94. A.P.Grekov, N.P.Shimanskaya, and A.P.Kilimov, in Sbornik "Khimicheskie Reaktivy i Preparaty" (Collected Papers on Chemical Reagents and Preparations), Moscow, 1961, p.137.
95. N.P.Shimanskaya, A.P.Kilimov, and A.P.Grekov, Optika i Spektrosk., 6, 194 (1959).
96. N.P.Shimanskaya, A.P.Kilimov, A.P.Grekov, L.M.Egupova, and R.S.Azen, Optika i Spektrosk., 7, 366 (1959).
97. Yu.P.Panov, N.A.Adrova, and M.M.Koton, Optika i Spektrosk., 7, 29 (1959).
98. P.Shestakov and V.Kind, Zhur.Russ.Fiz.-Khim.Obshch., 40, 330 (1908).
99. O.Diels and A.Wagner, Ber., 45, 878 (1912).
100. O.Diels and H.Okada, Ber., 46, 1872 (1913).
101. M.Freund and F.Kuh, Ber., 23, 2821, 2843 (1890).
102. G.Werber and F.Maggio, Ann.Chim.(Italy), 52, 747(1962).
103. A.P.Grekov and O.P.Shvaika, Zhur.Anal.Khim., 15, 732 (1960).
104. A.P.Grekov and O.P.Shvaika, in Sbornik "Khimicheskie Reaktivy i Preparaty" (Collected Papers on Chemical Reagents and Preparations), Moscow, 1961, p.285.
105. A.P.Grekov and R.S.Azen, Zhur.Obshch.Khim., 31, 1919 (1961).
106. N.S.Dokunikhin, B.M.Krasovitskii, R.M.Matskevich, V.A.Blinov, and Z.Ya.Vitokhina, Zhur.Prikl.Khim., 32, 664 (1959).
107. B.M.Krasovitskii, R.M.Matskevich, N.S.Dokunikhin, and N.A.Trubitsyna, Zhur.Obshch.Khim., 30, 2608 (1960).
108. H.Gehlen and G.Röbisch, Naturwiss., 48, 403 (1961).
109. H.Gehlen and G.Röbisch, Annalen, 663, 119 (1963).
110. C.Ainsworth, J.Amer.Chem.Soc., 78, 1636 (1956).
111. A.P.Grekov and V.I.Grigor'eva, in Sbornik "Stsintillyatory i Stsintillyatsionnye Materialy" (Collected Papers on Scintillators and Scintillation Materials), Khar'kov, No.3, 1963, p.15.
112. O.P.Shvaika and A.P.Grekov, *ibid.*, No.3, 1963, p.21.
113. M.Milone, Gazzetta, 62, 154 (1932).
114. L.M.Kutsyna and E.T.Verkhovtseva, Optika i Spektrosk., 12, 785 (1962).
115. P.Grammaticakis, Bull.Soc.chim.France, 86 (1953).
116. A.P.Grekov and O.P.Shvaika, in Sbornik "Stsintillyatory i Stsintillyatsionnye Materialy" (Collected Papers on Scintillators and Scintillation Materials), Khar'kov, No.2, 1963, p.60.
117. A.P.Grekov and O.P.Shvaika, *ibid.*, No.3, 1963, p.5.
118. O.P.Shvaika and A.P.Grekov, *ibid.*, No.3, 1963, p.17.
119. M.Milone and E.Borello, Gazzetta, 81, 677 (1951).
120. L.M.Kutsyna, A.P.Grekov, E.A.Lupashko, and E.T.Verkhovtseva, in Sbornik "Stsintillyatory i Stsintillyatsionnye Materialy" (Collected Papers on Scintillators and Scintillation Materials), Khar'kov, No.2, 1963, p.203.
121. R.Manzoni-Ansidei, Atti Accad.naz.Lincei, Rend.Classe Sci.fis.mat.nat., 22, 444 (1935).
122. M.Milone, Gazzetta, 65, 182 (1935).
123. E.Borello and S.Nocilla, Gazzetta, 84, 435 (1954).
124. N.P.Shimanskaya and V.D.Bezuglyi, Zhur.Obshch.Khim., 33, 1726 (1963).
125. N.P.Shimanskaya and V.D.Bezuglyi, in Sbornik "Stsintillyatory i Stsintillyatsionnye Materialy" (Collected Papers on Scintillators and Scintillation Materials), Khar'kov, No.3, 1963, p.65.
126. N.Hayes, D.Ott, and V.Kerr, Nucleonics, 13, 38 (1955).
127. O.P.Shvaika and A.P.Grekov, Optika i Spektrosk., 7, 824 (1960).
128. O.P.Shvaika and A.P.Grekov, in Sbornik "Stsintillyatory i Stsintillyatsionnye Materialy" (Collected Papers on Scintillators and Scintillation Materials), Khar'kov, No.2, 1963, p.130.
129. N.A.Adrova, M.M.Koton, and F.S.Florinskii, Dokl.Akad.Nauk SSSR, 114, 311 (1957).
130. N.A.Adrova, V.N.Andreev, M.M.Koton, Yu.P.Panov, and N.S.Musaliev, Optika i Spektrosk., 7, 128 (1959).
131. L.L.Nagornaya, V.D.Bezuglyi, and A.P.Grekov, Optika i Spektrosk., 10, 555 (1961).
132. E.Klingsberg, J.Amer.Chem.Soc., 80, 5786 (1958).
133. F.Stilmar, U.S.P. 2464831 (1949); Chem.Abs., 43, 4484 (1949).
134. F.Stilmar, U.S.P. 2567132 (1949); Chem.Zentr., 124, 449 (1953).
135. F.Stilmar, U.S.P. 2511018 (1950); Chem.Abs., 46, 270 (1952).
136. F.Stilmar, U.S.P. 2601179 (1952); Chem.Abs., 47, 2500 (1953).
137. F.Stilmar, U.S.P. 2628230 (1953); Chem.Abs., 47, 10234 (1953).
138. F.Stilmar, U.S.P 2650962 (1953); Chem.Abs., 48, 1014 (1954).
139. P.Belschaw and F.Irving, German P. 831432 (1950); Chem.Zentr., 123, 7261 (1952).
140. P.Belschaw and F.Irving, B.P. 676699 (1952); Chem. Abs., 11695 (1952).
141. P.Belschaw and F.Irving, B.P. 705920 (1954); Chem. Abs., 48, 10352 (1954).
142. P.Belschaw and A.Robson, B.P. 705928 (1954); Chem. Abs., 48, 10352 (1954).
143. P.Belschaw and A.Robson, B.P. 705929 (1954); Chem. Abs., 48, 10353 (1954).
144. G.Schwechten and J.Singer, German P. 825111 (1951); Chem.Abs., 49, 630 (1955).
145. F.Ebel and R.Randebrock, German P. 955174 (1955); Chem.Abs., 53, 4753 (1959).
146. O.Trauth, German P. 1049025 (1959); Ref.Zhur.Khim., 3L140 (1961).
147. V.A.Titkov, Khim.Nauka i Prom., 3, 174 (1958).
148. B.M.Krasovskii, R.M.Matskevich, and N.I.Mal'tseva, Zhur.Obshch.Khim., 31, 2259 (1961).
149. K.Futaki, Y.Oyama, and T.Iwasaki, Phot.Sci.Eng., 4, 97 (1960).
150. P.Merckx, U.S.P. 2473166 (1949); Chem.Abs., 43, 8924 (1949).
151. P.Merckx, German P. 806936 (1951); Chem.Abs., 46, 7918 (1952).

Institute of Organic Chemistry
and Institute of Chemistry of
Polymers and Monomers,
Academy of Sciences of the
Ukrainian SSR

U.D.C. 547.91 : 547.92.547.96 + 541.144.7

THE FORMATION OF BIOCHEMICALLY IMPORTANT COMPOUNDS IN THE PRE-BIOLOGICAL STAGE OF THE EARTH'S DEVELOPMENT

A. G. Pasynskii and T. E. Pavlovskaya

CONTENTS

1. Introduction 515

2. Possible conditions for primary syntheses on Earth 515
3. Amino-acids 516
4. Polypeptides 518
5. Purine and pyrimidine bases. Nucleosides and nucleotides 518
6. Carbohydrates 520
7. Aldehydes and organic acids 520
8. Amines and amides 520
9. Imidazole compounds 521
10. Porphyrins 521
11. General remarks 521

1. INTRODUCTION

The origin of life on Earth was preceded by a period of grandiose length, variously estimated at 1000–2500 million years, during which the compounds necessary for biological activity were formed. During this gigantic time interval, conditions were gradually created under which more and more complex compounds could be gradually formed from the simplest starting materials present on the Earth; these compounds included protein precursors, nucleic acids, lipids, etc., followed by more complex systems of these molecules directly leading to the appearance of life.

