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SPONTANEOUS ONSET OF HOMOCHIRALITY IN OLIGOPEPTIDE CHAINS GENERATED IN THE POLYMERIZATION OF N-CARBOXYANHYDRIDE AMINO ACIDS IN WATER

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Abstract. This article is concerned with the spontaneous onset of homochiral oligopeptide sequences. We will show that the polymerization of hydrophobic NCA (N-carboxyanhydride = cyclic anhydride)-amino acid racemates (i.e. tryptophane, leucine and isoleucine) in aqueous solution yields oligopeptides that are characterized by a high degree of homochiral sequences. Furthermore we will show that quartz enhances efficiently the mole fraction of oligopeptides with homochiral sequence by selectively adsorbing the more stereoregular oligopeptides from an aqueous solution of oligo-D,L-leucine. We find in particular that the mole fraction of the adsorbed homochiral 7mers is 17 times larger than the mole fraction calculated for a theoretical, random process. Experimentally the stereoisomer distribution for each oligomer length can be determined by the use of enantio-labeling and LC-MS (Liquid Chromatography-Mass Spectrometry). Furthermore, if we start the polymerization with an enantiomeric excess (e.e.) of 20% of L-leucine (L-amino acid : D-amino acid = 6 : 4, molar ratio) we observe a chiral amplification in the enantiomeric homochiral oligopeptides. We think that such processes are relevant to the chemical evolution of single handedness.

Keywords: chiral amplification, NCA-amino acid, oligopeptides with homochiral sequences, quartz, selective adsorption

1. Introduction

Despite the virtual simplicity, the polymerization of N-carboxyanhydrides (NCA) (for a review see Kricheldorf, 1990) presents a few aspects which have not been clarified to date (Kricheldorf, 1990; Karnup *et al.*, 1996). One of these concerns the polymerization of NCA-amino acid racemates in aqueous solution. Another aspect concerns the polymerization of chiral nonracemic NCA-amino acids in water with respect to chiral amplification of oligopeptides. Both aspects will be discussed in this study.

NCA-amino acid racemates polymerize slower than each of the pure NCA enantiomers does (Bartlett and Jones, 1957; Karnup *et al.*, 1996; Kricheldorf, 1990; Imanishi, 1981). A few hypotheses have been proposed to explain this difference and in particular it has been suggested that the higher rates of the polymerization of the pure enantiomers may correspond to a stereoselective or even stereospecific mechanism leading to homochiral sequences (Kricheldorf, 1990). Kinetic and

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NMR investigations appear to be consistent with a stereoselective mechanism for some of the amino acids used, and it was reported that the average length of the stereoblocks obtained in the racemic polymerization never exceeded 4 monomer units (Bartlett and Jones, 1957; Kricheldorf and Hull, 1979; Kricheldorf and Hull, 1982; Karnup *et al.*, 1996). However, it has not been possible to substantiate these kinetic data by determining directly the stereoisomer distribution of oligomers nor to quantitate the amount of homochiral sequence formed. A few years ago we started an investigation of the homochirality in oligopeptide chains obtained in the racemic NCA-amino acid polymerization in aqueous solution. Therefore we developed a technique to quantitate these homochiral sequences. In particular isotope labeling (deuteration) of one enantiomeric NCA-monomer in combination with liquid chromatography mass spectrometry (LC-MS) analysis leads to stereoisomeric subgroups (D_pL_q) of the same length ($n = p + q$), but having different masses. If the L-enantiomer is for example five-times deuterated, then each L-enantiomer inserted instead of a D-enantiomer leads to a 5 Da mass-increase in the resulting amino acid-oligomer. This permits a discrimination of D_pL_q stereoisomeric subgroups by their masses, since for $n = p+q$, D_pL_q-subgroups of length n have now different masses ($m_{\text{allD}} + 5q$) (where m_{allD} is the mass of the homochiral D-form of the amino acid-oligomer), and masses of different D_pL_q-groups are separated by at least 5 Da, maximally $5n$ Da. If the peaks in the selected ion monitoring (SIM)-chromatograms of the corresponding masses are integrated and compared to each other, the stereoisomer distribution (mole fraction) of D_pL_q-subgroups for each oligomer with length n can be determined, provided that the ionization sensitivity and the mass detection efficiency of the stereoisomers is similar under the conditions used. A typical SIM-chromatogram, including the mass spectra for each stereoisomeric subgroup, is shown in Figure 1. This kind of enantiolabeling has recently been used for the quantification of the stereoisomers formed in the polymerization of activated amino acid amphiphiles in two-dimensional crystalline self-assemblies at the air-water interface (Zepik *et al.*, 2002; Weissbuch *et al.*, 2002).

The first part of this article summarizes the results recently published by our group on the spontaneous formation of oligopeptides with homochiral sequences in the polymerization of NCA-amino acid racemates in water (Blocher *et al.*, 2001; Hitz *et al.*, 2001; Hitz and Luisi, 2002), while the second part will present some results on the polymerization of chiral nonracemic NCA-amino acids with respect to chiral amplification of oligopeptides (Hitz and Luisi, in press). For experimental details we refer the reader to our published papers (Blocher *et al.*, 2001; Hitz *et al.*, 2001; Hitz and Luisi, 2002; Hitz and Luisi, in press).

