EXPERIMENTS ON THE ABIOTIC AMPLIFICATION OF OPTICAL ACTIVITY

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I. ABSTRACT

Our earlier experiments are briefly reviewed, involving the abiotic generation of optical activity by exposure of DL-amino acids to various "chiral" physical forces. The enantiomeric enrichments so obtained were low, however, and additional experiments were undertaken with the objective of abiotically enhancing such small enantiomeric excesses. D ≠ L Mixtures of leucine N-carboxy anhydride gave enantiomerically enriched polymers on partial polymerization, while valine NCA mixtures behaved oppositely. Leucine polymers were also found to hydrolyze stereoselectively, providing for additional enantiomeric enhancement. A repetitive sequence of partial polymerization-hydrolysis steps is suggested as a possible mechanism for the abiotic genesis of optically enriched polypeptides on the primitive Earth.

II. INTRODUCTION

The origin of optically active molecules in nature poses a question - clearly bearing on the questions of the origin of chiral biopolymers and of life itself - which has intrigued scientists since the time of Pasteur, but which still lacks definitive answers. Over the intervening years a number of plausible physical mechanisms, recently reviewed (1-3), have been proposed for the abiotic genesis of chiral molecules. Because of the philosophical importance of the question, and since the experimental validity of these mechanisms bears directly on the applicability of optical activity per se as a criterion for

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extraterrestrial (4) or archean life, we have reinvestigated a number of these mechanisms using modern experimental techniques. In general our procedure has been to subject DL-amino acids (or derivatives), as prebiotically realistic substrates, to various chiral physical forces or environments, then to examine the recovered substrate for optical activity (i.e. an excess of one enantiomer, D $\neq$ L) using analytical gas chromatography (g.c.). The advantages of g.c. over polarimetry for such determinations has been summarized (5). The first section of this paper briefly reviews our experiments along these lines.

Several of the above experiments on the abiotic origin of optical activity were in fact successful in unambiguously generating small excesses of one enantiomer from a DL-amino acid precursor. The enantiomeric excesses (% major enantiomer - % minor enantiomer) thereby produced, however, were typically on the order of only a few percent - rather smaller than might resonably be thought adequate for the direct genesis of a biosphere. Clearly, additional abiotic mechanisms for the subsequent chemical amplification of such small, abiotically produced enantiomeric excesses would be stereochemically advantageous for prebiotic molecular evolution toward the stereospecific biomolecular processes existing today. Accordingly, our more recent experiments have focused on potential mechanisms for the abiotic amplification of small enantiomeric excesses. These experiments are discussed in the second section of this paper.

III. EXPERIMENTS ON THE ORIGIN OF OPTICAL ACTIVITY

A. Asymmetric Absorption on Quartz

The carefully executed negative experiments and critique of earlier positive experiments reported by Amariglio in 1968 (6) rendered the phenomenon of asymmetric adsorption of racemates by d- or l-quartz open to question. Since such a process had been suggested as a possible mechanism for the origin of optical activity (7), we have attempted to resolve the conflicting claims in the literature.

Our initial experiments (8,9) involved equilibrating ^{3}H- or ^{14}C-labeled D- or L-alanine hydrochloride in $10^{-5}M$ dimethylformamide solution with finely powdered d- and l-quartz. Comparison of radioactivity counts of the solutions before and after equilibration gave a measure of the percent of Ala•HCl adsorbed in each experiment. At 26-30% gross adsorption, d-quartz preferentially adsorbed D-Ala•HCl and l-quartz L-Ala•HCl, with the differential (i.e. asymmetric) adsorption ranging from 1-1.8%. These results were later confirmed (10) using labeled DL-Ala•HCl, with differential adsorption varying from 12-20%. Finally, the

adsorption of D- and L-alanine isopropyl ester hydrochloride from chloroform solution was studied using g.c. criteria for asymmetric adsorption (11). Here we observed that d-quartz preferentially adsorbed the L-Ala ester and l-quartz the D-enantiomer, with enantiomeric enrichment ranging from 1.5-12.4%. These positive asymmetric adsorption findings have been subsequently confirmed by others (12) and have been discussed in relation to a mechanism for the origin of optical activity (9).