As recently as 10–15 years ago, the main stages of this gigantic pathway remained entirely obscure. At present our knowledge of conditions existing on the Earth in its primary evolutionary period has been greatly extended. This has led to attempts to set up models for the synthesis of various biochemically important compounds on the basis of starting materials that could exist on the primary Earth. The number of papers on this subject has now increased to the point where it has become necessary to summarise and analyse this problem, which is of great general scientific interest. The present review is intended to meet this need.

2. POSSIBLE CONDITIONS FOR PRIMARY SYNTHESES ON EARTH

It is now generally accepted that the Earth's primary atmosphere contained mainly H_2, CH_4, NH_3, and water vapour[1,2]. In the upper layers of the atmosphere photodissociation of water molecules could have been caused by short-wave solar radiation and this probably led to the formation of a certain amount of oxygen and carbon monoxide, but undoubtedly the atmosphere retained its reductive character. The loss of hydrogen from the atmosphere by diffusion into cosmic space might have been considerable even at that time; if the present concentration of molecular hydrogen in the atmosphere is $\sim 10^{-6}$ atm at the Earth's surface, the pressure in the primary atmosphere considered here may be taken as $\sim 1.5 \times 10^{-3}$ atm,[3] although at the very beginning of the Earth's formation it was considerably higher. The giant planets (Jupiter, Saturn, and those more remote) contain tremendous amounts of H_2, CH_4, and NH_3, even at the present time. Meteorites and comets formed an important source of primary materials on the Earth. It is estimated that in the first 2000 million years of the Earth's existence comets alone contributed up to 10^{12} tons of these compounds, or frozen radicals such as CN, CH_2, NH, NH_2, etc.[4] Reduced materials also predominate in the composition of meteorites; various hydrocarbons have been observed in stony meteorites (chondrites).

These compounds might have accumulated in the primary hydrosphere of the Earth, and surface rock decomposition products as well as products separated from the internal layers might also have been taken up; these products include H_2, CH_4, NH_3, CO, and H_2S,[5] also NH_4Cl, and later $Ca(NO_3)_2$;[6] Miller and Urey[3] discuss equilibrium between $CaCO_3$ and NH_3. Activation of these molecules by various forms of energy led to the formation of more complex compounds.

Solar radiation was undoubtedly the most powerful energy source; the total energy from this source reaching the Earth's surface is 1.2×10^{21} kcal per year. The solar radiation of photochemical importance was mainly the ultraviolet (below 400 mμm); relative to the Earth it amounted to $\sim 10^{20}$ kcal per year, and this reached the surface in the prebiological period of the Earth's existence[1]; according to Sagan[7], the flux of ultraviolet radiation in the 2400–2900 Å region that reached the Earth's surface amounted to $\sim 10^4$ erg cm^{-2} s^{-1}. Effective cleavage of CH_4 occurs at $\lambda < 1450$ Å, of H_2O at $\lambda < 1850$ Å, of NH_3 at $\lambda < 2250$ Å, and of CO at $\lambda < 1545$ Å.[3,8] Water molecules adsorbed on zinc oxide or silicates are decomposed by radiation of wavelength in the region 2300 Å, but when gaseous ammonia is adsorbed on active aluminium oxide, the photodissociation threshold of NH_3 shifts to 2700 Å.[8] The formation of formaldehyde has been noted[9,10] when a mixture of $NH_3 + CH_4 + H_2O$ is exposed to ultraviolet radiation in the 1450–1900 Å region, and also when a mixture of CH_4 and H_2O is irradiated. The presence of formaldehyde has also been demonstrated[11] in an irradiated mixture of $CO + H_2O$. The photoionisation of gases and vapours by ultraviolet radiation has been reviewed by Vilesov[12].

Electrical discharges in the atmosphere formed the next important energy source, but they were less important than ultraviolet radiation. It is estimated[1] that electrical discharges accounted for $\sim 1.2 \times 10^{15}$ kcal over the whole Earth's surface. According to Miller and Urey[3], ultraviolet radiation of wavelength $\lambda < 2500$ Å amounted to 660 cal cm^{-2} per year, whereas the energy from electrical discharges was only 4 cal cm^{-2} per year. However, it must be borne in mind that the action of electrical discharges was localised in relatively small spaces, but the action of ultraviolet light was uniformly spread in the atmosphere; moreover it is possible that under primary Earth conditions thunderstorm activity was more intense. When a discharge occurs in a mixture of $CH_4 + NH_3 + H_2O$ the compounds formed include aldehydes and HCN;[13,14] when H_2S is added thiourea and ammonium thiocyanate are also formed[14].

The action of cosmic rays and charged particles emitted by the Sun might have been of great importance. At present, most ionising particles of this kind are held by the Earth's magnetic field and deflected to form a radiation belt. The role of this factor is therefore estimated[3] at three orders lower than that of electrical discharges, but this might have been different in the early period of the Earth's development. According to Uffen[15], the formation of radiation belts as a result of movements in the Earth's crust occurred 2500 million years ago. Up to that time corpuscular

radiation[16,17] reached the Earth's surface and led to the activation of simple compounds. Calvin and coworkers[18] detected formaldehyde in aqueous solutions of CO_2 that had been irradiated in a cyclotron with a stream of helium particles, but the real significance of this reaction is insufficiently based on geochemical data. Subsequently, Calvin and coworkers[19,20] subjected a mixture of methane, ammonia, and water to the action of fast electrons (5 MeV) and showed that under these conditions HCN, urea, and other products are formed.

The action of all the types of radiation mentioned is based on the breaking of C–C, C–H, H–O, and other bonds and on the formation of a number of radicals: OH, H, CH_2, CN, NH, etc.

In contrast, the action of heat — the most substantial non-ionising factor — consists in the activation of molecules of primary compounds by exciting their vibrational levels. Thermal solar radiation is undoubtedly the most significant here; as already mentioned, this amounts to 10^{21} kcal per year over the whole of the Earth's surface; about half this quantity is reflected. Heat flux from the interior to the surface is another factor in the Earth's heat balance; this is largely of radiogenic origin (disintegration of ^{40}K, ^{235}U, etc.) and amounts to $\sim 10^{17}$–10^{18} kcal per year[21]. The temperature of the Earth's surface was, at any rate, less than 100°.[22] However, in the same way as the density of electrical discharges in the path of lightning was much greater than the average values given above, so also the distribution of temperature on the Earth's surface was heterogeneous with sharp maxima at the points where volcanoes and geysers erupted. Volcanic eruptions produced large amounts of incandescent gases such as H_2S and SO_2; moreover, the liberation of NH_4Cl and other ammonium compounds by volcanoes and fumaroles must be taken into account[6].

In general, it may be assumed that in the first period of the Earth's existence as a planet H_2, CH_4, NH_3, CO, H_2S, CH_2O, HCN, and NH_4Cl and other compounds were present; these compounds themselves had no biochemical significance but they were the starting materials for the formation of compounds that entered into the composition of living organisms. In this period the main sources of energy were various ionising radiations, primarily short ultraviolet radiation, and, to a lesser extent, electrical discharges and heavy ionising particles; the role of these particles must be considered of greater significance than previously. Of the non-ionising types of energy, the action of heat must be taken into account.

Therefore, after 2000–2500 million years, when the reductive atmosphere gave place to an oxidative atmosphere, a layer of oxygen retained ultraviolet radiation; the radiation belts that arose at this time deflected the main mass of ionising particles from the Earth, and volcanic and thunderstorm activity began to die down. In this relatively quiet background the formation and development of life became possible. However, it can easily be seen that in the very first period of the Earth's existence the compounds present and the radiation conditions excluded the possibility of life, but were favourable to the chemical evolution of substances needed for the formation of various compounds that enter into the composition of living organisms.

We shall now consider possible paths in the formation of the main classes of biochemically important compounds from the starting compounds mentioned above, bearing in mind the sequence of energy sources.

3. AMINO-ACIDS

The formation of amino-acids has attracted much attention, because of the great significance of these compounds in the subsequent synthesis of polypeptides and proteins, and because of the relative ease with which a number of amino-acids can be prepared from simple starting materials.

Groth[23,24] found that glycine and alanine were formed when ultraviolet rays in the region of 1470 and 1295 Å (resonance lines of xenon lamp) acted on a mixture of $CH_4 + NH_3 + H_2O$ for 24 h, and when methane was replaced by ethane, α-aminobutyric acid was also formed. Terenin[8] used a hydrogen lamp with a spectrum in the region $\lambda > 1300$ Å, which is closer to the short-wave radiation spectrum of the Sun. He irradiated a mixture of $CH_4 + NH_3 + CO$ in contact with liquid water and found alanine in the reaction products. Later, Dodonova and Sidorova[9], working in Terenin's laboratory, irradiated the same mixture with ultraviolet rays in the 1800–1450 Å region and found that glycine, alanine, α-aminobutyric acid, valine, and leucine (or norleucine) were formed. When H_2S or CS_2 was added to the gas mixture, no sulphur-containing amino-acids were found[25]. When methane was replaced by ethane[10] the composition of the amino-acids formed remained unchanged.