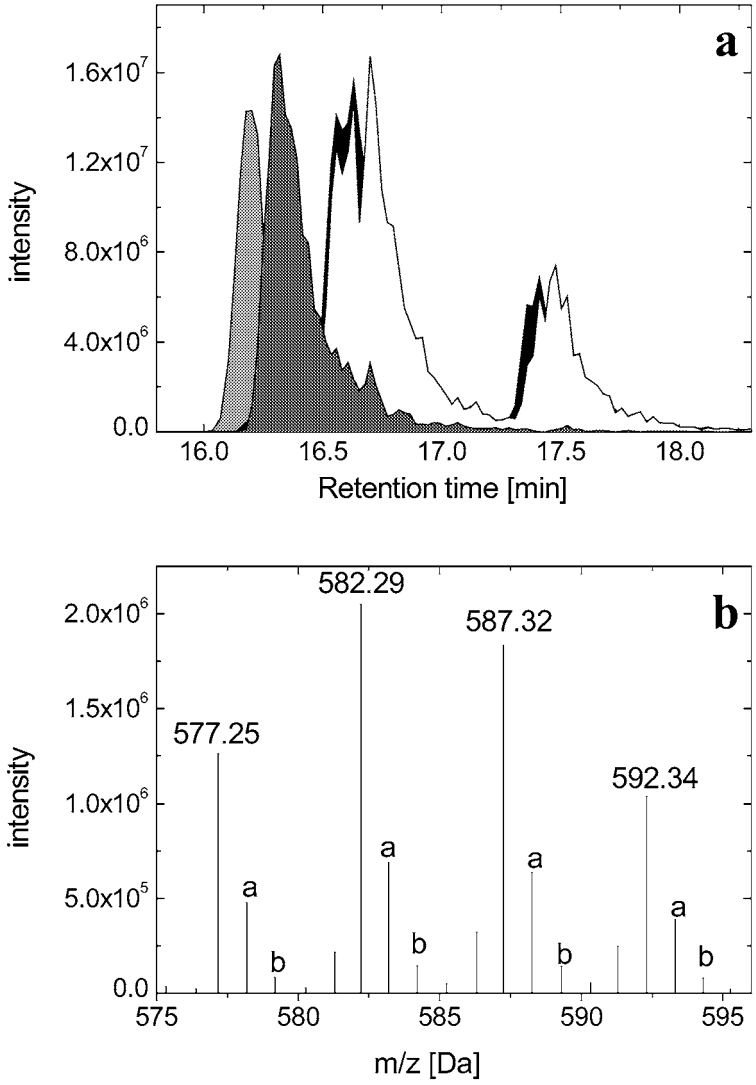
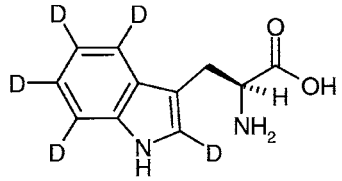
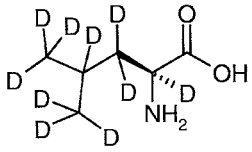


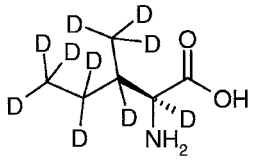
Figure 1. MS SIM chromatograms are shown for the stereoisomeric subgroups of oligo-Trp for $n = 3$ (trimers) in (a). The stereoisomeric subgroups consist of [L-Trp(d_5)])$_3$(L$_3$: light gray), [D-Trp]$_3$ (D$_3$: gray), [D-Trp][L-Trp(d$_5$)]$_2$ (DL$_2$: black) and [D-Trp]$_2$[L-Trp(d_5)] (D$_2$L: white). The corresponding m/z-values (ESI$^+$, z = 1: positively charged N-term of each peptide) and their intensities are shown in (b) for L$_3$: 592.34 Da, D$_3$: 577.25 Da, DL$_2$: 587.32 Da and D$_2$L: 582.29 Da. The letters a and b represent the isotopes of each stereoisomeric subgroup (a: $(m + 1)/z$ Da, b: $(m + 2)/z$ Da) (Blocher *et al.*, 2001).



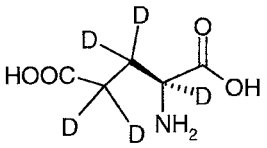
L-Trp(d_5)



L-Leu(d_{10})



L-Ile(d_{10})



L-Glu(d_5)

Scheme 1. Structures of the deuterated L-amino acids used in this study.

2. On the Polymerization with Hydrophobic NCA-Amino Acid Racemates

We have addressed the question, whether these polymerizations show a preferential formation of oligopeptides with homochiral sequences. In particular, we wanted to clarify whether the experimentally determined mole fractions of the homochiral oligopeptide sequences are higher than the mole fractions calculated for a theoretical, random polymerization process (binomial distribution). For this reason, racemic NCA-Trp, NCA-Leu and racemic NCA-Ile polymerizations have been performed in buffered aqueous solution (Ehler and Orgel, 1976). The L-isomer was in each case deuterated (Scheme 1, L-Trp(d_5), L-Leu(d_{10}), L-Ile(d_{10})).

Results are shown in Figure 2 for the longest detectable oligopeptides. It is apparent that the produced homochiral oligopeptides (L_n and D_n) are over-represented compared to the statistically expected distributions (i.e., 8.3-fold for the 7mers of Trp, 4-fold for the 6mers of Leu and 2.5-fold for the 5mers of Ile). It could therefore be concluded that the polymerization of these three hydrophobic NCA-amino acid racemates in aqueous solution is stereoselective. Here it is important to note that also the polymerization with mixtures of different hydrophobic NCA-amino acid racemates showed the preferential formation of co-oligopeptides with homochiral sequences (Hitz *et al.*, 2001).

Up to date, we have not studied in detail the mechanisms of these stereoselective polymerizations. Preliminary results appear rather interesting (Hitz *et al.*, 2001). The determination of the mole fractions of the different stereoisomeric subgroups of the oligopeptides as a function of time indicates for example higher order in the polymerization process. The time course of the 2mers of Leu, that are formed in the polymerization of the Leu-racemate, is shown in Figure 3. It can be seen that

