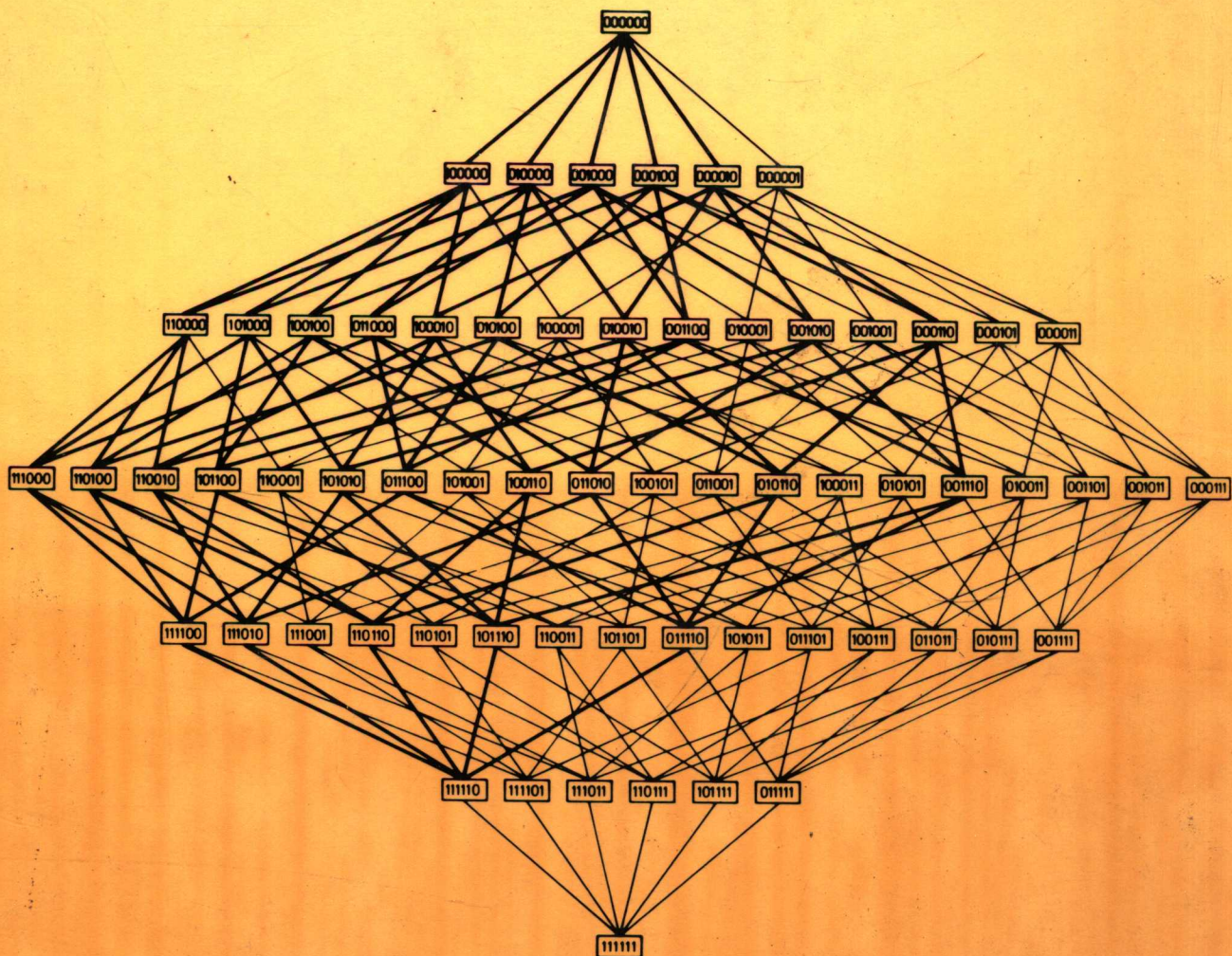


Molecular Evolution of Life

Edited by
Herrick Baltscheffsky
Hans Jörnvall
Rudolf Rigler



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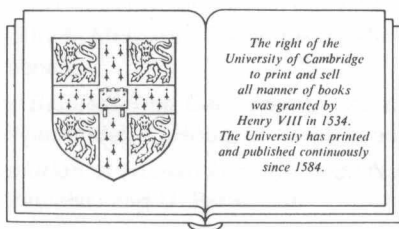
Molecular Evolution of Life

Proceedings of a conference held at Södergarn, Lidingö,
Sweden, 8–12 September 1985

Edited by

Herrick Baltscheffsky, Hans Jörnvall and Rudolf Rigler

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Molecular Evolution of Life

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Molecular Evolution of Life

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Preface

In the last few years great advances have been made in our understanding of fundamental molecular aspects of the prebiological and biological evolution of life. Nucleic acids and proteins are investigated with rapidly increasing efficiency. Molecular dimensions and dynamics are studied with biochemical and biophysical methods at high resolution and sensitivity. This has made possible discoveries of new relationships between functional forms and structural patterns in molecular evolution.