Pavlovskaya and Pasynskii[26] irradiated aqueous solutions containing 2.5% of CH_2O and 1–1.5% of NH_4NO_3 or NH_4Cl with ultraviolet light from a PRK-2 lamp (2.7×10^6 erg cm^{-2} min^{-1} at 40–45° for 20 h) and found that the following amino-acids were formed: serine, glycine, glutamic acid, alanine, valine, and also basic amino-acids; phenylalanine was found in small amounts in mixtures containing NH_4Cl at 40° and NH_4NO_3 at +1°. The reaction mixtures were analysed on columns and on paper, and a microphotometer was used to measure the chromatograms. In the presence of adsorbents (bentonite, kaolinite, limonite, and optical quartz)[27], the same amino-acids were found with the exception of basic amino-acids in some systems; moreover, the formation of isoleucine or phenylalanine (which have close R_f values) was also confirmed. In subsequent work[28] irradiation was carried out with a BUV-15 bactericidal lamp giving 80% of its radiation at 2537 Å; 1.5 litres of solution at 40° was irradiated for 20–40 h. The formation of amino-acids observed previously was confirmed and threonine was also found; phenylalanine and valine were not detected in these experiments. In some experiments formaldehyde was replaced by acetaldehyde and the resulting reaction mixtures showed the presence of arginine and tyrosine in addition to the acids previously mentioned; the presence of tyrosine confirms the formation of aromatic amino-acids. With the concentrations of starting materials mentioned above, the amino-acid content of the mixture after irradiation varied from 10^{-4} to 5×10^{-3} M, the lower figure referring to alanine. Thus, irradiation of a solution of simple starting materials leads to the formation of a number of important amino-acids.

Deschreider[29] showed that irradiation with ultraviolet rays of wavelength 2537 Å produced alanine, glycine, and aspartic acid, but the mixtures he used were too complex, maleic and succinic acid being used as starting materials. The work of Cultrera and Ferrari[30] suffers from the same disadvantage: they used dibasic acids, keto-acids, and hydroxycarboxylic acids as starting materials together with various nitrogenous compounds and their irradiation products included glycine, alanine, serine, and dicarboxylic amino-acids. Rid[31] demonstrated the formation of glycine,

but his irradiation mixture contained hydroxy-amines and CO_2. The work described in these three papers is therefore not fully justified by geochemical considerations.

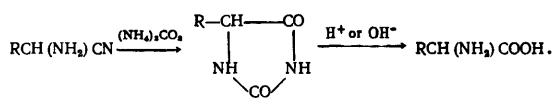
As early as 1913 Loeb[32] observed the formation of glycine when electrical discharged acted on a mixture of CO, NH_3, and H_2O, and also on 5–10% solutions of formamide. However, the most detailed work in this field is due to Miller[13,33,34], who found that glycine, alanine, aminodicarboxylic acids, aminobutyric acid, and sarcosine were formed in a continuously circulating mixture of $CH_4 + NH_3 + H_2 + H_2O$ subjected to spark and silent discharges for a week; the amino-acid concentration in the mixture was equivalent to 5×10^{-5}–5×10^{-3} M. It was shown that aldehydes (up to 10^{-3} M) and HCN (up to 4×10^{-2} M) are formed as intermediates; the kinetics of NH_3 loss, intermediate formation of HCN and aldehydes, and amino-acid accumulation were studied (Fig. 1).

Miller's results were confirmed by Pavlovskaya and Pasynskii[26], but they eliminated the excess of hydrogen in Miller's mixtures and replaced it by CO; this replacement was dictated by thermodynamic calculations. It was shown[26,34] that the irradiated solutions were sterile. With the spark discharge through the mixture for 100 h the formation of the same amino-acids was observed and HCN was found in the solution after the discharge.

The formation of the amino-acids appears to have been through a cyanhydrin stage by a mechanism closely related to that of the Strecker synthesis[35]. Strecker developed a method for preparing alanine from acetaldehyde by the following reaction:

$$RCHO + NH_3 \rightarrow RCH(NH_2)OH \xrightarrow{HCN} RCH(NH_2)CN \xrightarrow{2H_2O} RCH(NH_2)COOH.$$

This method was later used for the synthesis of various amino-acids (glycine, valine, phenylalanine, glutamic acid, etc.), but it was found most convenient for alanine, glycine, and serine. Bücherer[36] introduced an interesting modification in which an aminonitrile is heated with ammonium carbonate and the 5-hydantoin formed is hydrolysed:



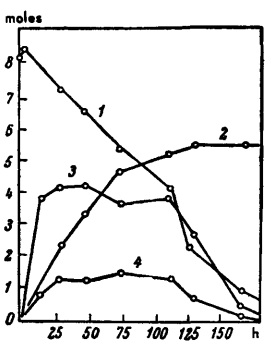


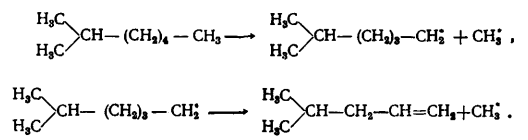
Fig. 1. Concentration of ammonia, hydrogen cyanide, aldehydes, and amino-acids during passage of a spark discharge through a mixture methane, ammonia, water, and hydrogen[13]: 1) NH_3 ($\times 100$); 2) amino-acids ($\times 10^3$); 3) HCN ($\times 10^2$); 4) aldehydes ($\times 10^3$).

Unfortunately, most other methods of synthesising amino-acids (with malonic ester, from keto-acids, etc.) are too complicated for the setting up of geochemical analogies. Here the Strecker synthesis has the undoubted advantage that it permits the assumption that any process that leads to the formation of aldehydes and HCN could have promoted the accumulation of α-amino-acids in the primary Earth's hydrosphere.

Abelson[37] who studied the action of a spark discharge on a mixture of various gases, found that NH_3 cannot be replaced by N_2; he also studied the effect of adding CO_2 and CO. He found that glycine, alanine, and sarcosine were formed. His results have been confirmed on mixtures corresponding in composition to those of Miller. That it was impossible to make do with $CO_2 + N_2$ has also been shown by Heyns and coworkers[14]; addition of H_2S to a reductive gas mixture yielded no sulphur-containing amino-acids. Frank[38] studied the action of a spark discharge on Miller's gas mixture, and also on a mixture in which $CH_4 + H_2$ was replaced by methanol and isooctane, but he could not extend the number of amino-acids formed. It appears that when an electrical discharge acts on hydrocarbon chains only small radicals are eliminated ($CH_3^{\cdot}$ type), as in the degradation of CH_4 and CH_3OH:

$$CH_4 \rightarrow CH_3^{\cdot} + H^{\cdot} \qquad (98.2 \text{ kcal}),$$

$$CH_3OH \rightarrow CH_3^{\cdot} + HO^{\cdot} \qquad (78.3 \text{ kcal}),$$



Oró[39] made a detailed study of the action of a spark discharge (spark length 1.5–3 cm) on conc. NH_4OH (15 M) at 30° for 5–7 h in an atmosphere of CH_4 and C_2H_6. ^{14}C-Hydrocarbons were used in some experiments and this enabled autoradiography to be used in the analysis of the two-dimensional chromatograms; the ultraviolet absorption of eluates of the spots was also measured. Glycine, alanine, aspartic acid, and isoleucine were found in the liquid phase; also, Oró refers to the production of valine and leucine in other experiments in which C_2- and C_3-hydrocarbons were used. He also obtained the amides, asparagine, and glycinamide, which probably played a part in the synthesis of polypeptides (see below); this is an entirely new result.

Using a spark discharge on a gaseous mixture of $NH_3 + CH_4 + H_2$ for 100–200 h, Grossenbacher[40] analysed the products on an automatic amino-acid analyser and found the following amino-acids: 2 moles of aspartic acid, 4 of threonine, 14 of serine, 16 of glycine, 14 of alanine, 4 of lysine, 2 of leucine, 2 of isoleucine, and 1 of glutamic acid; he also found some peptides (see below).

Dose and Rajewsky[41] subjected a gaseous mixture of $CH_4 + NH_3 + H_2 + CO_2 + N_2 + H_2O$ to the action of ionising radiation (X-rays in dose of 3.5×10^6 roentgen) and found that acid and neutral amino-acids were formed. Later, Dose and Ettre[42] found that lysine and asparagine were formed, but they irradiated more complex compounds (cadaverine and alanine bicarbonates).