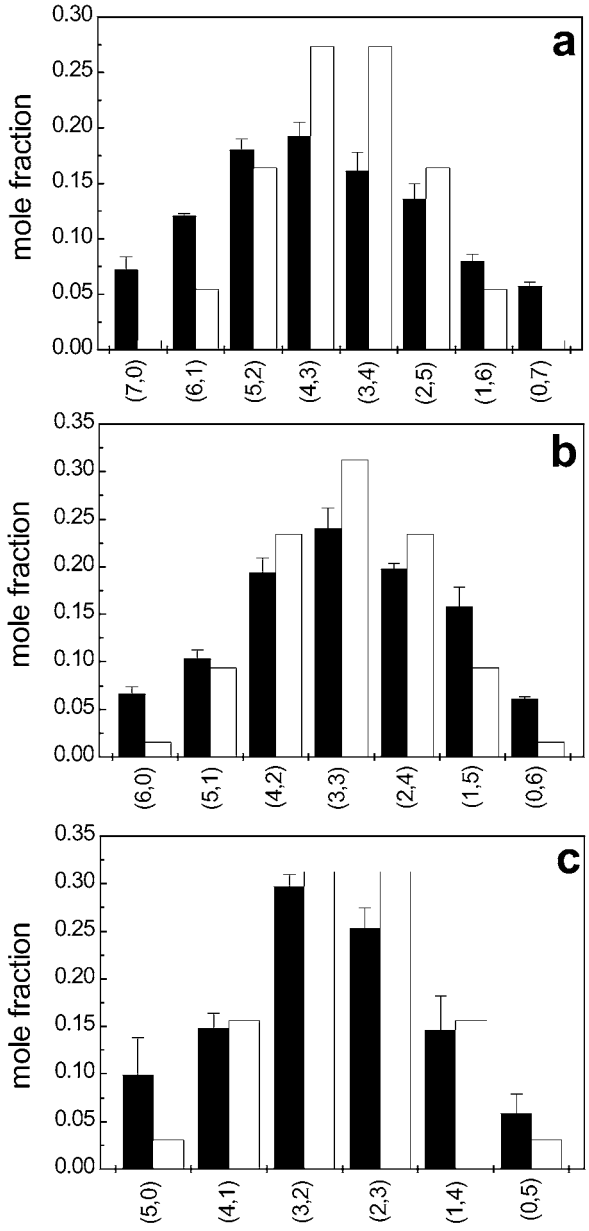


Figure 2. Mole fractions of the stereoisomeric subgroups $[D_p,L_q]$ of the oligo-amino acid n-mers obtained in the polymerization of (a) the Trp-racemate ($n = 7$), (b) the Leu-racemate ($n = 6$) and (c) the Ile-racemate ($n = 5$). The black columns correspond to the experimental determined mole fractions and are mean values of three measurements. The white columns correspond to the theoretical mole fractions assuming a random polymerization process. Concerning the description of the X-axis note that for example $[5(p),2(q)]$ stands for the stereoisomeric subgroup D_5L_2. The far-left columns correspond to the homochiral D_n-mer and the far-right columns to the homochiral L_n-mer (Blocher *et al.*, 2001; Hitz *et al.*, 2001).

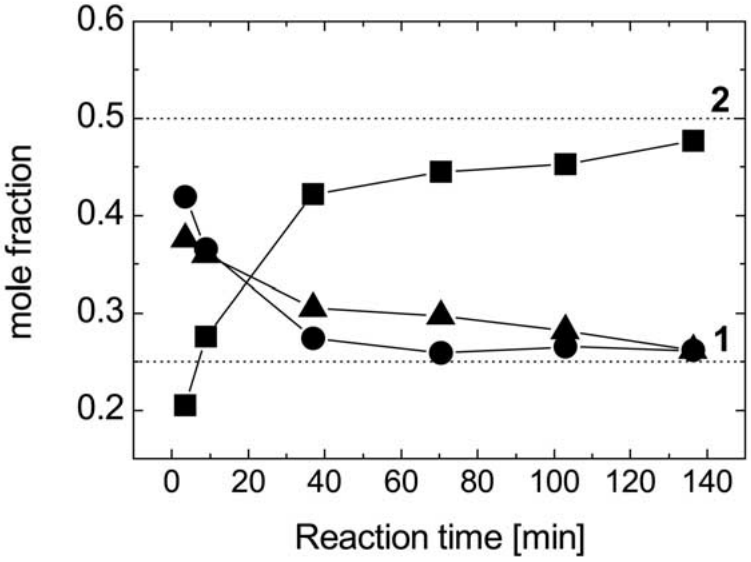


Figure 3. Racemic polymerization of NCA-D-Leu/NCA-L-Leu(d_{10}). Time progress of the mole fractions of the homochiral (● and ▲: L_2 and D_2) and heterochiral (■: DL) stereoisomers of Leu for $n = 2$. The dotted lines represent the theoretical, random distributions for the corresponding stereoisomeric subgroups (1: L_2 or D_2, 2: DL).

the mole fractions of the homochiral 2mers ([D-Leu]$_2$ and [L-Leu(d_{10})]$_2$) decrease with time whereas the mole fraction of the heterochiral 2mers increases. In other words, the homochiral dimers react faster than the heterochiral ones. Similar patterns are also observed for the 3mers and 4mers of oligo-Leu (data not shown). This behavior can be explained by a Markov process of second or higher order, in which namely at least the penultimate amino acid residue in the growing oligopeptide chain influences the next elongation step (Hitz *et al.*, 2001). Alternatively such a kinetic pattern can also be explained by amino acid cluster formation in aqueous solution, respectively at the air-water interface prior to the polymerization (i.e., L-amino acid clusters respectively D-amino acid clusters, Cooks *et al.*, 2001; Koch *et al.*, 2002; Zepik *et al.*, 2002; Weissbuch *et al.*, 2002). This possibility has to be investigated further.

3. On the Polymerization with Racemic NCA-Glutamic Acid (NCA-Glu)

We have also addressed the question, whether the polymerization of a negatively charged non-hydrophobic amino acid racemate in buffered aqueous solution also shows a preferential formation of oligopeptides with homochiral sequences. It is in fact interesting to compare the extend of homochirality in this case with the one found in the polymerization of the hydrophobic NCA-amino acid racemates.

Therefore we have investigated the polymerization of racemic NCA-Glu in aqueous solution (Hitz and Luisi, 2002; Hill and Orgel, 1996). The L-isomer was again deuterated (Scheme 1).

In the polymerization of racemic NCA-Glu a mixture of oligopeptides up to eight units is formed ($n = 2$–8). The extend of homochirality in the racemic NCA-Glu polymerization is shown in Figures 4a and 4b. It can be seen that the mole fractions of the shorter oligo-Glu are in a first approximation statistical with a slight under-representation of the homochiral oligo-Glu in the 3mers and 4mers. From the 6mer on, there is a clear trend towards enhanced formation of oligopeptides with homochiral sequence. The mole fraction of the homochiral oligo-Glu 8mers is approximately 3.3-fold higher than the expected mole fraction in random polymerization process (Hitz and Luisi, 2002). It can therefore be concluded that the polymerization of racemic NCA-Glu in aqueous solution is moderately stereoselective.