B. Asymmetric Photolysis with Circularly Polarized Light (CPL)

Before 1900 van't Hoff had suggested that optically active substances might have arisen in nature by the action on matter of right or left circularly polarized light (RCPL or LCPL), thought to be present in sunlight. After numerous others had failed (see (1)), Kuhn and coworkers (13,14) in 1929-30 reported the first successful asymmetric photolyses using CPL. They achieved rotations as high as +0.78° and -1.04°, for example, in the undecomposed residue from the partial photolysis of N,N-dimethyl-α-azidopropionamide, depending upon whether RCPL or LCPL (280-320nm) was employed. Several recent reviews (15,16) discuss the many successful asymmetric photodegradative and photosynthetic reactions with CPL which have been reported since Kuhn's initial experiments, and Kagan has recently shown (16,17) theoretically and experimentally the conditions necessary to achieve high optical purity on asymmetric photolysis - obtaining a residual optical purity of 20% on the 99% photodestruction of racemic camphor with 290-370 nm CPL. Our interest in this subject was to see if racemic amino acids might be capable of undergoing analogous asymmetric photolyses, thus providing a possible abiotic source of optically active monomers which might subsequently evolve to optically active polypeptides.

In our experiments (18) DL-leucine in 0.1M HCl was subjected to partial photolysis with 212.8 nm (circular dichroism maximum: 211 nm) RCPL and LCPL from a specially designed laser source. The enantiomeric composition of the unphotolyzed residual Leu was then determined by g.c., and the percent degradation by the g.c. "enantiomeric marker" technique (19,20). With RCPL the D-Leu component of the DL-Leu was preferentially destroyed, resulting in a L > D enantiomeric excess of 1.98% after 59% photolysis. Conversely, with LCPL the L-enantiomer was preferentially photolyzed, with a residual D > L excess of 2.50% after 75% gross decomposition. These enantiomeric enrichments are the second highest ever achieved during asymmetric photolysis. At about the same time Norden (21) reported the asymmetric photodegradation (and photoinversion) of racemic tartaric acid, alanine, and glutamic acid, with "enrichment yields" of 0.06 - 0.22%. We found no racemization of L-Leu after 7 hours exposure to 253.7 nm ultraviolet light and 96% gross photolysis, suggesting that

photoinversion was negligible in our experiments.

C. Asymmetric Radiolysis with Longitudinally Polarized Electrons

Shortly after the demonstration (22) of parity violation during β-decay (23), Vester (24) and Ulbricht (25) suggested that the circularly polarized Bremsstrahlen photons (26) produced by deceleration of natural "left-handed" (antiparallel spin) longitudinally polarized β-decay electrons might interact asymmetrically with racemic or prochiral substrates, ultimately affording optically active molecules by subsequent asymmetric degradations or syntheses. Vester (27) and Ulbricht (28) tested this interesting hypothesis in a number of synthetic and degradative experiments using a variety of β-emitters, but observed polarimetrically no optical activity in any of their products. In 1968 Garay (29) provided the first positive result regarding the Vester-Ulbricht hypothesis, reporting that D-tyrosine in alkaline solution was more decomposed than was L-tyrosine after 18-month exposure to the β-rays and Bremsstrahlen from 0.36 mCi of dissolved $^{90}SrCl_2$. Because of the potential importance of this observation and because of certain reservations about the experimental protocol employed (particularly the use of aqueous solutions, where symmetrical solution radiochemistry involving free radicals might obscure any asymmetric effect), we undertook to extend Garay's type of experiments using solid amino acid substrates and a variety of β-ray sources. The following sections briefly summarize our results.

1. ^{90}Sr-^{90}Y Source. Our initial experiments (30,31) involved irradiation of triplicate sets of 21 samples of amino acids (both solid and dissolved) in a 61,700 Ci ^{90}Sr-^{90}Y β-ray Bremsstrahlen source at Oak Ridge National Laboratory. Two of the sets have been retrieved and the samples examined for optical activity. Samples from the second set (irradiated for 1.34 years; 4.2×10^8 rads), including solid or dissolved DL-leucine, norleucine, norvaline, proline, and tyrosine proved totally void of optical activity by ORD examination. Samples of solid DL-leucine and its dissolved Na and HCl salts were extensively decomposed (13.8, 48.6 and 34.6%, respectively), but their enantiomeric composition (determined by g.c.) was D:L/50.0:50.0 within experimental error. The absence of asymmetric radiolyses in these experiments has been attributed (30,31) to symmetrical solution radiochemistry (for dissolved samples), insufficient degradation, and/or insufficient circular polarization of the majority of the Bremsstrahlen. The third set of samples is still being irradiated.