When a solution of ammonium acetate was irradiated with β-rays from a linear accelerator (2 MeV), glycine

and aspartic acid[43] were obtained; glycine and alanine[44] were formed by the γ-irradiation (^{60}Co, 5×10^8 r) of solid ammonium carbonate.

Palm and Calvin[19] found glycine, alanine, and aspartic acid in a mixture of $CH_3 + NH_3 + H_2 + H_2O$ which they irradiated with a beam of fast electrons (5 MeV with a dose of 10^{10} ergs).

Bakhadur[45,46] irradiated a mixture of paraformaldehyde, potassium nitrate, iron(II) chloride, and water under a 500–1000 W electric lamp and reported a large number of amino-acids in the product; however, his papers do not give sufficient grounds for his assumptions about the composition of the products and the mechanism of their formation. This remark also applies to the author's suggestion that it is possible to synthesise amino-acids by illuminating a mixture of paraformaldehyde, colloidal molybdenum oxide, and water, nitrogen being obtained by atmospheric fixation.

Finally, the formation of amino-acids by *heating* initial solutions has been studied in detail by Oró and coworkers[47,48]. In the first paper it was shown that a number of amino-acids (glycine, alanine, serine, aspartic acid, and threonine) can be obtained simply by heating aqueous mixtures of formaldehyde and hydroxylamine to 80–100° for 40 to 60 h, but the reaction had an appreciable velocity even at the lower temperature. The reaction mechanism here is also close to that of Strecker's syntheses, since formaldoxime and HCN are among the first reaction products of formaldehyde and hydroxylamine; the stationary concentration of these intermediates was $\sim 6 \times 10^{-3}$ M in the reaction $HCHO + NH_2 \rightarrow CH_2NOH \rightarrow HCN$; the amino-acid (mainly glycine) concentration reached 17.7×10^{-3} M. In the work described in the second paper[48], an aqueous solution of $HCN + NH_4OH$ was heated for 25 days at 75° and glycine, alanine, and aspartic acid were found amongst the products. These results have been confirmed by Lowe *et al.*[49], who heated a 1.5 M aqueous solution of NH_3 and HCN at 90° for 18 h; these workers also showed that considerable amounts of amino-acids are present in the form of peptides and other amino-acid derivatives, which are separated after the reaction products have been hydrolysed. Analysis in an automatic analyser showed the presence of leucine, isoleucine, serine, threonine, and glutamic acid (mostly serine) in addition to glycine, alanine, and aspartic acid. If the products had been hydrolysed in the work already mentioned here, a greater range of amino-acids might have been found.

Fox and coworkers[50] also heated the starting materials to obtain amino-acids but in their experiments the temperature was higher (140–200°) and the starting materials were too complex (salts of malonic acid); in our opinion this limits the value of their work.

4. POLYPEPTIDES

Lower peptides could be formed at the same time as amino-acids, but high-molecular peptides were probably formed in the later stages of evolution.

By the action of ultraviolet light on an aqueous solution of NH_4Cl in which FeS_2 was suspended, and through which methane was passed, Ellenbogen[51] observed the formation of a peptide which on hydrolysis gave phenylalanine, methionine, and valine. Bakhadur[52] and coworkers irradiated a solution of leucine and glutamic acid in the presence of sucrose with a 1000 W lamp and found that leucyl-leucine, leucyl-glutamic acid, and some other dipeptides were formed. However, both these reports lack confirmation.

Polyglycine has been obtained[53] by the action of a spark discharge on crystalline glycine at 13°, and on a 10% aqueous solution of glycine at 0°. Oró[39] has found that in addition to the production of amino-acids in a discharge, two compounds were obtained, the colour reactions and chromatographic behaviour of which indicate that they are low-molecular peptides formed with the participation of amides (see below), but the compounds were not identified. Grossenbacher[40], who made the most detailed examination of peptides formed in a spark discharge, found that the peptides he separated consisted of glycine and alanine (5 : 1), and also of glycine and isoleucine.

It is doubtful if peptides were actually formed in the work reported and, if they were formed, the amounts must have been insignificant. No doubt this is because peptides are readily degraded in a spark discharge or when they are irradiated. It is therefore natural that the formation of peptides and polypeptides should have been mainly observed when heat or catalysts were used. Fox and coworkers[54] studied the conditions for the thermal condensation of mixtures of various amino-acids. Linear polypeptides with a molecular weight up to 8600 were obtained by heating various amino-acid mixtures in the absence of water to 140–200° for several hours; the following mixtures were used: glutamic acid and glycine[55], aspartic and glutamic acids[56] (also in the presence of phosphoric acid[57]), lysine and alanine[54], glutamic acid and phenylalanine[54], and also a mixture containing an excess of aspartic and glutamic acids with 16 other amino-acids[58]. This work has been summarised by Fox[54]. It was shown by colour tests, infrared absorption spectra, solubility, electrophoretic mobility, and enzymic hydrolysis that the polypeptides obtained (Fox terms them "proteinoids") were not distinguishable from, for example, proteins of the caesin type. The preparation of poly-α-amino-acids has also been reported[60–62], but it has not been made clear how the results obtained are related to geochemical conditions.

The polypeptides prepared by Akabori[63] are of great interest; he suggested that the aminoacetonitrile formed from formaldehyde, ammonia, and HCN undergoes polycondensation on clay:

$$CH_2O + NH_3 + HCN \rightarrow H_2N{-}CH_2{-}CN + H_2O.$$

Experiments were done on kaolinite for 5 h at 130°. Side-chains could be introduced into the polyglycine obtained by reaction with aldehydes or unsaturated hydrocarbons; the molecular weight of the polyglycine was about 15 000. Unfortunately, these experiments were not further developed.

Oró[64] obtained polyglycine by heating glycinamide to 100° and also by heating glycine in 2 *N* NH_4OH solutions[65]; copolymers of eight different amino-acids were also obtained by heating the acids mixed with glycine in concentrated ammonia. The infrared and X-ray spectra of the products were examined, and they gave a positive biuret reaction. As has been pointed out already[49], considerable amounts of peptides have been obtained by heating an aqueous solution of HCN and NH_4OH.

5. PURINE AND PYRIMIDINE BASES. NUCLEOSIDES AND NUCLEOTIDES

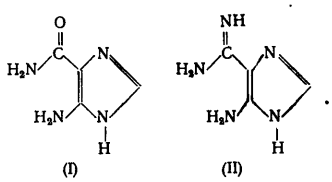
Apart from proteins, nucleic acids are the most important compounds of biological significance; for this reason,

a number of attempts have been made to synthesise nitrogenous bases, and also nucleosides and nucleotides. The main work in this field is due to Oró and Ponnamperuma.

On the action of ultraviolet light there is only a short report[66] on the formation of adenine by irradiation of an aqueous 10^{-4} M solution of HCN.

A more detailed study has been made[67] of the action of a beam of electrons (4.5 MeV, 7×10^8 rad) on a $CH_4 + NH_3 + H_2O$ mixture. In this irradiation the intermediate is HCN; according to Oró's scheme (see below) condensation of HCN leads to the formation of adenine. This purine base may be obtained because it is the most stable to radiation.

The majority of purine and pyrimidine bases were, however, obtained by Oró and coworkers[68-71] by heating aqueous solutions of HCN of various concentrations in aqueous ammonia to 70–90° for several days; in some experiments temperatures lower than 70° were also used. Adenine was obtained in this way[68] and its presence was demonstrated by eight different methods; Fig. 2 compares the ultraviolet and visible spectra of the picrates of the compounds separated with the spectra of a standard preparation of adenine. Fig. 3 shows Oró's mechanism for the formation of adenine, which is the product of condensation of five HCN molecules. It was shown that 4-aminoimidazole-5-carboxamide (I) and 4-aminoimidazole-5-carboxamidine (II)[69] were formed as intermediates; the compounds were separated and identified by various methods:



(I) (II)

Guanine was obtained from (I) by condensing it with guanidine in aqueous solution in closed vessels at 100–130°, and condensation with urea gave xanthine. Hypoxanthine (Fig. 4) was obtained from (I) by condensing it with formamidine and subsequently eliminating NH_3. The formation of adenine and hypoxanthine was also demonstrated when HCN + NH_4OH were heated at 90° for 18 h.[49]

Oró[70,71] also obtained pyrimidine bases (uracil and cytosine) by condensing other nitriles (aminopropionitrile or acrylonitrile) with urea at 135° in aqueous ammoniacal solutions. Uracil was also obtained by heating together malonic acid and urea in phosphoric acid solution at 100–140° for 1–2 h.[72]

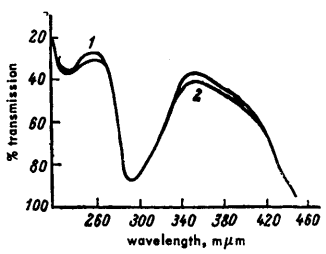


Fig. 2. Ultraviolet and visible absorption spectrum of picrate of standard adenine (1) and picrate of adenine obtained[68] from hydrogen cyanide (2).