4. On the Comparison of Hydrophobic and Negatively Charged NCA-Amino Acid Racemates

The excess of the mole fractions of the oligopeptides with homochiral sequence (mole fractions $[L_n + D_n]_{exp}$/mole fractions $[L_n + D_n]_{theoretical}$) formed in the polymerization of the hydrophobic NCA-Trp, NCA-Leu and NCA-Ile racemates and of the negatively charged NCA-Glu racemate is shown in Figure 5. It can be seen that there is a clear trend towards increasing excess with increasing chain length. This effect is stronger for the hydrophobic amino acid racemates than for the negatively charged Glu-racemate, indicating a stronger stereoselectivity in the polymerization of the hydrophobic NCA-amino acid racemates in aqueous solution. The hydrophobic amino acids and/or the short hydrophobic oligopeptides may interact more strongly in aqueous solution than the negatively charged Glu-monomers and/or the short Glu-oligopeptides do.

5. On the Polymerization with Racemic NCA-Leu in Presence of Racemic Quartz in Aqueous Solution

Because the longer oligopeptides with homochiral sequence are usually obtained in very low yields in the polymerization of NCA-amino acid racemates in aqueous solution, it is of general interest to find ways to concentrate such homochiral longer chains, possibly under plausible prebiotic conditions. To this aim we were prompted to the investigation of the possible role of quartz in the enhancement of homochirality in oligopeptide chains by two lines of observations. The first one is based on the 'adsorbed template' model, in which minerals serve as adsorbents for organic molecules (for example amino acids, oligopeptides and sugars) and/or as

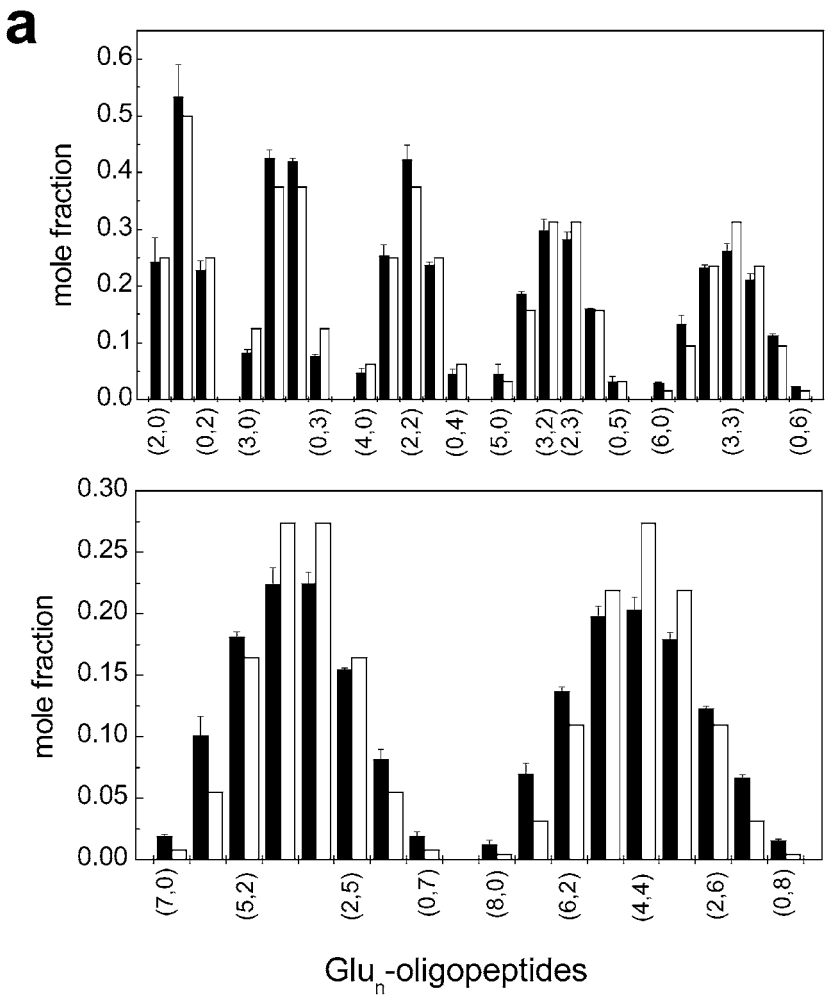


Figure 4a. Mole fractions for $[D_pL_q]$-stereoisomer groups of the oligo-Glu-n-mers are shown for the polymerization of the NCA-D-Glu/NCA-L-Glu(d_5) racemate in aqueous solution (80 mM, pH 7.0). For each oligomer length, the SIM-chromatograms for all the D_pL_q stereoisomer subgroup masses were integrated. The total of all SIM-peak areas of a particular n-mer corresponds to 1.0. The black columns correspond to the experimental determined mole fractions and are mean values of three measurements. The white columns correspond to the theoretical mole fractions assuming a random polymerization process. Note that for clarity not all the $[p, q]$-symbols have been included (Hitz and Luisi, 2002).

catalysts for a variety of organic reactions (for example protein synthesis) (Paecht-Horowitz and Eirich, 1970; Lahav *et al.*, 1978; Basiuk *et al.*, 1995; Lahav, 1994; Ferris *et al.*, 1996). The other observation is based on the data discussed above about the polymerization of activated α-amino acid racemates in aqueous solution, that yielded oligopeptides with a significant degree of homochirality (L_n and D_n)

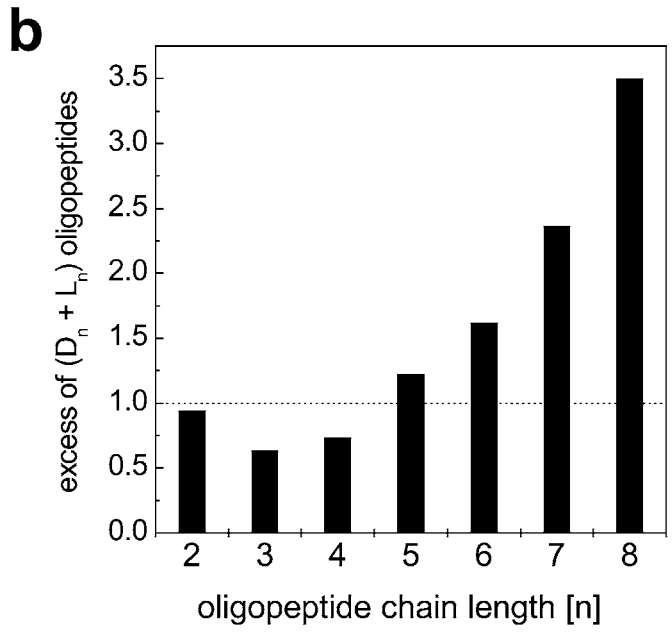


Figure 4b. Excess of the mole fractions of the oligopeptides with homochiral sequence (mole fractions $[L_n + D_n]_{exp}$/mole fractions $[L_n + D_n]_{theoretical}$) formed in the polymerization of racemic NCA-D-Glu/NCA-L-Glu(d_5). An excess equal to unity corresponds to a random polymerization process.