There is a mutual cause and effect situation between scientists in the current fast pace of development in molecular evolution and the intensified collaboration between biochemistry, biophysics, genetics, medical chemistry, medical physics, molecular biology, and related areas. It was considered timely and urgent to try to integrate the expanding knowledge in an international conference focusing, over the borders of different academic subjects, on the molecular evolution of life. The response, both national and international, was overwhelming. The number of active participants increased from a planned 40–50 to 73. The presence of so many qualified scientists contributing to the area was made possible thanks to generous grants from the Royal Swedish Academy of Sciences and the Nobel Institute of Chemistry, the Swedish Medical Research Council, the Swedish Natural Science Research Council, the Swedish Cancer Society, the Ministry of Education, and from the following industries with an active research interest in this and neighbouring fields: Astra AB, Boehringer-Mannheim GmbH, KabiGen AB, KabiVitrum AB, LKB Products AB, Pharmacia AB and Skandigen AB.

The conference took place at Södergarns kursgård, Lidingö, near Stockholm, 8–12 September, 1985. The final afternoon session with four overview lectures, was held at the Royal Swedish Academy of Sciences. These lectures were given by Professors C. Ponnampерuma, USA and Sri Lanka, M. Eigen, FRG, E. Davie, USA, and G. Edelman, USA.

This volume contains nearly all of the papers presented at the conference. The contributions are grouped according to the main topics treated at the conference. Naturally, the divisions in the list of contents are somewhat arbitrary since overlaps between sub-fields are considerable.

Stockholm, November, 1985

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Current Status of the Prebiotic Synthesis of Organic Molecules

Prebiotic Systems and Evolutionary Pathways

Current Status of the Prebiotic Synthesis of Small Molecules

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Paper presented at the Conference on 'Molecular Evolution of Life', Lidingö, Sweden, 8-12 September, 1985

Abstract

The prebiotic synthesis of small molecules has been accomplished using various simulated atmospheres with CH_4 , N_2 , NH_3 , H_2O being the most effective, but H_2 , CO , N_2 , H_2O and H_2 , CO_2 , N_2 , H_2O also give good yields of organic compounds provided $\text{H}_2/\text{CO} > 1$ and $\text{H}_2/\text{CO}_2 > 2$. The spark discharge is a very effective source of energy in such experiments, because it is a good source of HCN. Ultraviolet light would also have been important on the primitive earth. Almost all prebiotic amino acids are made by the hydrolysis of an amino nitrile formed from an aldehyde, NH_3 and HCN (Strecker synthesis). There are reasonable prebiotic syntheses worked out for the twenty amino acids that occur in proteins, with the exception of lysine, arginine and histidine. The purines are derived from the polymerization of HCN, and the precursor of the pyrimidines is cyanoacetylene. The sugars (including ribose), would have been formed from the base catalyzed polymerization of formaldehyde. There is no good prebiotic synthesis of straight chain fatty acids. Of the vitamin coenzymes, only nicotinic acid has been synthesized under prebiotic conditions.

Many of the molecules that are produced in these simulated primitive earth experiments are found in a group of meteorites that contain organic compounds, called the carbonaceous chondrites. Since such prebiotic syntheses took place on the parent body of the carbonaceous chondrites, generally thought to be an asteroid, it is plausible, but not proved, that such syntheses took place on the primitive earth, and that the first living organisms were formed out of these compounds.

Introduction

In the past three decades there has been a wide variety of experiments designed to simulate conditions on the primitive earth and to demonstrate how the organic compounds that made up the first living organisms were synthesized. This paper will review this work and indicate the status of such syntheses. There is too much material to review in detail, and the reader is directed to a number of more complete discussions [1-3].

1. The composition of the primitive atmosphere

There is no agreement on the constituents of the primitive atmosphere. It is to be noted that there is no geological evidence concerning the conditions on the earth from 4.5×10^9 years to 3.8×10^9 years since no rocks older than 3.8×10^9 years are known. Even the 3.8×10^9 years old Isua Rocks in Greenland are not sufficiently well preserved to infer details of the atmosphere at that time. Proposed atmospheres and the reasons given to favor them will not be discussed here. As shown in Sections 2-4, the more reducing atmospheres favor the synthesis of organic compounds both in terms of yields and the variety of compounds obtained. Some of the organic

chemistry can give explicit predictions about atmospheric constituents. Such considerations cannot prove that the earth had a certain primitive atmosphere, but the prebiotic synthesis constraints should be a major consideration.

2. Energy sources

A wide variety of energy sources has been utilized with various gas mixtures since the first experiments using electric discharges. The importance of a given energy source is determined by the product of the energy available and its efficiency for organic compound synthesis. Even though both factors cannot be evaluated with precision, a qualitative assessment of the energy sources can be made. It should be emphasized that a single source of energy or a single process is unlikely to account for all the organic compounds on the primitive earth [4]. An estimate of the sources of energy on the earth at the present time is given in Table I.