2. ^{14}C Source. In this study (32) we examined a series of ^{14}C-labeled DL-amino acids of high specific radioactivity (285-574 mCi/mole) which had been prepared (33) some 17-26 years

earlier, and had undergone self-β-radiolysis in the intervening period (radiation dose: 5-11x10^7 rads). Despite gross degradations to the extent of 17-68%, the D:L composition (by g.c.) of the residual samples was 50.0:50.0 within experimental error. The lack of optical activity of these samples confirmed results of their previous ORD examination by Calvin and coworkers (33).

3. ^{32}P Source. The recent remarkable claim of Darge et al. (34) that a 19% optical enrichment accompanied the 33% ^{32}P β-radiolysis of DL-tryptophan in frozen aqueous solution has prompted us (35) to duplicate Darge's experiment precisely. We relied, however, on analytical g.c. (rather than absorption spectra and optical rotation) to estimate percent degradation and enantiomeric enrichment. Although our gross degradations (42.5% av.) were somewhat larger than that of Darge et al. (34), we found no evidence whatsoever of asymmetric radiolysis. More recently we have extended such ^{32}P irradiations to DL-tryptophan and DL-leucine under low temperature (-196°) anhydrous conditions, again with no finding of asymmetric radiolysis (36).

4. Linear Accelerator Source. Our failure to detect asymmetric radiolyses using a 61.7 kCi ^{90}Sr-^{90}Y Bremsstrahlen source (30,31) prompted us to undertake experiments using an artificial source of monoenergetic, longitudinally polarized electrons, rather than their Bremsstrahlen. In these studies (37,38) we employed a linear accelerator which could provide both natural, anti-parallel spin (AP), "left-handed" electrons, as well as anti-natural, parallel spin (P), "right-handed" electrons of 120 KeV energy and 13-23% net polarization. Crystalline DL-leucine, under vacuum, was directly bombarded (dose: 0.9-2.4x10^9 rads) to produce gross degradations of 53-76%. In three experiments using AP-electrons the D-Leu component was selectively destroyed, producing a L > D excess in the residue of 0.60-1.42%. As a crucial "symmetry check", in three analogous irradiations with P-electrons the L-Leu was preferentially destroyed, yielding a residual D > L excess of 0.74-1.14%. Keszthelyi (39) and Walker (40) have since presented theoretical arguments that such asymmetric radiolyses could not have been due to a Bremsstrahlen effect, and we have accordingly suggested other possible mechanisms (41). Unfortunately, and for reasons as yet undetermined, the single, carefully executed attempt to duplicate our observations using AP- and P-electrons from another "artificial" source have been unsuccessful (42). In other papers we have recently discussed related aspects of the Vester-Ulbricht β-decay mechanism (43-46).

5. Radioracemization. In our earlier study of the self-radiolysis of ^{14}C-labeled amino acids (32), several of the optically active amino acids examined appeared unexpectedly to

have undergone some racemization along with their β-radiolysis. This prompted us to look into the question of the possible radioracemization of amino acids by ionizing radiation, and a series of experiments was undertaken in which optically pure amino acids were exposed to γ-radiation in a 3000 Ci ^{60}Co source, then were examined for percent degradation and enantiomeric composition by g.c. (47,48). It was found that radiation doses ($8-10\times10^{8}$ rads) which engendered 39-96% radiolysis of typical crystalline aliphatic amino acids also caused ca. 2-14% racemization in their undecomposed residues. The Na salts of these amino acids in aqueous solution were more susceptible both to radiolysis and radioracemization than were the solid samples, but the corresponding HCl salts in solution proved immune to radioracemization (48). The crystalline non-protein amino acid isovaline (α-amino-α-methylbutyric acid) which, lacking an α-hydrogen, is incapable of racemization by ordinary chemical agents (49), proved (50,51) nevertheless to be as susceptible to γ-radiolysis and radioracemization as the common amino acids studied (47,48), but its Na salt in aqueous solution was immune to radioracemization. These various observations have been qualitatively rationalized in terms of postulated mechanisms for the radiolysis of amino acids (48,51).