(Blocher *et al.*, 2001; Hitz *et al.*, 2001). In terms of chemical evolution it appeared therefore interesting to check whether the surface properties of minerals in general can enhance the naturally occurring homochirality in oligopeptide chains.

Naturally existing quartz displays enantiomorphic dextrorotatory (d) or levorotatory (l) chiral crystals (de Vries, 1958; Frondel, 1978; Evgenii and Wolfram, 2000). In this study we have been focussing on the polymerization of racemic NCA-Leu in aqueous solution in presence of racemic quartz (d/l-quartz: same amount of d- and l-quartz). Reactions were carried out with racemic mixtures of perdeuterated N-carboxyanhydride (NCA)-L-Leu (= NCA-L-Leu(d_{10})) and non-deuterated NCA-D-Leu (5.7 mM initial monomer concentrations) in presence of d/l-quartz in buffered aqueous solution. The adsorbed products and the products in the supernatant of the quartz system were analyzed by reverse-phase high performance liquid chromatography-mass spectrometry (RP-HPLC-MS, Scheme 2).

In typical experiments we have obtained oligo-Leu with $2 \leq n \leq 7$ in presence of quartz. It can be seen that all of the shorter oligopeptides (up to $n = 4$) are removed by washing with water (Figure 6a). After 20 washing cycles no more product is removed (Figure 6b). However longer oligopeptides remain bound to the surface, and the desorption of such longer oligopeptides ($5 \leq n \leq 7$) becomes possible when the washing is carried out with a 100 mM sodium pyrophosphate

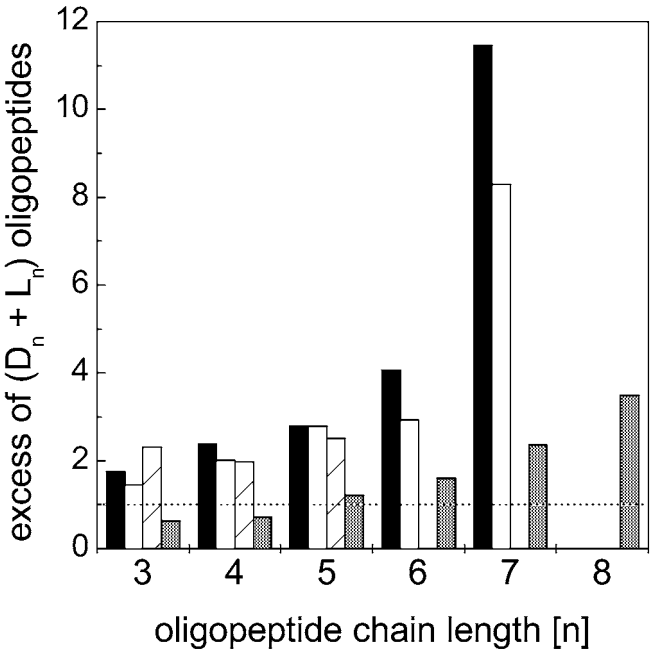
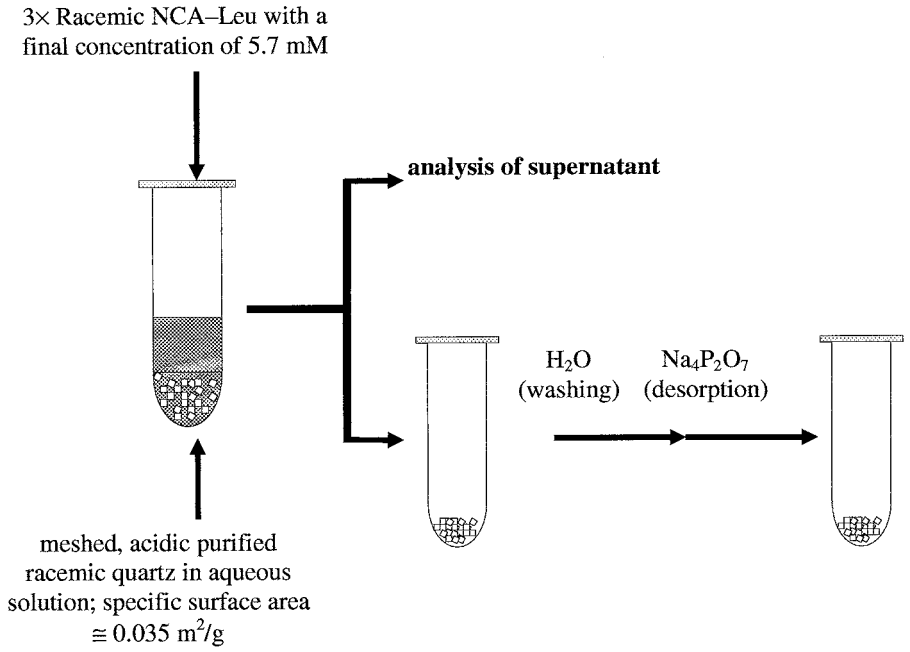


Figure 5. Excesses of mole fractions of oligopeptides with homochiral sequence (mole fractions $[L_n + D_n]_{exp}$/mole fractions $[L_n + D_n]_{theoretical}$) formed in the polymerization of the hydrophobic NCA-Leu (black columns), NCA-Trp (white columns) and NCA-Ile (hatched columns) racemates and of the negatively charged NCA-Glu (gray columns) racemate. An excess equal to unity corresponds to a random polymerization process.

solution, pH 10.4 (Figure 6c). It is assumed that mostly the pyrophosphate-anions are replacing the oligopeptides on the quartz surface (Iler, 1979). Also the reduction of the water activity (water that is bound to the salt ions) by the sodium pyrophosphate salt may further have decreased the oligo-Leu affinity to the surface (Iler, 1979). Here it is important to note that a mixture of acetonitrile/water 2 : 1 (v/v), that would solubilize simply precipitated oligo-Leu that are not bound to the quartz surface, does not desorb any oligopeptides (Blocher *et al.*, 2001; Hitz *et al.*, 2001). It could therefore be concluded that quartz can selectively uptake the longer hydrophobic oligo-D,L-Leu chains ($5 \leq n \leq 7$), that are formed in aqueous solution.