The energy from the decay of radioactive elements was probably not an important energy source for the synthesis of organic compounds on the primitive earth since most of the ionization would have taken place in silicate rocks rather than in the reducing atmosphere. The shock wave energy from the impact of meteorites on the earth's atmosphere and surface as well as the larger amount of shock waves generated in lightning bolts have been proposed as energy sources for

Table I. Present sources of energy averaged over the earth

Source	Energy	
	($\text{cal cm}^{-2} \text{ yr}^{-1}$)	($\text{J cm}^{-2} \text{ yr}^{-1}$)
Total radiation from sun	260000	1090000
Ultraviolet light		
< 3000 Å	3400	14000
< 2500 Å	563	2360
< 2000 Å	41	170
< 1500 Å	1.7	7
Electric discharges	4 ^a	17
Cosmic rays	0.0015	0.006
Radioactivity (to 1.0 km depth)	0.8	3.0
Volcanoes	0.13	0.5
Shock waves	1.1 ^b	4.6

^a 3 $\text{cal cm}^{-2} \text{ yr}^{-1}$ of corona discharge + 1 $\text{cal cm}^{-2} \text{ yr}^{-1}$ of lightning.

^b 1 $\text{cal cm}^{-2} \text{ yr}^{-1}$ of this is in the shock wave of lightning bolts and is also included under electric discharges.

primitive earth organic synthesis. Very high yields of amino acids have been reported in some experiments [5], but it is doubtful whether such yields would be obtained in natural shock waves. Cosmic rays are a minor source of energy on the earth at present, and it seems unlikely that any increase in the past could have been so great as to make them a major source of energy.

The energy in the lava emitted at the present time is a significant but not a major source of energy. It is generally supposed that there was a much greater amount of volcanic activity on the primitive earth, but there is no evidence to support this. Even if the volcanic activity was a factor of 10 greater than at present, it would not have been the dominant energy source. Nevertheless, molten lava may have been important in the pyrolytic synthesis of some organic compounds.

Ultraviolet light was probably the largest source of energy on the primitive earth. The wavelengths absorbed by the atmospheric constituents are all below 2000 Å except for ammonia (<2300 Å) and H₂S (<2600 Å). Whether it was the most effective source of organic compounds is not clear. Most of the photochemical reactions would occur in the upper atmosphere, and the products formed would, for the most part, absorb the longer wavelengths, and so be decomposed before they reached the protection of the oceans. The yield of amino acids from the photolysis of CH₄, NH₃, and H₂O at wavelengths of 1470 and 1294 Å is quite low [6], probably due to the low yields of hydrogen cyanide. The synthesis of amino acids by the photolysis of CH₄, C₂H₆, NH₃, H₂O, and H₂S mixtures by ultraviolet light of wavelengths greater than 2000 Å [7] is also a low yield synthesis, but the amount of energy is much greater in this region of the sun's spectrum. Only H₂S absorbs the ultraviolet light, but the photodissociation of H₂S results in a hydrogen atom having a high kinetic energy, which activates or dissociates the methane, ammonia, and water. This appears to be very attractive prebiotic synthesis. However, it is not clear whether a sufficient partial pressure of H₂S could be maintained in the atmosphere since H₂S is photolyzed rapidly to elemental sulfur and hydrogen.

The most widely used sources of energy for laboratory syntheses of prebiotic compounds are electric discharges. These include sparks, semicorona, arc, and silent discharges with the spark being the most frequently used type. The ease of handling and high efficiency of electric discharges are factors favoring its use, but the most important reason is that electric discharges are very efficient in synthesizing hydrogen cyanide, whereas ultraviolet light is not. Hydrogen cyanide is a central intermediate in prebiotic synthesis, being needed for amino acid synthesis by the Strecker reaction, or by selfpolymerization to amino acids, and most importantly for the prebiotic synthesis of adenine and guanine.

An important feature of all these energy sources is the activation of molecules in a local area followed by quenching of this activated mixture, and then protecting the organic compounds from further influence of the energy source. The quenching and protective steps are critical because the organic compounds will be destroyed if subjected continuously to the energy source.

3. Prebiotic synthesis of amino acids

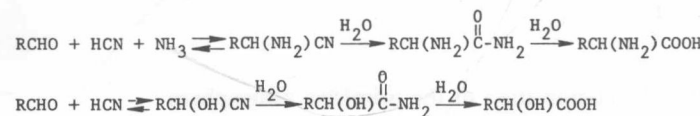
Mixtures of CH₄, NH₃, and H₂O with or without added H₂ are considered strongly reducing atmospheres. The atmosphere

Table II. Yields from sparking a mixture CH₄, NH₃, H₂O and H₂. The present yields are based on carbon. 59 mmoles (710 mg) of carbon was added as CH₄

Compound	Yield (μmol)	Yield (%)
Glycine	630	2.1
Glycolic acid	560	1.9
Sarcosine	50	0.25
Alanine	340	1.7
Lactic acid	310	1.6
N-Methylalanine	10	0.07
α-Amino-n-butyric acid	50	0.34
α-Aminoisobutyric acid	1	0.007
α-Hydroxybutyric acid	50	0.34
β-Alanine	150	0.76
Succinic acid	40	0.27
Aspartic acid	4	0.024
Glutamic acid	6	0.051
Iminodiacetic acid	55	0.37
Iminoacetic-propionic acid	15	0.13
Formic acid	2330	4.0
Acetic acid	150	0.51
Propionic acid	130	0.66
Urea	20	0.034
N-Methyl urea	15	0.051
Total		15.2

of Jupiter contains these species with the H₂ in large excess over the CH₄. The first successful prebiotic amino acid synthesis was carried out using an electric discharge as an energy source [8]. The result was a large yield of amino acids (the yield of glycine alone was 2.1% based on the carbon), together with hydroxy acids, short aliphatic acids, and urea. One of the surprising results of this experiment was that the products were not a random mixture of organic compounds, but rather a relatively small number of compounds were produced in substantial yield. In addition the compounds were, with a few exceptions, of biological importance.