Clearly, the phenomenon of radioracemization jeopardizes the potential efficacy of the Vester-Ulbricht β-decay mechanism for the origin of optical activity. If the rate of production of an optically active product by asymmetric β-radiolysis (or synthesis), for example, is less than its rate of radioracemization, then obviously no net optical activity will acrue. As we have discussed from the viewpoint of rate equations (48), the relative values of the several rate constants involved in such competing processes will determine if an excess of one enantiomer can be formed before gross radiolysis is complete. The radioracemization phenomenon also has serious potential implications in geochemistry and in cosmology, which we have recently discussed in some detail (52).

IV. EXPERIMENTS ON THE AMPLIFICATION OF OPTICAL ACTIVITY

A. Amplification of Amino Acid Chirality on Polymerization

In 1957 Wald (53) proposed a novel mechanism for the amplification of optical activity during polypeptide development, suggesting that the formation of the α-helix in the secondary structure of proteins, if "enhanced by the employment of a single configuration of the amino acids, ...should provide a sufficient basis for the selection of one configuration out of a mixture of enantiomorphs." The plausibility of Wald's hypothesis was soon enhanced by the results of a number of subsequent investigations

(briefly reviewed in (54)) on polymers from and polymerizations involving the D- and L-enantiomers of γ-benzylglutamate N-carboxy anhydride (NCA). The first experimental demonstration that an enantiomer in excess in a D ≠ L amino acid NCA monomer mixture could actually be selectively incorporated into a growing polymer was provided by Matsuura et al. in 1965 (55). They polymerized alanine NCA mixtures having the L-isomer in excess and found that the specific rotation of the polyalanine product decreased with time at the outset, reached a minimum at ca. 50% completion, and then increased - indicating that the L-isomer in excess was being preferentially incorporated into the polymer in the early stages of the polymerization. Similar observations were later made using other D ≠ L monomer mixtures of alanine (56) and γ-benzylglutamate NCA's (57). Because of these promising results and the possible importance of amino acid polymerization as a mechanism for the amplification of small, abiotically produced enantiomeric excesses, we have undertaken (54) a quantitative study of the polymerization of several amino acid NCA's as an experimental model for Wald's mechanism (53).

In these experiments (54) we induced partial polymerization of D ≠ L mixtures of leucine (or valine) NCA monomers containing a known excess of one enantiomer, then determined the enantiomeric composition of the resulting polymer (after hydrolysis) by g.c. The residual monomer NCA in each experiment was also analyzed for its enantiomeric composition. This provided an internal consistancy check, since any enantiomeric enrichment in the polymer should be reflected as a depletion in the unpolymerized monomer.

Table 1, showing our results with leucine NCA's, indicates that at ca. 50% completion the enantiomer predominant in the starting monomer is selectively incorporated into the polymer and (to a roughly comparable extent) depleted in the residual monomer. Furthermore, the extent of enantiomeric enrichement (Δ) in the polymer appears to increase to a plateau as the enantiomeric excess in the initial monomer NCA increases. These observations confirm and quantify conclusions of earlier workers (55-57) that for polymerizations affording helical polymers from D ≠ L NCA monomers, the enantiomer in excess at the outset is stereoselectively incorporated into the growing polymer in the early stages of reaction.

Table 2, which shows our results with valine NCA's, displays a novel and puzzling reversal of the effect noted for leucine. Here the enantiomeric excess of the initially predominant valine NCA monomer was decreased in the polymer and enhanced in the unreacted monomer. Furthermore, the magnitude of the effect (at least between 25-50% reaction) appears to be independent of the extent of polymerization. Thus, under our conditions, the growing

TABLE 1. PARTIAL POLYMERIZATION OF MIXTURES OF LEUCINE NCA'S OF INCREASING ENANTIOMERIC EXCESS

Initial Leucine NCA		Polymerization,	Hydrolyzed Product			
Excess of	% E.e.[a]	% Completion	Polymer		Unreacted NCA	
			% E.e.[a]	% Δ[b]	% E.e.[a]	% Δ[b]
D	8.5	51	11.8	3.3	5.1	-3.4
D	8.7	53	12.3	3.6	4.5	-4.2
L	9.0	54	13.3	4.3	4.7	-4.3
L	9.0	54	12.4	3.4	4.9	-4.1
L	27.0	56	39.5	12.5	18.3	-8.7
L	26.8	53	38.2	11.4	17.9	-8.9
D	31.2	52	42.1	10.9	21.8	-9.4
L	50.5	56	62.9	12.4	42.4	-8.1
L	50.6	54	57.9	7.3	42.1	-8.5
L	69.6	54	83.5	13.9	58.7	-10.9
L	69.6	53	77.0	7.4	61.1	-8.5
L	71.6	52	76.0	4.4	-	-

a) Absolute value of %D - %L

b) Product E.e. - Initial NCA E.e.