In the following we have analyzed the stereoisomer distribution of the adsorbed oligo-D,L-Leu chains. This is shown in Figure 7a. It can be seen that the experimentally determined mole fractions of the homochiral oligo-Leu are one order of magnitude larger than what is expected according to a theoretical, random polymerization process (i.e. 13-fold for $n = 5$, 15-fold for $n = 6$ and 17-fold for $n = 7$). Figure 7b compares the stereoisomer distribution of the adsorbed 5mers with the stereoisomer distribution of the 5mers left in the supernatant (similar chromatograms are also observed for $n = 6$ and $n = 7$, data not shown). The



Scheme 2.

under-representation of homochiral 5mers in the supernatant and the strong over-representation of the homochiral 5mers adsorbed on quartz are a strong indication for a selective uptake of the homochiral oligo-Leu chains from aqueous solution.

In conclusion we have shown that quartz can selectively adsorb the longer homochiral chains of oligo-D,L-Leu, that are formed in aqueous solution and that the selective removal of shorter peptide chains by water washings permits the enrichment of these longer homochiral oligomers.

6. On the Polymerization of NCA-Leu Starting with a Given Enantiomeric Excess (e.e.)

The problem of understanding chirality in nature is usually debated in terms of two major aspects. One is the breaking of symmetry, the question namely of the possible mechanism(s) that produced an initial enantiomeric excess (e.e.). The other aspect is concerned with the chiral amplification, the question namely of the mechanism(s) that have permitted to increase this initial e.e. up to complete single handedness (single chirality). In order to test a possible chiral amplification of an initial e.e., we performed the NCA-Leu polymerization starting with an e.e. of 20% of the L-enantiomer (L-amino acid : D-amino acid = 6 : 4, molar ratio) in buffered aqueous solution (Hitz and Luisi, in press). In an ideal random system one

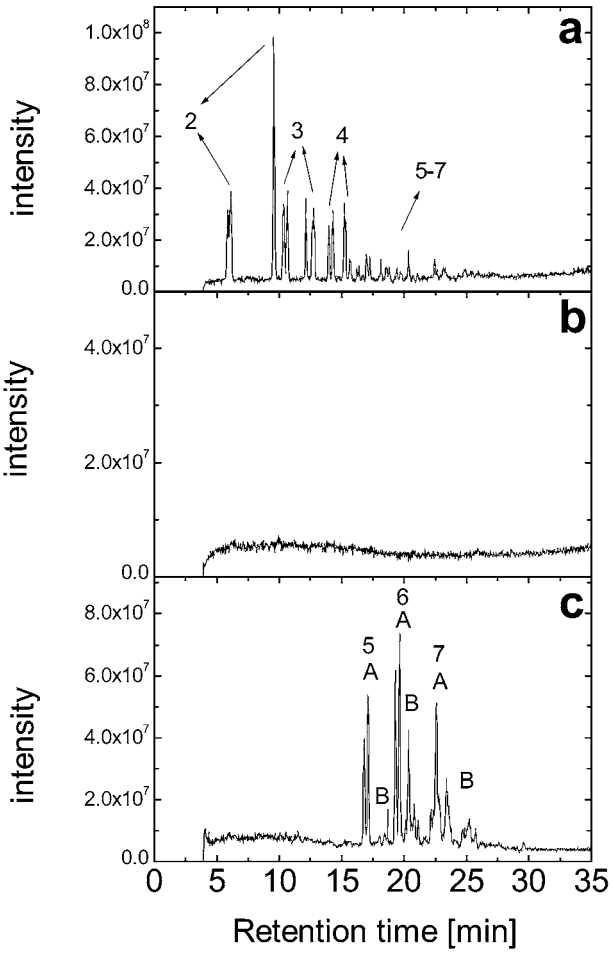


Figure 6. Typical TIC (total ion current)-chromatograms for the washing and desorption of the oligo-Leu products from the d/l-quartz-surface for racemic NCA-Leu polymerizations in presence of d/l-quartz powder (1 : 1, (w : w)). (a) Chromatogram after one washing with millipore water. (b) Chromatogram after 20 times washing with millipore water. (c) Chromatogram after 20 times washing and adding 100 mM sodium pyrophosphate pH 10.4. The numbers indicate the oligopeptide chain length [n]. The letter A stands for the products with homochiral sequence and the letter B for the products with heterochiral sequence of the adsorbed 5 to 7mers (Hitz and Luisi, 2002).

would expect, with increasing chain length n, a trivial statistical amplification of the L_n/D_n-ratio according to

$$\left(\frac{L_n}{D_n}\right)^n = \left(\frac{0.6}{0.4}\right)^n .$$

This is illustrated in Figure 8a. When for example starting with an e.e. ($[(L-D)/(L+D)]\times 100$) of 20% it can be seen, that at the level of the enantiomeric homochiral decamers the e.e. ($[(L_n - D_n)/(L_n + D_n)] \times 100$) has increased up to 96.6%.