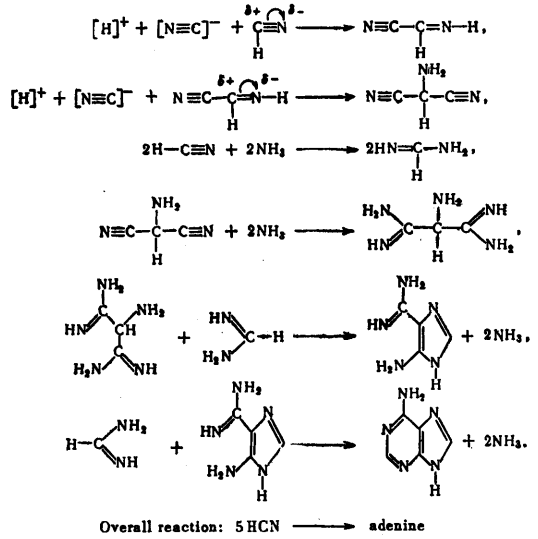


Fig. 3. Mechanism of formation of adenine from hydrogen cyanide[69].

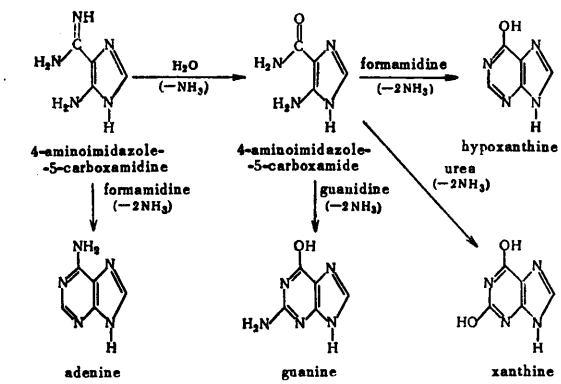


Fig. 4. Proposed mechanism for the synthesis of purines on the primary Earth[70].

The next important step was made by Ponnamperuma and coworkers[73], who showed that ultraviolet irradiation of an aqueous solution of adenine and ribose (2537 Å, 1 h, dose 10^8 r, 40°) in the presence of phosphoric acid (or better ethyl metaphosphate) caused them to condense to give the nucleoside adenosine, although the yield was very low (0.01%); the quantum yield of the process was 10^{-5}. It was also found that the nucleoside phosphates or nucleotides (adenylic acid, ADP, and even ATP) were obtained in 0.05–0.08% yield in the presence of ethyl metaphosphate; irradiation of a mixture of AMP and ethyl metaphosphate gave ATP in 0.3% yield[66,74].

Schramm and coworkers[75] have drawn attention to the catalytic part played by polyphosphates in the adenine–ribose condensation, but in Ponnamperuma's work in addition to its catalytic action the phosphate is directly included in the nucleoside, thanks to activation by ultraviolet rays. Because of the high stability of adenine to radiation, the accumulation of ATP and other adenine nucleotides takes

preference over the formation of nucleotides with other nitrogen bases. Since ATP is an energy-rich compound, which is characteristic of all forms of living organisms right down to the simplest, it is likely that organisms would have available pre-formed ATP and some other nucleotides at their origin.

6. CARBOHYDRATES

The formation of carbohydrates was in itself of great importance, since these compounds form an important biochemical class; moreover, ribose and deoxyribose were required for the formation of the nucleosides and nucleotides mentioned above.

As has been pointed out, formaldehyde was one of the main primary starting materials. Since the classical synthesis of Butlerov, it has been shown that formaldehyde could be condensed to form carbohydrates, and this subject has been repeatedly reviewed in the literature. Recently[76], it has been shown that when formaldehyde is condensed in a basic medium, up to 30 monosaccharides are formed, mainly pentoses and hexoses, which are the most stable simple carbohydrates; ribose was among the products. The intermediates included glycollic aldehyde, glyceraldehyde, and dioxyacetone[77,78]. Oró[70] obtained 2-deoxyribose and 2-deoxyxylose in ~5% yield by condensing acetaldehyde and glyceraldehyde in aqueous systems in the presence of bivalent metal (Ca^{2+}, Mg^{2+}) oxides at temperatures from 0° to 50°.

Ponnamperuma[79] has reported the formation of ribose and deoxyribose among other products when a 3×10^{-4} M aqueous solution of formaldehyde was subjected to ultraviolet irradiation.

7. ALDEHYDES AND ORGANIC ACIDS

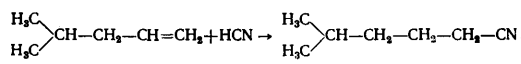
The formation of the lower aldehydes, formaldehyde and acetaldehyde, was of great practical importance for the production of amino-acids and carbohydrates and their oxidation led to the formation of a number of organic acids; as mentioned above, the preparation of amides of organic acids was an important intermediate step in the formation of nucleic acid fragments.

When ultraviolet rays act on gases of a reductive atmosphere, lower aldehydes and organic acids are among the primary compounds formed. Thus the action of rays of wavelength 1850 and 2537 Å on a mixture of $C_2H_6 + NH_3 + H_2O$ gave formic, acetic, and propionic acids[24]; with rays of wavelength 1295 Å acting on a mixture of $CO + H_2$ or CH_4, formaldehyde and glyoxal were obtained[11]; formaldehyde was obtained by the action of rays of wavelength 1450 Å on a mixture of CO, CH_4, or C_2H_6 with water vapour. The following mechanism has been proposed[10] for the formation of formaldehyde in hydrocarbon–water mixtures:

$$2H_2O \rightarrow 2H + 2OH \rightarrow H_2O + H_2 + O,$$
$$CH_4 \rightarrow CH_3 + H,$$
$$CH_3 + O_2 \rightarrow CH_2O + OH.$$

Losanitsch[80] observed the formation of aldehydes when electrical discharges acted on $CO_2 + CH_4$. Various organic acids were obtained in Miller's experiments[13,34], including formic, acetic, propionic, lactic, and glycollic; formic acid was the most abundant (23 mmoles). We found that formic, acetic, and traces of propionic acid are formed by the action of discharges on a mixture of $C_4H_{10} + H_2O$.[28] Frank found only formic acid in the acid fraction of a mixture of isooctane and water that had been subjected to discharges[38]; he explains this by the fact that only CH_3 radicals are eliminated in the degradation of linear hydrocarbons (*cf.* p. 517).

Frank obtained organic acids in higher yield by the action of discharges on the mixtures $CH_4 + H_2 + NH_3$, $CH_3OH + NH_3$, and isooctane + NH_3, all in the presence of water vapour. Since the intermediate compound in these mixtures is HCN, its addition to the terminal double bond of an unsaturated hydrocarbon probably leads to the formation of a nitrile, oxidation of which gives fatty acids (in Frank's work these were obtained in the non-volatile fatty acid fraction):



The formation of formaldehyde, formic acid, and some other acids was also observed[18,43,44] when various ionising radiations acted on aqueous solutions of CO_2 and NH_4 and Na bicarbonates.

Oró found[47] that formic acid, acetic acid, glycollic acid, and lactic acid were formed by heating a 0.25 M solution of CH_2O and $NH_2OH.HCl$ to 100°; the acids were separated and identified by column chromatography. Lowe and coworkers[49] also mention the formation of fatty acids.

8. AMINES AND AMIDES

In addition to amino-acids and organic acids, the formation of amines and amides has been mentioned in a number of papers. Formamide has been obtained[81] by the action of short-wave ultraviolet radiation (1850 Å) on a mixture of NH_3 + CO, and urea has been obtained by the action of rays of wavelength 1800–1450 Å on a mixture of the same composition (also with the addition of $CH_4 + H_2O$).[9] Hydrazine and hexamethylenetetramine have been obtained[10] by the action of rays of wavelength 1450 Å on a mixture of CH_4 (or C_2H_6) + NH_3 + H_2O; hexamethylenetetramine was also formed by 1850 Å radiation acting on a mixture of $CH_2O + NH_3 + H_2O$.[31] When a mixture of formaldehyde and ammonium salts was irradiated[28] a fraction containing methylamine, ethanolamine, isopropylamine, urea, and hexamethylenetetramine was separated.

Miller[13] obtained urea and *N*-methylurea (total amount 2×10^{-5} moles) by the action of electrical discharges on a mixture of $CH_4 + NH_3 + H_2 + H_2O$; methylamine and ethylamine were obtained by the action of a corona discharge on the same mixture[82]. Thiourea and thioacetamide have been obtained[14] by the action of a discharge on a mixture of $CH_4 + NH_3 + H_2S + H_2O$, and urea has been obtained[83] from a mixture of $N_2 + H_2$ + CO.