The mechanism of synthesis of the amino and hydroxy acids was investigated [9]. It was shown that the amino acids were not formed directly in the electric discharge but were the result of solution reactions of smaller molecules produced in the discharge, in particular hydrogen cyanide and aldehydes. The reactions are shown in Scheme 1. These reactions were



Scheme 1

studied subsequently in detail, and the equilibrium and rate constants of these reactions were measured [10]. These results show that amino and hydroxy acids can be synthesized at high dilutions of HCN and aldehydes in a primitive ocean. It is also to be noted that the rates of these reactions were rather rapid. The half-lives for the hydrolysis of the amino and hydroxy nitriles are less than 10³ years at 0 °C.

This synthesis of amino acids, called the Strecker synthesis, requires the presence of NH₄⁺ (and NH₃) in the primitive

ocean. On the basis of the experimental equilibrium and rate constants it can be shown [10] that equal amounts of amino and hydroxy acids are obtained when the NH_4^+ concentration is about 0.01 M at pH 8 and 25 °C with this NH_4^+ concentration being insensitive to temperature and pH. This translates into a p_{NH_3} in the atmosphere of 2×10^{-7} atm at 0 °C and 4×10^{-6} atm at 25 °C. This is a low partial pressure, but it would seem to be necessary for amino acid synthesis. A similar estimate of the NH_4^+ concentration in the primitive ocean can be obtained from the equilibrium decomposition of aspartic acid [11]. Ammonia is decomposed by ultraviolet light, but mechanisms for resynthesis are available. The details of the ammonia balance on the primitive earth remain to be worked out.

In a typical electric discharge experiment, the partial pressure of CH_4 is 0.1–0.2 atm. This pressure is used for convenience, and it is likely, but never demonstrated, that organic compound synthesis would work at much lower partial pressures of methane. There are no estimates available for p_{CH_4} on the primitive earth but 10^{-5} to 10^{-3} atm seems plausible. Higher pressures are not reasonable because the sources of energy would convert the CH_4 to organic compounds in the oceans too rapidly for higher pressures of CH_4 to build up.

As discussed above, ultraviolet light acting on this mixture of gases is not effective in producing amino acids except at very short wavelengths or in the presence of an absorber such as H_2S .

Pyrolysis of CH_4 and NH_3 gives very low yields of amino acids. The pyrolysis conditions are from 800 to 1200 °C with contact times of a second or less [12]. However, the pyrolysis of CH_4 and other hydrocarbons gives good yields of benzene, phenylacetylene, and many other hydrocarbons. It can be shown that phenylacetylene would be converted to phenylalanine and tyrosine in the primitive ocean [13]. Pyrolysis of the hydrocarbons in the presence of NH_3 gives substantial yields of indole, which can be converted to tryptophan in the primitive ocean [14].

A mixture of CH_4 , N_2 , and traces of NH_3 , and H_2O is a more realistic atmosphere for the primitive earth because large amounts of NH_3 would not have accumulated in the

atmosphere since the NH_3 would dissolve in the ocean. It is still, however, a strongly reducing atmosphere.

This mixture of gases is quite effective with an electric discharge in producing amino acids [15]. The yields are somewhat lower than with higher partial pressures of NH_3 , but the products are more diverse. Hydroxy acids, short aliphatic acids, and dicarboxylic acids are produced along with the amino acids. Ten of the 20 amino acids that occur in proteins are produced directly in this experiment. Counting asparagine and glutamine, which are formed but hydrolyzed before analysis, and methionine, which is formed when H_2S is added [16], one can say that 13 of the 20 amino acids in proteins can be formed in this single experiment. Cysteine was found in the photolysis of CH_4 , NH_3 , H_2O , and H_2S [7]. The pyrolysis of hydrocarbons, as discussed above, leads to phenylalanine, tyrosine, and tryptophan [13, 14]. This leaves only the basic amino acids: lysine, arginine, and histidine. There are so far no established prebiotic syntheses of these amino acids. There is no fundamental reason that the basic amino acids cannot be synthesized, and this problem may be solved before too long.

4. Mildly reducing and non-reducing atmospheres

There has been less experimental work with gas mixtures containing CO and CO_2 as carbon sources instead of CH_4 .