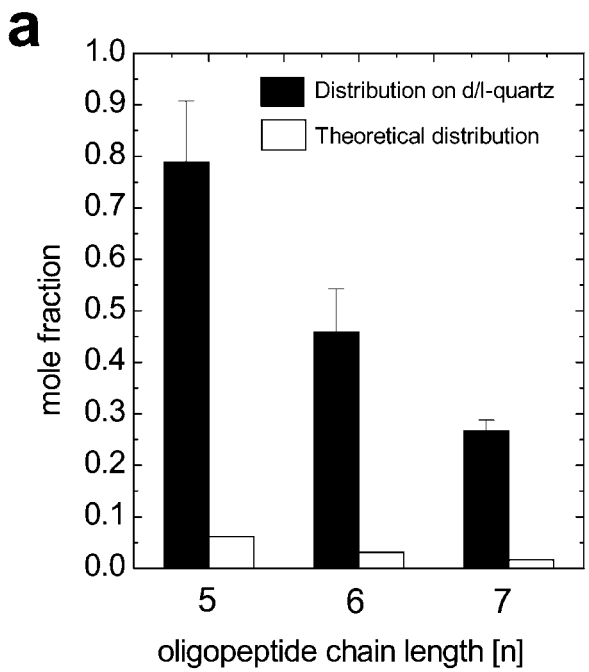


Figure 7a. Comparison of the experimentally determined mole fractions of the oligo-Leu with homochiral sequence adsorbed on quartz with the values calculated on the basis of a random polymerization process (white columns). The black columns correspond to the experimental determined mole fractions and are mean values of three measurements. Standart deviations are given as error bars (Hitz and Luisi, 2002).

In other words the simple binomial propagation would bring about a strong amplification of the initial e.e. Of course in the mean time the homochiral oligomers (L_n and D_n) would become extremely diluted by all the heterochiral diastereomers formed in this random polymerization process. This dilution would increase with increasing chain length (Figure 8b). Bonner (1999) has made such considerations.

Let us now compare the experimental results of the Leu-system with the theoretical, random distribution. It can be seen that the oligopeptides with homochiral sequence are obtained in excess with respect to the theoretical, random distribution (i.e., 2.5-fold for the 5mers of Leu, Figure 9a). It can therefore be concluded that the system behaves stereoselectively. Focussing on the homochiral oligomers of Leu it can be seen that the L_n/D_n-ratio increases strongly with increasing n (Figure 9b). In fact the intensity of the homochiral 5mer of D-Leu becomes negligible small with respect to the intensity of the homochiral 5mer of L-Leu(d_{10}). The whole system behaves therefore stereoselectively including chiral amplification of the obtained enantiomeric oligopeptides with homochiral sequence. It is of interest to quantitatively analyze the statistical and the chemical influence on the observed chiral amplification.

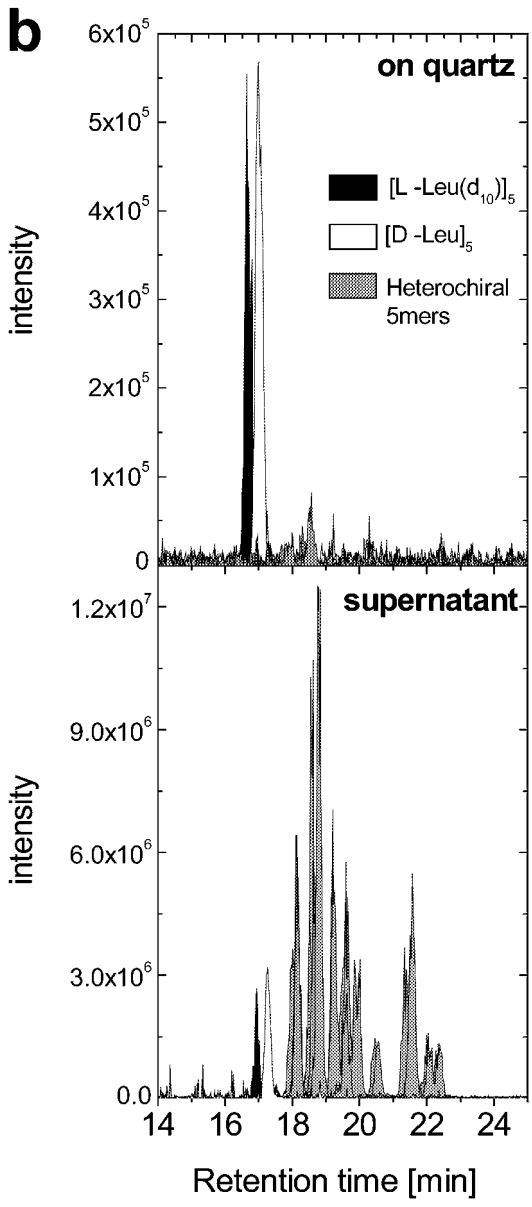


Figure 7b. Stereoisomer distribution of oligo-Leu for $n = 5$ (5mers). (a) Distribution on d/l-quartz. (b) Distribution in the supernatant of d/l-quartz. The corresponding m/z values (pos. ESI, $z = 1$) of the stereoisomeric subgroups are 634.8 Da for [L-Leu(d_{10})]$_5$, 584.43 Da for [D-Leu], 624.74 Da for [D-Leu][L-Leu(d_{10})]$_4$, 614.67 Da for [D-Leu]$_2$[L-Leu(d_{10})]$_3$, 604.59 for [D-Leu]$_3$[L-Leu(d_{10})]$_2$ and 594.51 Da for [D-Leu]$_4$[L-Leu(d_{10})] (Hitz and Luisi, 2002).