Oró obtained aliphatic amines, asparagine, and glycinamide by the action of a spark discharge (7 h, 15–30 kV) on a mixture of $CH_4 + C_2H_6 + H_2O$ over conc. NH_4OH. The two amides are significant not only because they are the direct precursors of amino-acids, but also because of their participation in the formation of polypeptides (see above). By heating conc. HCN and NH_4OH to 70° Oró and Kimball obtained[69] glycinamide, formamide, and formamidine. According to these workers[4], the hydroxylamine used in

their reactions might have been formed by the recombination of NH_2 and OH radicals contained in materials from comets.

A considerable amount of urea was obtained[19] by the action of a beam of electrons (5 MeV) on a mixture of $CH_4 + NH_3 + H_2 + H_2O$. Heyns and coworkers[84] noted the formation of a number of guanidine compounds when a discharge was passed through a mixture of $CH_4 + NH_3 + H_2O$, but they added a certain amount of oxygen to the mixture on the assumption that this is formed in the photodissociation of water. There are no other references to the formation of guanidine compounds.

9. IMIDAZOLE COMPOUNDS

Imidazole compounds form an important group, being intermediates in the formation of nucleic bases (see above), which are also closely connected with the formation of histidine and histamine. 4-Aminoimidazole-5-carboxamide and the corresponding amidine have been formed[69] by heating a mixture of HCN + NH_4OH. The formation of imidazole, 4-hydroxymethylimidazole, and 4-methylimidazole has been shown to occur[28] in a mixture of $CH_2O + NH_4NO_3$ exposed to ultraviolet light (2537 Å); when a mixture of $CH_3CHO + NH_4NO_3$ was irradiated, in addition to the foregoing compounds 2-methylimidazole, 4,5-dimethylimidazole, and an unidentified compound, probably an alkylimidazole, were also obtained; however, the presence of histidine could not be demonstrated in the irradiated solutions.

10. PORPHYRINS

The formation of tetrapyrrole compounds was of great importance for the subsequent development of catalase activity[7] and for the formation of the main compound that absorbs visible light in the process of photosynthesis. Chichibabin[85] obtained pyrrole by heating acetylene and NH_3 in the presence of sesquioxides. Szutka and coworkers found that tetraphenylporphyrin was formed by the action of γ-rays (^{60}Co, 5×10^5 r h^{-1}, 10 h)[86] or ultraviolet rays (3000 Å, 5×10^{16} quanta-seconds on irradiated surface)[87,88] on a mixture of pyrrole and benzaldehyde in the presence of zinc acetate. Rothemund[89] synthesised porphyrin by heating a mixture of pyrrole and formaldehyde in methanol and pyridine in sealed ampoules. Krasnovskii and Umrikhina[90] obtained porphyrin by heating (8–10 h, 100°) pyrrole and formaldehyde in methanol containing 10% of water; the reaction was accelerated by water, oxygen, and some catalysts.

11. GENERAL REMARKS

It is now known with sufficient certainty that a large number of diverse compounds of biochemical importance could have been formed by the action of various kinds of energy (ultraviolet, electrical discharge, ionising, and thermal) on the simplest compounds (CH_4, NH_3, HCN, CH_2O, etc.) that could exist under primary Earth conditions, although these simple compounds were themselves rather antibiogenic. Of necessity, this review has been restricted to those compounds of biochemical importance (amino-acids, purines, pyrimidines, organic acids, etc.), which can be obtained experimentally direct from primary non-biological substances, since the number of secondary biochemically important compounds which can be obtained in this way is very great and could only be touched on here.

In all the reactions for the formation of biochemically important compounds from simple primary substances, a prerequisite for a yield of the products was their rapid removal from the reaction zone, to avoid destruction of the compounds formed. Favourable conditions were created at the points of contact of two different reaction zones, for example, at a water surface absorbing the products of ultraviolet radiation from the atmosphere, and also at zones due to a cold atmosphere, electrical discharges, or volcanic eruptions. In all cases the accumulation of products in the ocean was of great importance[1]; at sufficient depth the absorbed compounds were protected from ultraviolet and ionising radiations and so preserved from further degradation. The quantity of organic compounds that could have settled from the primary atmosphere in 1000 million years is ~ 1 kg cm^{-2}; according to Urey[2] and Sagan[7] this would give a concentration of $\sim 1\%$ at the end of the time interval.

The work covered in this review shows that extraordinarily diverse biochemically important compounds could have been formed in the early stages of the Earth's development, but many problems have, of course, been left unsolved. Only half the amino-acid components of proteins have been obtained experimentally. Either suitable abiogenic methods of synthesis have not been found for the other amino-acids, or they were formed as secondary products, or even by biosynthesis in living cells. It is possible that the primary polypeptides or protein-like compounds did not contain a full complement of amino-acids, but they may nevertheless have had catalytically active groupings. For example, the active centres of the present-day enzymes, phosphoglucomutase, trypsin, and chymotrypsin contain the amino-acid sequence aspartic acid–serine–alanine (Asp–Ser–Ala), a sequence that might have occurred in primary polypeptides. However, many amino-acids such as histidine and cysteine that have not been obtained experimentally from primary materials play an important part in the active centres of enzymes. Elucidation of the possibility of their abiogenic synthesis would be of great interest.

In general, the problem of preparing polypeptides of fairly high molecular weight on suitable catalysts without the use of organic solvents, high temperatures, or complex organic amino-acid derivatives has received little attention; an interesting attempt at such a polymerisation[63] under the geochemical conditions of the primary Earth was not sufficiently developed.

Closely linked to the polycondensation of amino-acids on catalysts is the important problem of the origin of the optical activity of natural amino-acids. Up to now the absolute asymmetric synthesis of L-amino-acids by means of circularly polarised light has not been achieved; in all the work dealt with in this review the amino-acids were obtained as racemates, and all known methods of making optically active compounds are based on the use of existing optically disymmetry (compounds, crystals, adsorbents, etc.)[91]. Stereospecific polymers with spatially arranged side groups can be prepared on catalysts having no optical activity; in our opinion[92], the elucidation of this is of the greatest importance. It is possible that optical asymmetry developed not by the initial formation of optically active monomers and their conversion into optically active polymers, but by the reverse process; high-molecular-weight asymmetric cata-

lysts might have been formed by stereospecific polymerisation and then the secondary optical symmetry of low-molecular compounds might have developed on the basis of the polymers. The appearance of optically asymmetric and catalytically active polypeptides was important for accelerating the reaction and was therefore secured by evolution. The conditions for the formation of such polypeptides are still unknown and their experimental preparation would be a significant achievement.

A great achievement of recent years, apart from the preparation of amino-acids, has been the abiogenic synthesis of purine and pyrimidine bases, some nucleosides and mononucleotides, and also ATP (Oró; Ponnamperuma and coworkers). The preparation of such complex compounds is, of course, of great interest not only in connection with the conditions for the formation of such important compounds as nucleic acids, but also because it raises the whole question of the length of the biological stage in the Earth's evolution. Since such important compounds as nucleotides and ATP, which were previously considered to be products of the biological stage of evolution, have now been obtained by abiogenic synthesis under relatively simple conditions, the chemical stage of evolution can be reduced to 1000–1500 million years, and the origin of life can be extended into the depths of time; according to Sagan's estimate[7], life might have originated 4000 million years ago. This would explain the discovery of fossil algae in rocks 2700 million years old, or the appearance of signs of an oxidative atmosphere on the Earth 3400 million years ago[7].

It is well known that ATP passes through all the evolution of living things from the simplest organism to man; if ATP were entirely a product of biological evolution, uncountable generations would have been required for the formation of ATP precursors. Recent experiments have shown that this assumption is unnecessary and that primary living organisms could have obtained ATP in a prepared form from the surrounding medium[73]. The abiological formation of ATP was considered by Blum[93], but experimental confirmation of this possibility was only obtained recently. If ATP was present its participation in the synthesis of polypeptides or polynucleotides may be assumed. The important problem of the conversion of nucleotides into polynucleotides, similar to the simplest nucleic acids, has still not been solved experimentally under the geochemical conditions of the primary Earth. It is possible that in the presence of nucleoside diphosphates and triphosphates further condensation could occur by the Kornberg–Ochoa mechanism, the low specificity of the catalysts present and the slowness of the process being compensated for by geological periods of time.

The formation of simple carbohydrates, including such important compounds as glucose, ribose, and deoxyribose has been demonstrated experimentally beyond doubt[70,79]. In contrast, the important problem of the formation of higher fatty acids has not been solved experimentally; these formed the main basis for lipoprotein membranes and films. The interaction of higher hydrocarbons with HCN in a discharge may have been important here (p. 520), or the fatty acids may have originated at a stage when the Earth's oxidative atmosphere had been formed. The formation of porphyrins undoubtedly occurred in the later stages of chemical evolution, or even at the initial stage in the evolution of primary living organisms[3].