Table III. Yields from sparking CH_4 (336 mmoles); N_2 , and H_2O with traces of NH_3

	μmol
Glycine	440
Alanine	790
α -Amino- <i>n</i> -butyric acid	270
α -Aminoisobutyric acid	~30
Valine	19.5
Norvaline	61
Isovaline	~5
Leucine	11.3
Isoleucine	4.8
Alloisoleucine	5.1
Norleucine	6.0
tert-Leucine	<0.02
Proline	1.5
Aspartic acid	34
Glutamic acid	7.7
Serine	5.0
Threonine	~0.8
Allothreonine	~0.8
α,γ -Diaminobutyric acid	33
α -Hydroxy- γ -aminobutyric acid	74
α,β -Diaminopropionic	6.4
Isoserine	5.5
Sarcosine	55
<i>N</i> -Ethylglycine	30
<i>N</i> -Propylglycine	~2
<i>N</i> -Isopropylglycine	~2
<i>N</i> -Methylalanine	~15
<i>N</i> -Ethylalanine	<0.2
β -Alanine	18.8
β -Amino- <i>n</i> -butyric acid	~0.3
β -Amino-isobutyric acid	~0.3
γ -Aminobutyric acid	2.4
<i>N</i> -Methyl- β -alanine	~5
<i>N</i> -Ethyl- β -alanine	~2
Pipecolic acid	~0.05

Yield based on the carbon added as CH_4 . Glycine = 0.26%, Alanine = 0.71%, total yield of amino acids in the table = 1.90%.

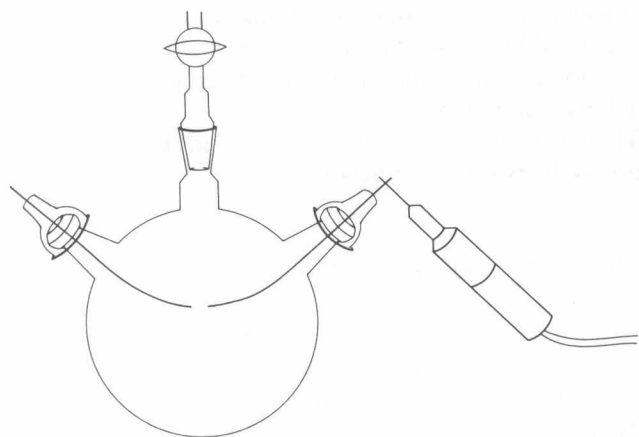


Fig. 1. Spark discharge apparatus. The 3 l flask is shown with the two tungsten electrodes and a spark generator. The second electrode is usually not grounded. In the experiments described in Table III, the flask contained 100 ml of 0.05 M- NH_4Cl brought to pH 8.7 giving p_{NH_3} of 0.1 torr. The p_{CH_4} was 200 torr and p_{N_2} was 80 torr. Since the temperature was about 30 °C during the sparking, $p_{\text{H}_2\text{O}}$ was 32 torr.

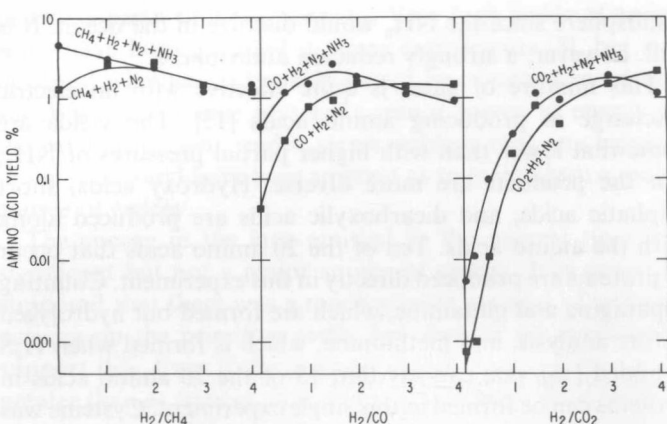


Fig. 2. Amino acid yields based on initial carbon. The apparatus of Fig. 1 was used with a sparking time of 48 h. In all experiments $p_{N_2} = 100$ torr, p_{CH_4} or p_{CO} or $p_{CO_2} = 100$ torr. For experiments containing NH_3 , the spark discharge flask contained 100 ml of 0.05 M- NH_4Cl brought to $\sim pH$ 8.7 so that p_{NH_3} was 0.1 torr. For experiments not containing NH_3 , the flask had 100 ml of H_2O .

Spark discharges have been the source of energy most extensively investigated [17, 18]. Figure 2 compares amino acid yields using CH_4 , CO , and CO_2 as a carbon source with various amounts of H_2 [18]. Separate experiments were performed with and without added NH_3 . In the case of CH_4 without added NH_3 , the yield of amino acids is 4.7% at $H_2/CH_4 = 0$ and drops to 1.4% at $H_2/CH_4 = 4$. With CO and no added NH_3 , the amino acid yield is 0.05% at $H_2/CO = 0$ and rises to a maximum of 2.7% at $H_2/CO = 3$. With CO_2 and no added NH_3 , the amino acid yield is 7×10^{-4} at $H_2/CO_2 = 0$. This is close to the level of reagent contamination and is so low that this could not be considered as a significant source of amino acids on the primitive earth. At higher H_2/CO_2 ratios, however, the yield rises to about 2%. With both CO and CO_2 , the presence of added NH_3 increases the yield of amino acids by a factor of ~ 10 at low H_2/CO and H_2/CO_2 ratios. The amino acids produced in the CH_4 experiments were similar to those shown in Table III. With CO and CO_2 , glycine was the predominant amino acid with only a small amount of alanine being produced.

The hydrogen cyanide and formaldehyde yields were also measured in these experiments. In both cases the yields paralleled those of the amino acids but were a factor 5 to 10 higher. Considerable amounts of NH_3 were also produced in these experiments.