TABLE 2. PARTIAL POLYMERIZATION OF MIXTURES OF VALINE NCA'S OF COMPARABLE ENANTIOMERIC COMPOSITION

Initial Valine NCA		Polymerization,	Hydrolyzed Product			
Excess of	% E.e.[a]	% Completion	Polymer		Unreacted NCA	
			% E.e.[a]	% Δ[b]	% E.e.[a]	% Δ[b]
D	12.3	25[c]	7.3	-5.0	14.6	2.3
D	12.2	25[c]	7.0	-5.2	15.0	2.8
L	13.3	35	8.6	-4.7	15.6	2.3
D	12.3	50	7.0	-5.3	-	-
D	12.1	50	7.2	-4.9	15.9	3.8

a) Absolute value of %D - %L

b) Product E.e. - Initial NCA E.e.

c) Approximated by: % Completion = 100 DP/(A/I)

polyvaline appears at the outset selectively to incorporate either the minor enantiomer or the racemate as the polymerization advances. While several explanations for this "reverse" stereoselectivity have been advanced (54), the precise cause of the effect is curently unknown and is presently under our investigation.

While amino acid NCA's can hardly be considered as prebiotically realistic monomer precursors, we believe that the above and earlier (55,56) preliminary studies with leucine NCA's do at least establish the principle that small, abiotically engendered enantiomeric excesses in amino acid monomers might be abiotically enhanced during subsequent polymerization to polypeptides.

B. Amplification of Peptide Chirality on Partial Hydrolysis

If, as seen above with leucine NCA, the optical purity of an amino acid can be enhanced by partial polymerization to a polypeptide, it is perhaps reasonable to suspect that polypeptides might also show stereoselectivity during their degradation by such means as hydrolysis, pyrolysis or radiolysis. In a preliminary investigation of this possibility we have undertaken several model experiments involving peptide hydrolysis (58). Polyleucine was chosen as a model substrate since, when optically pure, it has an extremely stable α-helix structure (59).

Samples of poly-D-, -L-, and -DL-leucine were partially hydrolyzed (160°; 2-PrOH/6N HCl; 21 hours) under identical conditions, whereupon each amount of monomeric leucine produced by hydrolysis was determined by g.c. Table 3 shows that in all cases the DL-polymer was hydrolyzed more extensively than the stereohomogeneous D- or L-peptide. Since poly-D- or -L-leucine is predominantly in the α-helix conformation (59, 60), and since configurational randomness weakens such structures (61), it seems possible that the increased ease of hydrolysis of the poly-DL-Leucine may be due to the diminished integrity of its helical structure.

The results in Table 3 suggested a more pertinent experiment (58). D ≠ L Leucine polymers of intermediate enantiomeric excess were partially hydrolyzed and the hydrolysates, along with the unhydrolyzed residual polymers, were each analyzed for their new enantiomeric compositions. As seen in Table 4, the leucine monomer hydrolysate was uniformly of lower enantiomeric purity than the initial polymer, while the residual unhydrolyzed polymer showed a uniform enhancement of the initial enantiomeric excess. In the final experiment in Table 4 this enrichment totalled as much as 10.1% after ca. 57% hydrolysis of the starting polymer. Recognizing that the initial polyleucine consisted of a