The mechanism and kinetics of none of the syntheses mentioned here have been studied; up to now attention has been directed to the qualitative composition and the yields of the unusually diverse products of these syntheses.

Available results show that polypeptides and polynucleotides could have arisen independently of each other under the conditions of the primary Earth. Polynucleotides could have been formed by mutual union; these would, of course, be very different from existing specific nucleoproteins but they would have the important property of forming coacervate layers due to the mutual saturation of polar groups and reduction in solubility. Although coacervates may be formed by low-molecular compounds (*e.g.* phenol–water) of limited solubility, typical coacervates are formed from compounds of high-molecular-weight, in particular from proteins and polysaccharides, two proteins with very different isoelectric points, mixtures of proteins and nucleic acids, etc. Oparin and coworkers[94] have obtained coacervates from polypeptides and polynucleotides. Thus at the state of formation of polynucleotides, or even earlier, the formation of complex molecules inevitably gave rise to more or less complex systems.

Within such systems of molecules (coacervate drops, etc.) new molecular interactions occurred that do not occur in dilute homogeneous solutions. In particular, the inclusion of catalysts in these systems led to differences in concentration between the drop and the medium and automatically converted them into chemically open macrosystems constantly exchanging matter with the surroundings.

Open systems, the stability of which was dynamically maintained by chemical reactions in the medium must have been of great evolutionary importance. These processes have been experimentally examined in simple equilibrium coacervates[95] and also in stabilised suspensions of enzymes, the stability of which resulted from the dynamic balance of surface precipitation forces of the stabilised surface layer and its enzymic hydrolysis from inside the drop[96]. In more ideal types of enzyme coacervates, the stabilising membrane was a product of synthetic reactions in the drops, and their stability resulted from the dynamic balance of chemical synthetic and degradation reactions in the drops; this made the behaviour of these systems similar to that of the simplest living organisms.

At the limit of the origin of primary living organisms, macromolecules were hardly characterised by a rigid definite specificity in their composition, but probably differed significantly from existing types of these molecules; for example, protein-like compounds might not have had a full complement of amino-acids, and nucleic compounds might have contained only relatively simple nucleotides. Division of the coacervate drops occurred with a very low specificity for transmitting "genetic information", and the development of nucleic acid and nucleoprotein molecules that ensured a higher level of specificity for this transmission might have been the result of long evolution[97]. The idea that life originated at the moment when there was a synthesis[98] coded by nucleic acids, of specific protein-like compounds is, in our opinion, erroneous; this interpretation disregards a tremendous initial period in the evolution of living organisms. It is difficult to imagine how the existing mechanism for the biosynthesis of proteins with matrix, information, and soluble nucleic acids, necessarily involving ATP and a number of amino-acids, could be built up to any extent before the origin of life, as Buchanan[99] suggests. All these multi-stage controlling processes could only have been built up in morphologically specialised open chemical systems exchanging matter with their surroundings. At a definite stage in the development of such

systems, the system as a whole and not just one component (either protein or nucleic acid) might have been reproduced. It is probably at this stage that the first living beings arose†.

1. A.I.Oparin, "Vozniknovenie Zhizni na Zemle" (The Origin of Life on Earth), 3rd Edn., Izd.Akad.Nauk SSSR, 1957.
2. H.C.Urey, "The Planets: Their Origin and Development", Yale Univ.Press, 1952.
3. S.Miller and H.C.Urey, Science, 130, 245 (1959).
4. J.Oró, Nature, 190, 389 (1961).
5. G.Yuri [H.C.Urey], in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd. Akad.Nauk SSSR, Moscow, 1959, p.22.
6. A.P.Vinogradov, *ibid.*, p.34.
7. C.Sagan, Radiation Res., 15, 174 (1961).
8. A.N.Terenin, in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd.Akad.Nauk SSSR, Moscow, 1959, p.144.
9. N.Ya.Dodonova and A.I.Sidorova, Biofizika, 6, 149 (1961).
10. N.Ya.Dodonova and A.I.Sidorova, Biofizika, 7, 31 (1962).
11. W.Groth, Z.phys.Chem., 37B, 315 (1937).
12. F.I.Vilesov, Uspekhi Fiz.Nauk, 81, 669 (1963).
13. S.Miller, Biochim.Biophys.Acta, 23, 480 (1957).
14. K.Heyns, W.Walter, and E.Meyer, Naturwiss., 44, 385 (1957).
15. R.Uffen, Nature, 198, 143 (1963).
16. J.A.Van Allen and L.Frank, Nature, 183, 430 (1959).
17. S.N.Vernov, A.E.Chudakov, P.V.Vakulov, and Yu.I.Logachev, Dokl.Akad.Nauk SSSR, 125, 304 (1959).
18. W.Garrison, D.Morrison, J.Hamilton, A.Benson, and M.Calvin, Science, 114, 416 (1951).
19. C.Palm and M.Calvin, J.Amer.Chem.Soc., 84, 2115 (1962).
20. M.Calvin, "Horizons in Biochemistry" (Edited by M.Kasha and B.Pullman), Academic Press, 1962, p.43.
21. G.V.Voitkevich, Dokl.Akad.Nauk, 74, 771 (1950).
22. V.I.Baranov, in Sbornik "Vozniknovenie Zhizni vo Vselennoi" (Symposium on the Origin of Life in the Universe), Izd.Akad. Nauk SSSR, 1963, p.23.
23. W.Groth, Angew.Chem., 69, 681 (1957).
24. W.Groth and H.Weyssenhoff, Ann.Physik, 4, 69 (1959).
25. N.Ya.Dodonova, Biofizika, 7, 367 (1962).
26. T.E.Pavlovskaya and A.G.Pasynskii, in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd.Akad.Nauk SSSR, Moscow, 1959, p.161.
27. T.E.Pavloskaya, A.G.Pasynskii, and A.I.Grebenikova, Dokl.Akad.Nauk SSSR, 135, 743 (1960).
28. T.E.Pavloskaya and A.G.Pasynskii, in Sbornik "Problemy Evolyutsionnoi i Tekhnicheskoi Biokhimii" (Symposium on Problems of Evolutionary and Technical Biochemistry), Izd. "Nauka", Moscow, 1964, p.70.
29. A.Deschreider, Nature, 182, 528 (1958).
30. R.Cultrera and G.Ferrari, Agrochimica, 5, 108 (1961).
31. S.Rid, in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd.Akad.Nauk SSSR, Moscow, 1959, p.622.
32. W.Loeb, Ber., 46, 690 (1913).
33. S.Miller, Science, 117, 528 (1953).
34. S.Miller, J.Amer.Chem.Soc., 77, 2351 (1955).
35. A.Strecker, Annalen, 75, 27 (1850).
36. H.Bücherer and V.Lieb, J.prakt.Chem., 141, 5 (1934).
37. P.Abelson, Ann.N.Y.Acad.Sci., 69, 274 (1957).
38. B.Frank, Chem.Ber., 93, 446 (1960).
39. J.Oró, Nature, 197, 862 (1963).
40. K.Grossenbacher, Proceedings of Symposium "The Origin of Prebiological Systems", Florida, 28th October 1963, p.269.
41. K.Dose and B.Rajewsky, Biochim.Biophys.Acta, 25, 225 (1957).
42. K.Dose and K.Ettre, Naturforsch., 13b, 784 (1958).
43. T.Hasselstrom, M.Henry, and B.Murr, Science, 125, 350 (1957).
44. R.Paschke, R.Chang, and D.Yaung, Science, 125, 881 (1957).
45. K.Bakhadur, in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd.Akad.Nauk SSSR, Moscow, 1959, p.149.
46. K.Bakhadur and R.Srivastava, Zhur.Obshch.Khim., 31, 3017 (1961).
47. J.Oró, A.Kimball, R.Fritz, and F.Master, Arch.Biochem. Biophys., 85, 115 (1959).
48. J.Oró and S.Kamat, Nature, 190, 442 (1961).
49. C.Lowe, M.Ress, and R.Markham, Nature, 199, 219 (1963).
50. S.Fox, J.Johnson, and A.Vegotsky, Science, 124, 923 (1956).
51. E.Ellenbogen, *Abstracts of American Chemical Society* Meeting, Chicago, 1958, p.47C, cited by Miller and Urey[3].
52. O.Perti, K.Bakhadur, and N.Potan, Biokhimiya, 27, 708 (1962).
53. K.Otozai, S.Kume, S.Nagai, T.Yamamoto, and S.Fukushima, Bull.Chem.Soc.Japan, 27, 476 (1954).
54. S.Fox, Science, 132, 200 (1960).
55. K.Harada and S.Fox, J.Amer.Chem.Soc., 80, 2694 (1958).
56. K.Harada and S.Fox, Arch.Biochem.Biophys., 86, 274 (1960).
57. S.Fox and K.Harada, Arch.Biochem.Biophys., 86, 281 (1960).
58. S.Fox, K.Harada, and A.Vegotsky, Experientia, 15, 81 (1959).
59. S.Fox and K.Harada, J.Amer.Chem.Soc., 82, 3745 (1960).
60. E.Katchalsky, Adv.Protein Chem., 6, 123 (1951).
61. G.Krampitz, Naturwiss., 46, 558 (1959).
62. J.Kovács and H.Nagy (Kovács), Nature, 190, 531 (1961).
63. Sh.Akabori, in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd.Akad.Nauk SSSR, Moscow, 1959, p.197.
64. J.Oró and C.Guidry, Nature, 186, 156 (1960).
65. J.Oró and C.Guidry, Arch.Biochem.Biophys., 93, 166 (1961).
66. C.Ponnamperuma, C.Sagan, and R.Mariner, Nature, 199, 222 (1963).
67. C.Ponnamperuma, R.Lemmon, R.Mariner, and M.Calvin, Proc.Nat.Acad.Sci.U.S.A., 49, 737 (1963).