A mixture of $CO + H_2$ is used in the Fischer-Tropsch reaction to make hydrocarbons in high yields. The reaction requires a catalyst, usually Fe or Ni supported on silica, a temperature of 200–400 °C and a short contact time. Depending on the conditions, aliphatic hydrocarbons, aromatic hydrocarbons, alcohols, and acids can be produced. If NH_3 is added to the $CO + H_2$, then amino acids, purines, and pyrimidines can be formed [19]. The intermediates in these reactions are not known, but it is likely that HCN is involved together with some of the intermediates postulated for the electric discharge processes.

A mixture of $CO + H_2O$ with electric discharges is not particularly effective in organic compound synthesis, but ultraviolet light that is absorbed by the water ($< 1849 \text{ \AA}$) results in the production of formaldehyde and other aldehydes, alcohols, and acids in fair yields [20, 21]. The mechanism seems to involve splitting the H_2O to $H + OH$ with the OH

converting CO to CO_2 and the H reducing another molecule of CO .

Electric discharges and ultraviolet light do not give substantial amounts of organic compounds with a mixture of $CO_2 + H_2O$. Ionizing radiation (e.g. 40 MeV helium ions) gives small yields of formic acid and formaldehyde [24].

Calculations using one dimensional photochemical models of $CO_2 + H_2O$ atmospheres show that substantial amounts of H_2CO can be produced in these atmospheres by solar ultraviolet light [22, 23].

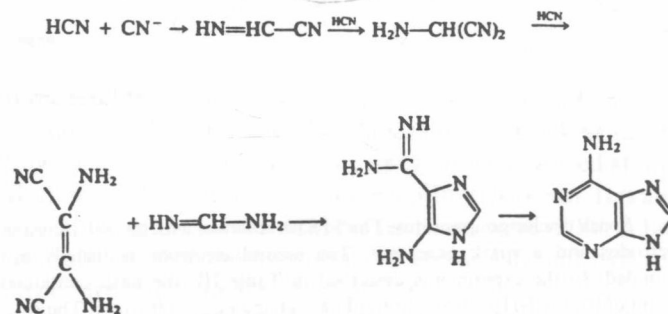
The action of gamma-rays on an aqueous solution of CO_2 and ferrous ion gives fair yields of formic acid, oxalic acid, and other simple products [25]. Ultraviolet light gives similar results. In these reactions, the Fe^{2+} is a stoichiometric reducing agent rather than a catalyst. Nitrogen in the form of N_2 does not react, and experiments with NH_3 have not been tried.

The implications of these results in considering the composition of the primitive earth is that CH_4 is the best carbon source for prebiotic synthesis, especially for amino acid synthesis. Although glycine was essentially the only amino acid synthesized in the spark discharge experiments with CO and CO_2 , other amino acids (e.g. serine, aspartic acid, alanine) would probably have been formed from this glycine with the H_2CO and HCN in the primitive ocean over longer periods of time. Since we do not know which amino acids were required for the origin of the first living organism, atmospheres containing CO and CO_2 can not be excluded, but a CH_4 containing atmosphere is favored if a wide variety of amino acids is needed. The synthesis of purines and sugars described below would not be greatly different with CH_4 , CO or CO_2 with adequate H_2 . Although the spark discharge yields of amino acids, HCN and H_2CO are about the same with CH_4 and with $H_2/CO > 1$ and $H_2/CO_2 > 2$, it is not clear how such high H_2 /carbon ratios could have been maintained in the primitive atmosphere since H_2 escapes from the earth's atmosphere into outer space. These problems are poorly understood and beyond the scope of this outline.

5. Purine and pyrimidine synthesis

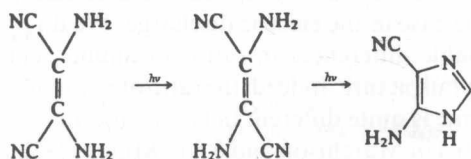
Hydrogen cyanide is used in the synthesis of purines as well as amino acids. This is illustrated in a remarkable synthesis of adenine. If concentrated solutions of ammonium cyanide are refluxed for a few days, adenine is obtained in up to 0.5% yield along with 4-aminoimidazole-5-carboxamide and the usual cyanide polymer [26].

The mechanism of adenine synthesis in these experiments is probably as shown in Scheme 2.



Scheme 2

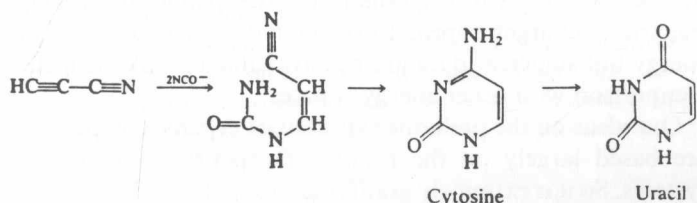
The difficult step in the synthesis of adenine just described is the reaction of tetramer with formamidine. This step may be bypassed by the photochemical rearrangement of tetramer to aminoimidazole nitrile, a reaction that proceeds readily in contemporary sunlight [27] (Scheme 3).



Scheme 3

A further possibility is that tetramer formation may have occurred in a eutectic solution. High yield of tetramer (>10%) can be obtained by cooling dilute cyanide solutions to between -10 and -30 °C for a few months [27].