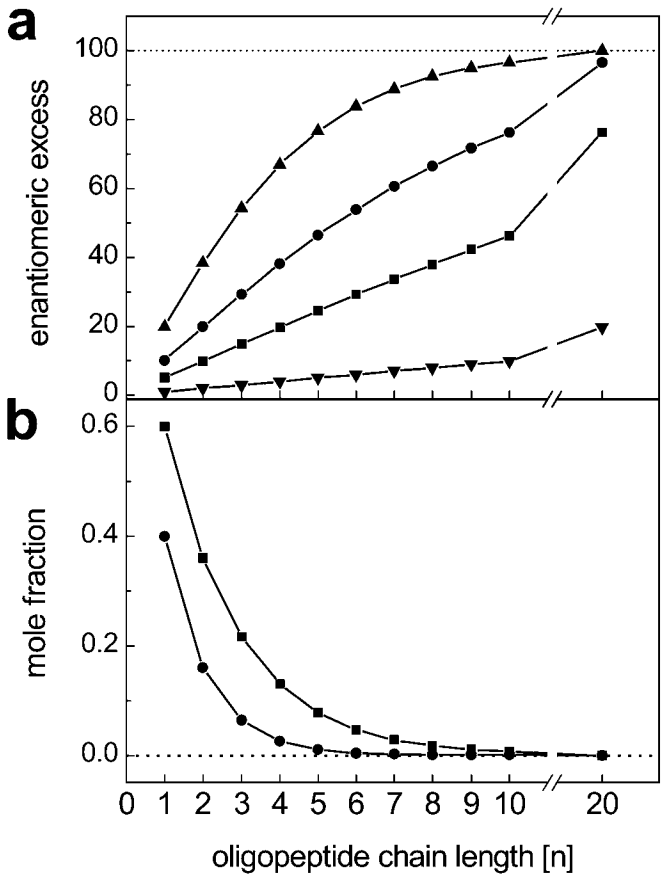


Figure 8. (a) Theoretical enantiomeric excesses ($[(L_n - D_n)/(L_n + D_n)] \times 100$) in the enantiomeric oligomers with homochiral sequence as a function of n, when starting the polymerization with various enantiomeric excesses ($[(L - D)/(L + D)] \times 100$) of the L-enantiomer – (▼): 1%; (■): 5%; (●): 10%; (▲): 20%. (b) Theoretical mole fractions of the enantiomeric oligomers with homochiral sequence as a function of n, when starting the polymerization with an e.e. of 20% of the L-enantiomer – (■): $(\text{L-Leu})_n$ and (●): $(\text{D-Leu})_n$

We think that such processes may be of general importance concerning chiral amplification of oligopeptides and studies with other amino acids are in progress in our group.

7. Conclusion and Outlook

We have established on the level of a direct product analysis that there is in the polymerization of activated amino acid racemates in buffered aqueous solution a natural tendency towards homochirality: the formation of homochiral sequences is preferred to the heterochiral ones either because of kinetic or thermodynamic

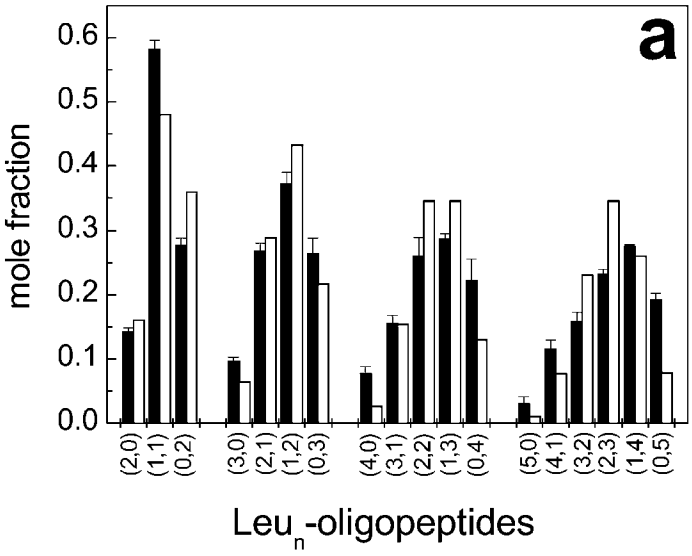


Figure 9a. Mole fractions of the stereoisomeric subgroups $[D_p, L_q]$ of the oligo-Leu n-mers obtained in the polymerization of NCA-Leu with an initial enantiomeric excess of 20% of the L-enantiomer (L-amino acid : D-amino acid = 6 : 4, molar ratio). For each oligomer length, the SIM-chromatograms for all the D_pL_q stereoisomer subgroup masses were integrated. The total of all SIM–peak areas of a particular n-mer corresponds to 1.0. The mole fractions of the D_pL_q stereoisomer subgroups are mean values of three measurements. The far-left columns correspond to the homochiral D_n-mer and the far-right columns to the homochiral L_n-mer. Standard deviations are given as error bars. The white columns correspond to the theoretical mole fractions assuming a random polymerization process (Hitz and Luisi, in press).

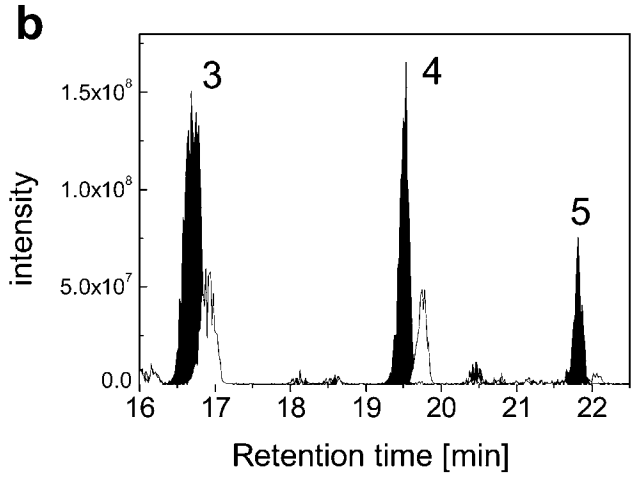


Figure 9b. MS SIM chromatograms for the homochiral tripeptides to pentapeptides (n = 3–5) of oligo–Leu obtained in the polymerization of NCA-Leu with an initial enantiomeric excess of 20% of the L-enantiomer (L-amino acid : D-amino acid = 6 : 4, molar ratio). The black SIM-peaks correspond to [L-Leu(d_{10})]$_n$, the white peaks to [D-Leu]$_n$ (Hitz and Luisi, in press).

reasons. The mechanisms are not yet fully understood and clearly require further investigations. Possible mechanisms are the 'growing chain end control' (Kricheldorf, 1990), 'cluster formation' (Weissbuch *et al.*, 2002; Zepik *et al.*, 2002), the 'helix control' (helical secondary structure, Kricheldorf, 1990) and other 'chain effects' (Kricheldorf, 1990). Furthermore we observed chiral amplification of oligopeptides formed in the polymerization of chiral nonracemic NCA-Leu (Hitz and Luisi, in press). Here it is interesting to see whether this chiral amplification can also be observed with other amino acids than Leu.

The spontaneous formation of oligopeptides with homochiral sequence and the observed chiral amplification might be relevant for the general question of the origin of single chirality on Earth. Our studies are not directly concerned with the breaking of symmetry. However, the fact that homochiral chains can be accumulated on a solid surface may correspond to a novel way to look at the separation of enantiomeric compounds. What immediately comes to mind is the use of chiral surfaces for the separation of enantiomeric longer chains. Preliminary attempts with chiral quartz have not shown enantiomeric discrimination (Hitz and Luisi, 2002), but studies with other chiral surfaces may be more successful.

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