TABLE 4. ENANTIOMERIC EXCESS CHANGES ON PARTIAL HYDROLYSIS OF D ≠ L POLYLEUCINES

Initial Polymer, % E.e.	Yield of Leucine Monomer,%	Recovered Leucine, % E.e.	Recovered Polymer, % E.e.
45.4[a]	10.4	31.2[a]	49.5[a]
45.4	16.9	30.5	50.1
45.4	27.0	39.2	54.9
45.4	46.4	43.7	54.6
41.4[b]	57.0	39.5[b]	51.5[b]

a) L > D

b) D > L

TABLE 3. STEREOSELECTIVITY ON HYDROLYSIS OF POLYLEUCINES

Polyleucine from Leucine of Configuration	DP_{av}[a]	Yield of Leucine Monomer, %[b]
D	16.6	45
L	16.2	41
DL	16.0	55
D	29.9	30
L	28.8	31
DL	29.6	39
D	41.4	30
L	49.2	35
DL	40.7	56

a) Determined by end group analysis of crude peptide

b) 100x(amount of Leu recovered)/theoretical amount of Leu in peptide)

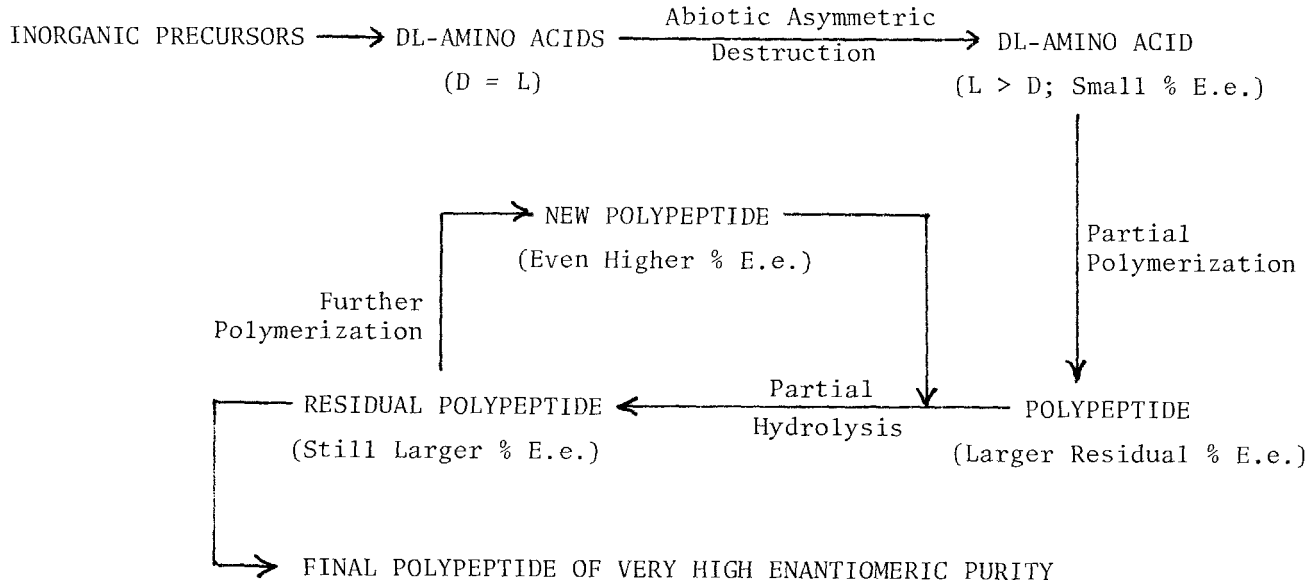

FIGURE 1. POSSIBLE MECHANISM FOR THE ABIOTIC FORMATION OF OPTICALLY ENRICHED POLYPEPTIDES

distribution of oligomers of various sizes and enantiomeric compositions, the results in Table 4 can be explained by assuming that the polyleucine components of lower enantiomeric purity were hydrolyzed more rapidly than the components of greater enantiomeric purity.

C. A Cyclic Mechanism for the Amplification of Optical Acitivity

The 45.4% enantiomeric excess L > D polymer in Table 4 was prepared, as discussed above, by the partial polymerization (to 52%) of a 31.1% enantiomeric excess L > D mixture of leucine NCA's. This constituted a 14.3% enhancement of the original enantiomeric excess on polymerization. The 45.4% enantiomeric excess in the resulting polymer could subsequently be increased by as much as 9.5% (to 54.9%) by partial hydrolysis (Table 4). Thus in one combined polymerization-hydrolysis sequence the intial 31% enantiomeric excess of the monomer was enhanced to ca. 55%, an increase of some 24%. Thus a combined partial polymerization-hydrolysis process appears potentially quite efficient as a mechanism for the abiotic enrichment of small enantiomeric excesses.