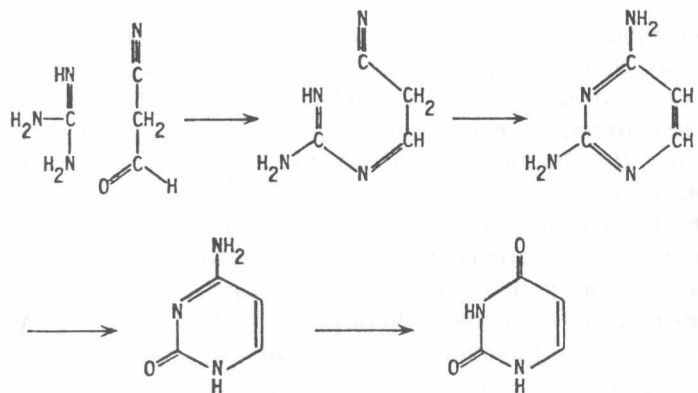
The prebiotic synthesis of the pyrimidine cytosine involves cyanoacetylene, which is synthesized in good yield by sparking mixtures of $\text{CH}_4 + \text{N}_2$. Cyanoacetylene reacts with cyanate to give cytosine [28] (Scheme 4), and the cytosine can be



Scheme 4

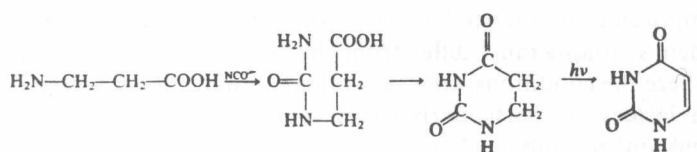
converted to uracil. Cyanate can come from cyanogen or by the decomposition of urea.

A related synthesis starts with cyanoacetaldehyde, from the hydration of cyanoacetylene, which reacts with guanidine to give diaminopyrimidine. This is then hydrolyzed to cytosine and uracil [29] (Scheme 5).



Scheme 5

Another prebiotic synthesis of uracil starts from β -alanine and cyanate and ultraviolet light [30] (Scheme 6).

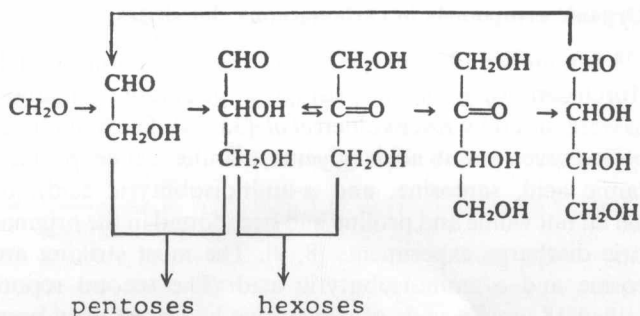


Scheme 6

6. Sugars

The synthesis of reducing sugars from formaldehyde under alkaline conditions was discovered long ago. However, the process is very complex and incompletely understood. It depends on the presence of a basic catalyst, with calcium hydroxide and calcium carbonate being frequently used. In the absence of catalysts, little or no sugar is obtained. Particularly attractive is the finding that at 100 °C, clays such as kaolin serve to catalyze formation of monosaccharides, including ribose, in good yield from dilute (0.01 M) solutions of formaldehyde [31, 32].

The reaction is autocatalytic and proceeds in stages through glycolaldehyde, glyceraldehyde, and dihydroxyacetone, tetroses, and pentoses to give finally hexoses including glucose and fructose. One proposed reaction sequence is as shown in Scheme 7.



Scheme 7

The problem with sugars on the primitive earth is not their synthesis, but rather their stability. They decompose in a few hundred years at most at 25 °C. There are a number of possible ways to stabilize sugars, the most interesting being to convert the sugar to a glycoside of a purine or pyrimidine.

7. Other prebiotic compounds

There are a number of compounds that have been synthesized under primitive earth conditions, but space does not permit an adequate discussion. These include:

dicarboxylic acids, tricarboxylic acids, fatty acids (C_2 – C_{10} , branched and straight), fatty alcohols (straight chain via Fischer–Tropsch reaction), Porphin, nicotinonitrile and nicotinamide, triazines, imidazoles.

Other prebiotic compounds that may have been involved in polymerization reactions include:

cyanate [NCO^-], cyanamide [H_2NCN], cyanamide dimer [$\text{H}_2\text{NC}(\text{NH})\text{NH-CN}$], dicyanamide [NC-NH-CN], cyanogen [NC-CN], HCN tetramer, diimino succinonitrile, acylthioesters, phosphate polymers.

8. Compounds that have not been synthesized prebiotically

It is a matter of opinion as to what constitutes a prebiotic synthesis. In some cases the conditions are so forced (e.g. the use of anhydrous solvents) or the concentrations so high (e.g. 10 M formaldehyde) that such conditions could not have occurred extensively on the primitive earth. Reactions under these and other extreme conditions can not be considered prebiotic.

There have been many claimed prebiotic synthesis in which the compound has not been properly identified. The best method for unequivocal identification these days is gas chromatography-mass spectrometry of a suitable derivative, although melting points and mixed melting points can sometimes be used. The amino acid analyzer alone or chromatography in multiple solvent systems does not prove the identification of a compound.

