

can be oxidized to cyanogen either during electrical discharge in the gaseous phase or by photo-oxidation in aqueous solution. Clearly the prebiotic synthesis of amino-acids and purines presents few problems, but what about the pyrimidines uracil and cytosine?

Uracil has been obtained by heating malic acid, urea and poly-phosphoric acid at 100° to 140° C and, in very low yields, by heating aqueous solutions of acrylonitrile, urea and ammonium chloride in aqueous solution at 135° C, but it is stretching the imagination too far to claim these as plausible prebiotic conditions. Ferris, Sanchez and Orgel, however, have just reported in the current issue of *J. Mol. Biol.* (**33**, 693; 1968) the synthesis of both cytosine and uracil under much milder and therefore more plausibly prebiotic conditions. They have found that cyanoacetylene, a major product of electrical discharges on nitrogen-methane mixtures, reacts with aqueous cyanate at 100° C to yield cytosine. Apparently up to 19 per cent of the products of reaction can be cytosine. When cyanoacetylene is added to cyanate at room temperatures, three chromatographically separable products are obtained and all three yield cytosine on heating in aqueous solution. Furthermore, cyanogen on cyanofornamide can replace cyanate in the reaction. Once cytosine has been formed it is a simple step to hydrolyse it to yield uracil.

Although the concentrations of reactants necessary to give a reasonable yield of cytosine are quite low, both cyanate and cyanoacetylene are unstable. The half-life of cyanoacetylene in aqueous solution is at most a few years and cyanate hydrolyses to ammonium carbonate within a hundred years. This severely restricts the range of possible prebiotic environments which could sustain pyrimidine synthesis. It seems very unlikely that sufficiently high concentrations could ever have accumulated in the primeval oceans or in ponds for that matter. A possible alternative is reaction in a eutectic phase.

What makes these latest results particularly significant is that they show that all the purines and pyrimidines and many of the amino-acids can all be obtained from a small family of cyanides which have closely related structures and are produced in a plausible prebiotic simulation. Could the primeval amino-acids and bases have been formed by any other route?

Deformylase

from our Cell Biology Correspondent

Few, if any, of the completed proteins of *E. coli* have N-formylmethionine as the N-terminal residue. As Waller (1963) proved, the great majority have either methionine, alanine or serine at the N-terminus. If this is accepted, one of the consequences of the model of protein synthesis, in which formylmethionine initiates all protein chains, is that bacteria contain an enzyme, or enzymes, which removes the formyl group, and in some cases the methionine as well, from the N-terminus of the polypeptide. Last year, Fry and Lamborg (*J. Mol. Biol.*, **28**, 423; 1967) reported some preliminary evidence for an enzyme in *E. coli* that deformylates peptides, and Weissbach and Redfield (*Biochem. Biophys. Res. Commun.*, **27**, 7; 1967) also reported the presence in *E. coli* of an enzyme that removes the formyl group from N-formylmethionine but not from other N-formyl amino-acids.

Adams, who with Capecchi initially proposed that N-formylmethionine is the chain initiating amino-acid, has just reported the isolation of a deformylase from *E. coli* (*J. Mol. Biol.*, **33**, 571; 1968). Unfortunately the enzyme is very labile under experimental conditions and strongly inhibited by thiols and this has prevented any significant purification. It also prompted Adams to isolate the same enzyme from *Bacillus stearothermophilus*, a bacterium which grows happily at 65° C. The idea is that enzymes from this species might be more stable at experimental temperatures and this seems to be so. Extracts from both species contain an activity which cleaves the formyl group from the peptide F-met-ala-ser to yield formate and met-ala-ser. Neither extract cleaves off the methionine residue nor does it cleave formylmethionine alone. The *E. coli* extract has also been shown to cleave formate from *E. coli* proteins made *in vitro*. As Capecchi (1966) showed, most of the *E. coli* proteins made in a cell free system have the formyl group intact presumably because the deformylase does not survive the cell fractionation procedures used to make the cell free system.

Although the peptide deformylase does not split formate from formylmethionine, *E. coli*, but not *B. stearothermophilus*, contains a second activity which hydrolyses formylmethionine. This is probably the enzyme Weissbach and Redfield worked with, and Adams believes it to be acetyl-ornithine deacetylase which has nothing to do with initiation.

Formylmethionine peptides are hydrolysed by the deformylase much faster than other formyl peptides, the dipeptide acetyl-met-ala or formylmethionine alone. This argues that the deformylase is specifically designed to cleave formate from proteins initiated with formylmethionine and the reaction seems to be a straightforward hydrolysis. As the deformylase only clips off the formate group, there must be a second enzyme to remove the methionine residue, but so far this activity has not been isolated. This hypothetical enzyme is probably a methionine-specific aminopeptidase. And from the limited data on N-terminal residues and sequences of *E. coli* proteins, Adams proposes that the enzyme might have specificity such that if the N-terminal formylmethionine is followed by alanine or serine the methionine is removed. But if methionine is followed by other amino-acids, it is left at the N-terminus.

Odd Proteins

from our Molecular Biology Correspondent

THE postulate, embodied in the formulation of the allosteric hypothesis, that sub-unit enzymes should have high symmetry and an even number of sub-units has so far held good, and it has been reasonable to suspect that it might be a general rule, applicable irrespectively of whether allosteric regulation obtains. The few apparent contradictions have hitherto always turned out to be false alarms.

A new study of the enzyme arginine decarboxylase (from *E. coli*) has now appeared (Boeker and Snell, *J. Biol. Chem.*, **243**, 1678; 1968), which gives seemingly irrefutable evidence that this can dissociate into five sub-units, each containing two polypeptide chains. The enzyme contains pyridoxal phosphate, and its isolation in homogeneous form is described in an accompanying