On the basis of the above model experiments it is tempting to speculate that repeated polymerization-hydrolysis reactions, induced by environmental dry-wet cycles, might have been operative on the primitive Earth to enhance small, abiotically produced enantiomeric excesses in amino acid monomers. One can imagine a repetitive cycle of partial polymerization-hydrolysis steps, as illustrated in Figure 1, which could in principle abiotically enhance the optical purity of polypeptides to a degree sufficient to permit the eventual evolution of a stereohomogeneous biosphere.

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REFERENCES

1. Bonner, W. A.: 1972, in "Exobiology", C. Ponnamperuma, ed., North-Holland, Amsterdam, pp. 117-181.
2. Thiemann, W.: 1974, Naturwiss. 61, pp. 476-483.
3. Norden, B.: 1978, J. Molec. Evol. 11, pp. 313-332.
4. Stryer, L.: 1966, in "Biology and the Exploration of Mars", C.S. Pittendrigh, W. Vishniac and J. P. T. Pearman, eds., Nat.Acad.Sci. - Nat.Res.Conc., Washington, D.C., pp.141-146.
5. Bonner, W. A., Van Dort, M. A. and Flores, J. J.: 1974, Analyt. Chem. 46, pp. 2104-2107.
6. Amariglio, A., Amariglio, H., and Duval, X.: 1968, Helv. Chim. Acta 51, pp. 2110-2132.
7. Bernal, J. D.: 1949, Proc. Phys. Soc. 62A, pp. 537-558.
8. Bonner, W. A., Kavasmaneck, P. R., and Martin, F. S.: 1974, Science 186, pp. 143-144.
9. Bonner, W. A., Kavasmaneck, P. R., Martin, F. S., and Flores, J. J.: 1975, Origins of Life 6, pp. 367-376.
10. Bonner, W. A., and Kavasmaneck, P. R.: 1976, J. Org. Chem. 41, pp. 2225-2226.
11. Kavasmaneck, P. R., and Bonner, W. A.: 1977, J. Am. Chem. Soc. 99, pp. 44-50.
12. Furuyama, S., Kimura, H., Sawada, M., and Morimoto, T.: 1978, Chem. Lett. (Japan), pp. 381-382.
13. Kuhn, W., and Braun, E.: 1929, Naturwiss. 17, pp. 227-228.
14. Kuhn, W., and Knopf, E.: 1930, Naturwiss. 18, p. 183.
15. Burchardt, O.: 1974, Angew. Chem. Int. Ed. Engl. 13, pp. 179-185.
16. Kagan, H. B., Balavoine, G., and Moradpour, A.: 1974, J. Molec. Evol. 4, pp. 41-48.
17. Balavoine, G., Moradpour, A., and Kagan, H. B.: 1974, J. Am. Chem. Soc. 96, pp. 5152-5158.
18. Flores, J. J., Bonner, W. A., and Massey, G. A.: 1977, J. Am. Chem. Soc. 99, pp. 3622-3625.
19. Bonner, W. A.: 1973, J. Chromatogr. Sci. 11, pp. 101-104.
20. Blair, N. E., and Bonner, W. A.: 1980, J. Chromatogr. (In press).
21. Norden, B.: 1977, Nature 266, pp. 567-568.
22. Wu, C. S., Ambler, E., Hayward, R. W., Hoppes, D. D., and Hudson, R. P.: 1957, Phys. Rev. 105, pp. 1413-1415.
23. Lee, T. D., and Yang, C. N.: 1956, Phys. Rev. 104, pp. 254-257.
24. Vester, F.: 1957, Seminar at Yale University, Feb. 7.
25. Ulbricht, T. L. V.: 1959, Quart. Rev. 13, pp. 48-60.
26. Goldhaber, M., Grodzins, L., and Sunyar, A. W.: 1957, Phys. Rev. 106, pp. 826-828.
27. Vester, F., Ulbricht, T. L. V., and Krauch, H.: 1959, Naturwiss, 46, p. 68.
28. Ulbricht, T. L. V., and Vester, F.: 1962, Tetrahedron 18, pp. 629-637.

