The results can be reasonably explained in terms of the intermediate formation of the isomeric chlorosulfite esters V and VI which then undergo dissociation to the common intimate ion pair VII. Subsequent loss of sulfur dioxide from the chlorosulfite anion generates chloride ion which then attacks randomly the *exo*-allylic positions C-2 and C-4 to give the *exo*-allylic chlorides III and IV. Diversion from the expected S_Ni' process is probably due to the exceptional stability of the rigid bicyclo-[3.2.1]octenyl cation.

It has been suggested that although the S_Ni' process is often depicted as a cyclic transition state [3], the formation and collapse of highly oriented ion pairs [2] could produce the same stereochemical result. It can now be concluded that in a symmetrical allylic intimate ion pair, such selective orientation does not exist, or at least is difficult to attain. Indeed, in these cases any net allylic rearrangement of the reactant should be just a reflection of the relative rates of attack at the alternative allylic termini by the gegenion. Accordingly, a prerequisite for the occurrence of an S_Ni' reaction appears to be a low stability of the related allylic cation.

Experiments are under way to re-investigate several long-standing claims for classic S_Ni' processes by means of our NMR. spectroscopic method.

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155. Note on the rôle of cyanides and polyphosphates in the formation of peptides in aqueous solutions of amino acids, at room temperature, as a possible prebiotic process

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(30. IV. 71)

Résumé. Les cyanures et les polyphosphates jouent un rôle important dans l'évolution chimique. Des solutions aqueuses d'acides aminés additionnées de trimétaphosphate et de cyanure, amenées à pH 11,5–12 par NH_3 et maintenues à ce pH 4 jours à température ordinaire, contiennent les dipeptides correspondants, formés avec des rendements à peu près doubles de ceux obtenus en présence du seul trimétaphosphate. En présence uniquement de cyanure, il ne se forme pas de peptides. Dans ces mêmes conditions, une solution de cyanure ne fournit ni acides aminés ni peptides. Pour la formation abiotique de peptides à partir d'amino-acides, le système polyphosphate-cyanure est donc plus efficace que chacun de ses composants individuellement.

Hydrocyanic acid, HCN, formed by electric discharge in mixtures simulating supposed primitive atmospheres, *e.g.* $CH_4 + NH_3 + H_2O$, is known to be a precursor

and a key intermediate for the abiotic preparation of many important substances of biological interest such as amino acids, peptides, purines (adenine), etc. It may also be considered as a condensing agent in prebiotic reactions. Its central rôle in chemical evolution has already been pointed out (for a discussion of the subject and for an extensive bibliography see *e.g.* [1]).

We have shown that amino acids are condensed to peptides (mainly dipeptides) in aqueous solutions of linear or cyclic polyphosphates, at room temperature and at pH's above 7 [2]. The best yields are obtained with trimetaphosphate and the optimum pH for the reaction seems to be around 9.5 ($H_2NCHROO^-$), although the reaction proceeds well at higher or at lower pH (8.0 which is that of the ocean and probably that of the primitive ocean too). Polyphosphates are known to be good condensing agents for other types of reaction and also good phosphorylating agents even in aqueous solution, under appropriate conditions [2] [3]. Their possible rôle as condensing and/or phosphorylating agents during the course of chemical evolution has already been discussed in several papers [2] [3] [4].

In this paper we report some preliminary results, using mixtures of sodium trimetaphosphate and sodium cyanide as the condensing agent for amino acids.

The results, summarized in the table, show that an aqueous solution of glycine (0.1 M) containing trimetaphosphate (0.1 M) and cyanide (0.3 M) brought to pH ~11.5 with conc. aqueous ammonia and maintained at that pH (by addition of conc.