† *Note added in proof*. After this review had been written, some papers appeared that we were unable to include in the text; they are however included in the list of references. These additional references are: a review[100], an asymmetric Strecker synthesis of L-alanine based on *d*-methylbenzylamine[101], an examination of the conditions for the formation of the Earth's primary atmosphere[102], a paper on the chemical evolution of the primary Earth[103], and also a paper on the thermal synthesis of natural amino-acids under primary atmosphere conditions[104].

68. J.Oró and A.Kimball, Arch.Biochem.Biophys., 94, 217 (1961).
69. J.Oró and A.Kimball, Arch.Biochem.Biophys., 96, 293 (1962).
70. Dzh.Oro [J.Oró], in Sbornik "Problemy Evolyutsionnoi i Tekhnicheskoi Biokhimii" (Symposium on Problems of Evolutionary and Technical Biochemistry), Izd."Nauka", Moscow, 1964, p.63.
71. J.Oró, Proc.Lunar Planet.Explor.Colloquim, 3, 9 (1963).
72. S.Fox and K.Harada, Science, 133, 1923 (1961).
73. C.Ponnamperuma and R.Mariner, Nature, 198, 1199 (1963).
74. C.Ponnamperuma, Proceedings of Symposium "The Origin of Prebiological Systems", Florida, 28th October 1963, p.335.
75. G.Schramm, H.Grotsch, and W.Pollmann, Angew.Chem., 74, 53 (1962).
76. E.Mariani and G.Torraca, Intern.Sugar J., 55, 309 (1953).
77. R.Meyer and L.Jäschke, Annalen, 635, 145 (1960).
78. E.Pfeil and H.Ruckert, Annalen, 641, 121 (1961).
79. C.Ponnamperuma and R.Mariner, Radiation Res., 19, 183 (1963).
80. S.Losanitsch, Ber., 30, 135 (1897).
81. H.J.Emeléus, Trans.Faraday Soc., 28, 89 (1932).
82. H.Rathsack, Z.phys.Chem.(Leipzig), 206, 285 (1957).
83. G.Grieppe and M.Galotti, Gazzetta, 59, 507 (1929).
84. K.Heyns, W.Walter, and E.Meyer, Naturwiss., 46, 667 (1959).
85. A.E.Chichibabin, Zhur.Russ.Fiz.-Khim.Obshch., 47, 703 (1915).
86. A.Szutka, J.Hazel, and W.McNabb, Radiation Res., 5, 597 (1959).
87. A.Szutka, Radiation Res., 19, 183 (1963).
88. A.Szutka, Proceedings of Symposium "The Origin of Prebiological Systems", Florida, 28th October 1963, p.381.
89. P.Rothemund, J.Amer.Chem.Soc., 58, 625 (1936).
90. A.A.Krasnovskii and A.V.Umrikhina, Dokl.Akad.Nauk SSSR, 155, 691 (1964).
91. A.P.Terent'ev and E.I.Klabunovskii, in Sbornik "Vozniknovenie Zhizni na Zemle" (Symposium on the Origin of Life on Earth), Izd.Akad.Nauk SSSR, Moscow, 1959, p.99.
92. A.G.Pasynskii, *ibid.*, p.184.
93. H.F.Blum, "Time's Arrow and Evolution", Princeton, 1951.
94. A.I.Oparin, K.B.Serebrovskaya, N.V.Vasil'eva, and T.O.Balaevskaya, Dokl.Akad.Nauk SSSR, 154, 471 (1964).
95. K.B.Serebrovskaya and N.V.Vasil'eva, Dokl.Akad.Nauk SSSR, 155, 212 (1964).
96. A.G.Pasynskii and V.P.Slobodskaya, Dokl.Akad.Nauk SSSR, 153, 473 (1963).
97. A.G.Pasynskii, Vestnik Akad.Nauk SSSR, No.4, 27 (1962).
98. A.Rich, in "Horizons in Biochemistry" (Edited by M.Kasha and B.Pullman), Academic Press, New York, 1962, p.117.
99. J.M.Buchanan, Proceedings of the Symposium "The Origin of Prebiological Systems", Florida, 28th October 1963, p.185.
100. M.A.Kolomiichenko, Ukrain.Biokhim.Zhur., 36, 132, 216 (1964).
101. K.Harada, Nature, 200, 1201 (1963).
102. S.Miller and G.Yuri [H.C.Urey], in Sbornik "Problemy Evolyutsionni i Tekhnicheskoi Biokhimii" (Symposium on Problems of Evolutionary and Technical Biochemistry), Izd. "Nauka", Moscow, 1964, p.357.
103. C.Ponnamperuma, Nature, 201, 337 (1964).
104. K.Harada and S.Fox, Nature, 201, 335 (1964).

Bakh Institute of Biochemistry,
Academy of Sciences of the USSR

U.D.C. 547.244:541.6

POLYMERIC BORON COMPOUNDS

V.A.Zamyatina and N.I.Bekasova

In the three years since the publication of our earlier review of the scientific literature on polymeric compounds containing boron[1], the number of papers published in this field has considerably increased, as well as their penetration of the subject. Investigators no longer restrict themselves to reporting the production of a polymer, but now describe its properties, give the results of investigations which confirm its structure, and, in particular cases, draw conclusions regarding the features of behaviour which reflect the specific chemical nature of boron.

However, as a whole, the chemistry of polymeric boron compounds still lags far behind the monomeric chemistry of boron in time spent on it and in the vigour of its development. It is as though it were passing through an induction period of hidden development, which is necessary for the assimilation of the huge amount of original material made available by the monomer chemistry and for the working out of the basic methods for the production of the polymers.

In this review we follow the order of presentation of material used in our previous review.

Only a few polymers are known in which the main chain contains B–B bonds. Thus Kuchen and Brinkmann[2] reacted metallic sodium with phenylboron dichloride and obtained the linear polymer of composition $[(C_6H_5)B]_n$ having molecular weight 820, corresponding to $n = 9–10$. The product is a yellow amorphous powder which is slowly oxidised in air and darkens above 200°, and it was considered to be the phenyl derivative of the previously described linear polyboron hydride $[BH]_x$.[3] A polymer of analogous structure was obtained by the pyrolysis of tricyclohexylboron, with elimination of cyclohexene and cyclohexane[4]:

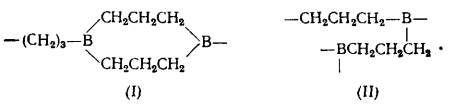
$$x\,B(C_6H_{11})_3 \xrightarrow{250^\circ} (BC_6H_{11})_x + x\,C_6H_{10} + x\,C_6H_{12}.$$

In their investigation of the chemical reactions of diboron tetrachloride, Holliday and coworkers obtained a solid polymeric boron subchloride $[BCl]_n$ from it by pyrolysis[5], and reacted it with epoxyethane to obtain tetrakis-(2-chloroethoxy)diboron $B_2(OCH_2CH_2Cl)_4$ which decomposes on heating to give the polymer $(BOCH_2CH_2Cl)_n$.[6]

According to a British patent[7], tetraethoxydiboron $B_2(OCH_2CH_3)_4$ is also converted into a polymer on heating at 100°.

The pyrolysis of decaborane gives hydrogen and a condensation product $B_{20}H_{24}$, which can evolve further hydrogen and is converted into a non-volatile solid boron hydride[8].

New polymers containing B–C bonds in the main chain have been described. These are most simply prepared by hydroboration of unsaturated compounds; thus by the action of diborane on triallylboron Mikhailov and Pozdnev[9] obtained a solid polymer which they consider contains both cyclic (I) and acyclic (II) units:



(I) (II)