Some of the compounds which do not yet have adequate prebiotic syntheses are: arginine, lysine, histidine, straight-chain fatty acids, porphyrins, pyridoxal, thiamine, riboflavin, folic acid, lipoic acid, biotin. It is probable that prebiotic syntheses will be available before too long for some of these compounds. In other cases the compounds may not have been synthesized prebiotically, so their occurrence in living systems started after the origin of life.

9. Organic compounds in carbonaceous chondrites

On 28 September 1969 a type II carbonaceous chondrite fell in Murchison, Australia. Surprisingly large amounts of amino acids were found by Kvenvolden *et al.* [33, 34]. The first report identified seven amino acids (glycine, alanine, valine, proline, glutamic acid, sarcosine, and α -aminoisobutyric acid), of which all but valine and proline had been found in the original electric discharge experiments [8, 9]. The most striking are sarcosine and α -aminoisobutyric acid. The second report identified 18 amino acids of which nine had previously been identified in the original electric discharge experiment, but the remaining nine had not.

At that time we had identified the hydrophobic amino acids from the low temperature electric discharge experiments described above, and therefore we examined the products for the non-protein amino acids found in Murchison. We were able to find all of them [15].

There is a striking similarity between the products and relative abundances of the amino acids produced by electric discharge and the meteorite amino acids. Table IV compares

Table IV. *Relative abundances of amino acids in the Murchison meteorite and in an electric discharge synthesis*

Amino acid	Murchison meteorite	Electric discharge
Glycine	****	****
Alanine	****	****
α -Amino- <i>n</i> -butyric acid	***	****
α -Aminoisobutyric acid	****	**
Valine	***	**
Norvaline	***	***
Isovaline	**	**
Proline	***	*
Pipecolic acid	*	<*
Aspartic acid	***	***
Glutamic acid	***	**
β -Alanine	**	**
β -Amino- <i>n</i> -butyric acid	*	*
γ -Aminoisobutyric acid	*	*
γ -Aminobutyric acid	*	**
Sarcosine	**	***
<i>N</i> -Ethylglycine	**	***
<i>N</i> -Methylalanine	**	**

Mol. ratio to glycine (= 100): * 0.05–0.5; ** 0.5–5; *** 5–50; **** < 50.

the results. The most notable difference between the meteorite and the electric discharge amino acids is the pipecolic acid, the yield being extremely low in the electric discharge.

Proline is also present in relatively low yield from the electric discharge. The amount of α -aminoisobutyric acid is greater than α -amino-*n*-butyric acid in the meteorite, but the reverse is the case in the electric discharge. We do not believe that reasonable differences in ratios of amino acids detract from the overall picture. Indeed, the ratio of α -aminoisobutyric acid to glycine is quite different in two meteorites of the same type, being 0.4 in Murchison and 3.8 in Murray [35]. A similar comparison has been made between the dicarboxylic acids in Murchison [36] and those produced by an electric discharge [37], and the product ratios are quite similar.

The close correspondence between the amino acids found in the Murchison meteorite and those produced by an electric discharge synthesis, both as to the amino acids produced and their relative ratios, suggests that the amino acids in the meteorite were synthesized on the parent body by means of an electric discharge or analogous processes. A quantitative comparison of the amino acid and hydroxy acid abundances [38] shows that these compounds can be accounted for by a Strecker–Cyanohydrin synthesis on the parent body [39]. Electric discharges appear to be the most favored source of energy but sufficient data are not available to make realistic comparison with other energy sources.

Our ideas on the prebiotic synthesis of organic compounds are based largely on the results of experiments in model systems. So it is extremely gratifying to see that such synthesis really did take place on the parent body of the meteorite, and so it becomes quite plausible that they took place on the primitive earth.

10. Interstellar molecules

In the past 15 years a large number of organic molecules have been found in interstellar dust clouds mostly by emission lines in the microwave region of the spectrum (for a summary see ref. 40). The concentration of these molecules is very low (a few molecules per cm³ at the most) but the total amount in a dust cloud is large. The molecules found include formaldehyde, hydrogen cyanide, acetaldehyde, and cyanoacetylene. These are important prebiotic molecules, and this immediately raises the question of whether the interstellar molecules played a role in the origin of life on the earth. In order for this to have taken place it would have been necessary for the molecules to have been greatly concentrated in the solar nebula and to have arrived on the earth without being destroyed by ultraviolet light or pyrolysis. This appears to be difficult to do. In addition, it is necessary for some molecules to be continuously synthesized (unless life started very quickly) because of their instability, and an interstellar source could not be responsible for these.

For these reasons, it is generally felt that the interstellar molecules played at most a minor role in the origin of life. However, the presence of so many molecules of prebiotic importance in interstellar space, combined with the fact that their synthesis must differ from that on the primitive earth where the conditions were very different, indicates that some molecules are particularly easily synthesized when radicals and ions recombine. Another way of saying this is that there appears to be a universal organic chemistry, which shows up

in interstellar space, in the atmospheres of the major planets, and in the reducing atmosphere of the primitive earth.

Acknowledgement

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