Dipeptide formation in aqueous 0.1 M solutions of amino acids in the presence of trimetaphosphate and/or cyanide after 4 days, at room temperature and at pH 11.5–12.0

The pH is maintained by addition of conc. ammonia when necessary

Amino Acid	Trimeta-phosphate M	Cyanide M	Peaks (Elution time in min)				Yield of di-peptide %
			(23) [c]	(36) [c]	Glycine (99) M	Diglycine (146) M	
Glycine	0.1	–	*m*	–	0.101	0.007	12
Glycine [a]	0.1	0.3	*m*	*s*	0.088	0.011	20
Glycine	–	0.3	–	*vs*	0.100	0	0
–	–	0.3 [b]	–	*vs*	0	0	0
Alanine	0.1	–					~ 5
Alanine	0.1	0.3					~ 9

m = medium, *s* = strong, *vs* = very strong

[a] Hydrolysis in 6 N HCl at 100° for 24 h yields glycine only.

[b] Hydrolysis yields no amino acids or peptides.

[c] Not identified: peaks with low elution times; they may be the reaction products of trimetaphosphate (23 min) or cyanide (36 min) with ammonia.

ammonia when necessary), at room temperature, for 4 days, yielded 20% of diglycine. This is almost twice the yield (12%) obtained in a parallel experiment with trimetaphosphate alone.

In order to ascertain if the effect of the system trimetaphosphate-cyanide on the yield of dipeptide was synergistic or additive we ran parallel experiments using a 0.1 M solution of glycine containing only NaCN (0.3 M) and ammonia, and a blank

solution of NaCN (0.3 M) + ammonia. In both cases, no diglycine was detected. In the blank no amino acids or peptides were present even after hydrolysis.

Although at this point we cannot exclude that a fraction of the diglycine found may have resulted from the direct interaction of trimetaphosphate with glycine according to a mechanism we have previously discussed [2], the available data (see table) suggest that trimetaphosphate *plus* cyanide leads to a more efficient system in condensation reactions than either trimetaphosphate or cyanide alone. This is why we intend to study the mechanism of this reaction as well as the trimetaphosphate-cyanide system, in aqueous solutions at various pH's in the presence or absence of ammonia, and its application to other condensations and/or phosphorylation reactions.

The data described in this paper emphasize once more that cyanides and polyphosphates may have played a crucial role in chemical evolution.

Experimental. – 1. *Analysis of amino acids and peptides.* Performed on a *Beckman* 120C Amino acid analyzer. The elution times and peak areas enabled identification of each peak (except two with low elution times: 23 and 36 min. respectively) and assay of the products.

2. *Condensation of amino acids in aqueous solutions of sodium trimetaphosphate and/or cyanide.* 153 mg of sodium trimetaphosphate and/or 147 mg of sodium cyanide were added to 5 ml of an 0.1 M aqueous solution of the amino acid. The pH was adjusted to 11.5–12.0 with concentrated ammonia and was maintained at room temperature at that value for 4 days by addition of ammonia when necessary (once or twice daily). Aliquots of the solution were then analyzed (Amino acid analyzer) and the yields of the dipeptides were determined by comparing the area of the peaks on the chromatogram with those obtained with known amounts of authentic products. The solution of glycine and trimetaphosphate plus cyanide showed 4 peaks on the chromatogram; the two with low elution times were not identified. The results are summarized in the table.

3. *Behaviour of cyanide + ammonia in aqueous solution at pH 11.5 – 12.* A 0.3 M solution of sodium cyanide was adjusted to pH 11.5–12 with concentrated ammonia and analyzed after 4 days at that pH (maintained by addition of ammonia), at room temperature. Besides an unidentified peak with low elution time (36 min.) no peak corresponding to an amino acid or a peptide was detected on the chromatogram. After hydrolysis of the solution (6 N HCl at 100° for 24 hours) no amino acids or peptides were fond, and the peak with low elution time had vanished (see table).

4. *Hydrolysis of the reaction solutions obtained under 2.* After hydrolysis (6N HCl, 24 hours at 100°) of the reaction solution of glycine plus trimetaphosphate and cyanide which had shown 4 peaks (see table), all the peaks but that of glycine had disappeared (see table).

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