29. Garay, A. S.: 1968, Nature 219, pp. 338-340.
30. Bonner, W. A.: 1974, J. Molec. Evol. 4, pp. 23-29.
31. Bonner, W. A., and Flores, J. J.: 1975, Origins of Life 6, pp. 187-194.
32. Bonner, W. A., Lemmon, R. M., and Noyes, H. P.: 1978, J. Org. Chem. 43, pp. 522-524.
33. Bernstein, W. J., Lemmon, R. M., and Calvin, M.: 1972, in "Molecular Evolution, Prebiological and Biological", D. L. Rolfing and A. I. Oparin, eds., Plenum, New York, pp. 151-155.
34. Darge, W., Laczko, I., and Thiemann, W.: 1976, Nature 261, pp. 522-524.
35. Bonner, W. A., Blair, N. E., and Flores, J. J.: 1979, Nature 281, pp. 150-151.
36. Blair, N. E., and Bonner, W. A.: 1980, J. Molec. Evol. 15, pp. 21-28.
37. Bonner, W. A., Van Dort, M. A., and Yearian, M. R.: 1975, Nature 258, pp. 419-421.
38. Bonner, W. A., Van Dort, M. A., Yearian, M. R., Zeman, H. D., and Li, G. C.: 1976/77, Israel J. Chem. 15, pp. 89-95.
39. Keszthelyi, L.: 1976, Nature 264, p. 197.
40. Walker, D. C.: 1976, Origins of Life 7, pp. 383-387.
41. Bonner, W. A., Van Dort, M. A., and Yearian, M. R.: 1976, Nature 264, p. 198.
42. Hodge, L. A., Dunning, F. B., Walters, G. K., White, R. H., and Schroepfer Jr., G. J.: 1979, Nature 280, pp. 250-252.
43. Noyes, H. P., and Bonner, W. A.: 1975, J. Molec. Evol. 6, pp. 91-98.
44. Noyes, H. P., Bonner, W. A., and Tomlin, J. A.: 1977, Origins of Life 8, pp. 21-23.
45. Bonner, W. A., Van Dort, M. A., and Yearian, M. R.: 1978, Nature 271, p. 186.
46. Bonner, W. A., Van Dort, M. A., and Yearian, M. R.: 1979, Nature 280, p. 252.
47. Bonner, W. A., and Lemmon, R. M.: 1978, J. Molec. Evol. 11, pp. 95-99.
48. Bonner, W. A., and Lemmon, R. M.: 1978, Bioorg. Chem. 7, pp. 175-187.
49. Pollock, G. E., Cheng, C. N., Cronin, S. E., and Kvenvolden, K. A.: 1975, Geochim. Cosmochim. Acta 39, pp. 1571-1573.
50. Bonner, W. A., Blair, N. E., and Lemmon, R. M.: 1979, J. Am. Chem. Soc. 101, p. 1049.
51. Bonner, W. A., Blair, N. E., Lemmon, R. M., Flores, J. J., and Pollock, G. E.: 1979, Geochim. Cosmochim. Acta 43, pp. 1841-1846.
52. Bonner, W. A., Blair, N. E., and Lemmon, R. M.: 1979, Origins of Life 9, pp. 279-290.
53. Wald, G.: 1957, Ann. N. Y. Acad. Sci. 69, pp. 352-368.
54. Blair, N. E., and Bonner, W. A.: 1980, Origins of Life, (In press).

55. Matsuura, K., Inoue, S., and Tsuruta, T.: 1965, Makromolec. Chem. 85, pp. 284-286.
56. Tsuruta, T., Inoue, S., and Matsuura, K.: 1967, Biopolymers 5, pp. 313-319.
57. Inoue, S., Matsuura, K., and Tsuruta, T.: 1968, J. Polymer Sci., Part C, 23, pp. 721-732.
58. Blair, N. E., Dirbas, F. M., and Bonner, W. A.: 1980, Tetrahedran, (In press).
59. Fasman, G. D.: 1962, in "Polyamino Acids, Polypeptides and Proteins", M. A. Stahman, ed., Univ. of Wisconsin Press, Madison, Wisc., pp. 221-224.
60. Blout, E. R.: 1962, in "Polyamino Acids, Polypeptides and Proteins", M. A. Stahman, ed., Univ. of Wisconsin Press, Madison, Wisc., pp. 275-279.
61. Blout, E. R., Doty, P., and Yang, J. T.: 1957, J. Am. Chem. Soc. 79, pp. 749-750.