

Amplification of enantiomeric concentrations under credible prebiotic conditions

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Solutions with as little as 1% enantiomeric excess (ee) of D- or L-phenylalanine are amplified to 90% ee (a 95/5 ratio) by two successive evaporations to precipitate the racemate. Such a process on the prebiotic earth could lead to a mechanism by which meteoritic chiral α -alkyl amino acids could form solutions with high ee values that were needed for the beginning of biology.

amino acids | crystallization | transamination

One of the most interesting questions about the prebiotic world is the origin of homochirality, the fact that biological molecules are generally found in only one enantiomeric form. Various theories about the origination of homochirality by terrestrial processes have been advanced, but a striking finding is that some compounds are delivered to the earth by carbonaceous chondritic meteorites with α -alkyl amino acids that have enantiomeric excesses (ee's). Normal amino acids, also found in such meteoritic deposits, are racemic and racemizable by ionization of their α -proton. The α -alkylated amino acids cannot racemize, and are found in from 2.8% to 15% ee, normally as the S enantiomers (1).

These α -alkyl amino acids could be the seeds of terrestrial homochirality if two conditions are met: (i) they must be able to transfer their chirality to biomolecules such as simple amino acids and sugars; and (ii) there must be a mechanism for amplification of the modest chiralities produced up to the very large enantiomeric excesses seen in living systems.

We have shown that R α -methylvaline can transaminate α -keto acids to form amino acids with some chirality transfer. With 100% ee, we produced L-alanine with only 3% ee, and L-phenylalanine with only 9.5% ee (2, 3). Some microorganisms use both the D and L forms of amino acids for different purposes, so the chiral sense is not a problem. However, because S α -methylvaline is found in only 2.8% ee in the Murchison meteorite, only a tiny ee of amino acids could be produced by our transamination process.

Pizzarello (1) has reported that 100% S α -ethylvaline can catalyze the aldol self condensation of glycolaldehyde to form L-erythrose in 4.8% ee, and D-threose in 10.6% ee. Because S α -ethylvaline is found in the Murchison meteorite in only 15.2% ee, again the process will produce these simple sugars in very low ee's. Amplification is needed.

Soai *et al.* (4) have reported a striking process of chiral amplification by using compounds that catalyze their own formation with chiral retention. Furthermore, the S form of the catalyst binds the R form selectively into an inactive heterodimer; starting with a small ee of the R form, only that small amount of residual R form is left to catalyze its own production. In this way, a small ee can selectively catalyze reproduction to amplify the ee of the material. However, no version of this kind of process has yet been proposed or demonstrated that could occur under credible prebiotic conditions.

It occurred to us that the selective formation of an R/S heterodimer could result in enantiomeric amplification of a concentration if there were simply phase separation, requiring no catalysis. Many compounds, including amino acids and tartaric acids, for instance, are less soluble as their racemates than as the pure enantiomers (5). Thus, it seemed likely that, if a solution with a small ee of an amino acid component were allowed to evaporate,

Table 1. Enantiomeric concentration amplification of phenylalanine after two crystallizations from water

Component	Initial ee, %	Final ee, %
D	10	90.0 \pm 3.7
	5	91.7 \pm 1.5
	1	87.2 \pm 2.0
L	10	88.3 \pm 1.1
	5	88.6 \pm 0.9
	1	90.9 \pm 0.3

there would be selective precipitation of the racemate crystals, leading to amplification of the ee concentration in solution.

Results

We have tested that idea with phenylalanine, the amino acid we formed in modest ee by transamination from a meteoritic amino acid, and the results are striking (Table 1). When we started with a water solution of \approx 500 mg of phenylalanine with a 1% excess of the L component and allowed it to evaporate slowly until the bulk of the material ($>$ 400 mg) had crystallized from solution, we found that the crystals were racemic and that the solution now contained a few mg of phenylalanine with a 40% ee of the L component, a 70/30 ratio of L to D. When we started with 500 mg of such a 40% L ee in water solution and allowed it to concentrate, the racemate again separated, and the solution now had \approx 100 mg that had a 90% ee in the L enantiomer, a 95/5 ratio of L to D. Similar results were found with D-phenylalanine.

Discussion

The ee increase in solution from 1% to 90% by two simple evaporations solves the concentration amplification problem. We are examining further such processes with other amino acids, including some of those found with enantiomeric excesses in meteoritic deposits.

We propose that such a process could occur and may have occurred under prebiotic conditions. As a water solution of one of the meteoritic amino acids or of one of the products from it dried, there would be an increased enantiomeric concentration in the solution. If that solution ran off from the solid racemate, or indeed if subsequent chemistry simply occurred in the solution, the modest ee's from the meteoritic components or their subsequent products could be amplified in solution to start the processes leading to our observed homochiralities in life today (Klussman *et al.* have reported some relevant studies after our work was completed; ref. 6).

Materials and Methods

D-phenylalanine, L-phenylalanine, and DL-phenylalanine were obtained from Aldrich (St. Louis, MO). The enantiome-

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Abbreviation: ee, enantiomeric excess.

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ric compositions of the products were determined by hplc chromatography of diastereomers prepared from the phenylalanine, *o*-phthaldehyde, and *N*-acetyl L-cysteine, as we have described (2). The data in Table 1 reflect duplicate runs in which the product ee's were subjected to duplicate analyses.

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Note Added in Proof. We have now determined that S α -methylvaline, the amino acid that we used previously (2, 3), can be amplified from its 2.8% ee, as found in meteorites, by a process similar to that described in our paper.

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