Spoilt for choice: assessing phase behavior models for the evolution of homochirality

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Received (in Cambridge, UK) 19th June 2007, Accepted 6th September 2007
First published as an Advance Article on the web 17th September 2007
DOI: 10.1039/b709314b

The observation of single chirality in biological systems has intrigued scientists for more than one hundred years. Here we discuss several recent experimental studies showing amplification of enantiomeric excess based on amino acid phase behavior. Comparing observations of solution–solid and gas–solid phase transitions highlights the underlying fundamental physical chemistry principles that rationalize the observed enantioenrichment in both cases.

Introduction

A recent article in *Chemistry World*[1] highlighted the work of several groups in developing models to explain ''one of the biggest puzzles in understanding how life began'', the fact of homochirality in biological molecules. While theoretical models for how single chirality might have evolved from a presumably racemic prebiotic environment have been discussed for more than half a century,[2,3] it was only in the last decade of the twentieth century that experimental studies of both physical[4] and chemical[5] behavior in chiral systems attempted to address the question more directly. In the past several years, however, a number of distinct models based on phase behavior have emerged,[6–8] leading *Chemistry World* to remark that scientists are now ''spoilt for choice'' amongst possible explanations for how one enantiomer came to dominate over the other in biological molecules.

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The *Chemistry World* article focused on recent work by our group, reported in *Nature*[7] and *Angew. Chem.*,[9] on amplification of solution *ee* for amino acids under solution–solid equilibrium conditions, and on Cooks and coworkers' studies of the sublimation of solid serine, which appeared in *Chem. Commun*.[8] Most recently, *Chem. Commun*. also published important related work by Feringa[10] that helps to shed further light on the mechanism of enantioenrichment *via* sublimation of amino acids.

This Feature article aims to compare these different observations in the context of the underlying theory for solution–solid and gas–solid phase transitions.† We propose that the intrinsic mechanism for enantioenrichment is identical in the two cases, is unrelated to cluster formation, and is based on fundamental principles first reported in studies dating back to the turn of the 20th century. It might be said that we are ''spoilt for choice'' because we are lucky enough to have access to the pioneering work of the great minds that came before us, including the likes of Gibbs, van't Hoff, Pasteur, and Roozeboom, and in contemporary times, Jacques, Collet,

† The model presented in Ref. 6*a* describes enrichment obtained in the solid phase and hence is outside the scope of the present discussion. See also: Refs. 6*b* and 6*c*.

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and Wilen.[11] We find that the concepts required to rationalize these observations of asymmetric amplification in organic molecules have been well understood for almost as long as the question of homochirality has been posed.

Solution–solid equilibrium: time is on our side

The description of Pasteur meticulously separating mirror-image L and D crystals of sodium ammonium tartrate using a magnifying glass and a needle is many a scientist's first introduction to the fascinating subject of chirality. It is lucky that Pasteur was working with crystals from the racemate of this double salt rather than with those from the neutral tartaric acid. In that case, he would have observed only one type of crystal, one that is formed from a network of bonds between L and D molecules. In fact, the majority of known enantiomeric molecules preferentially form such heterochiral L–D crystals, known as *racemic compounds*, rather than *conglomerates*, compounds that form when homochiral interactions are stronger than heterochiral interactions, that is, when the thermodynamic preference is for L and D to crystallize separately. These latter account for only *ca.* 15% of known molecules, including only two out of the twenty proteinogenic amino acids.[11]

Does the particular form that a molecule exhibits as a crystal impact the issue of the emergence of homochirality based on phase transitions? To answer that question, let's consider what happens when we partially dissolve a racemic compound (such as serine), or a conglomerate (such as threonine), in water or solvent, starting in each case with unequal amounts of the two enantiomers and allowing the system to come to solution–solid equilibrium, as shown in Fig. 1. For a conglomerate, a saturated solution in equilibrium with both D and L solid phases exhibits roughly *double* the solubility of a system containing either the D or the L solid alone. This is because each solution phase enantiomer establishes its own solution–solid equilibrium, ignorant of the presence of the other. This is a property known as ''Meyerhoffer's double solubility rule''[12] that has been recognized for more than a century as a characteristic of chiral compounds forming conglomerates. Even if the D and L solids differ in amount, the solution phase will contain identical concentrations of each. Therefore at equilibrium a conglomerate always exhibits a solution *ee* of 0% (eutectic point), as shown in Fig. 1a. This is the case for threonine.

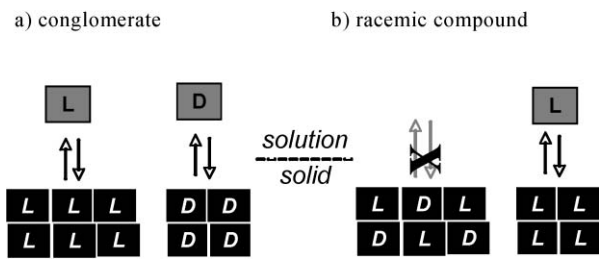

Fig. 1 Depiction of solid–solution equilibrium for the case of a) a conglomerate such as threonine, giving $ee^{eut} = 0$; and b) a racemic compound with $ee^{eut} > 99\%$ ee, such as serine. Black squares denote solid phase, grey squares denote solution phase.

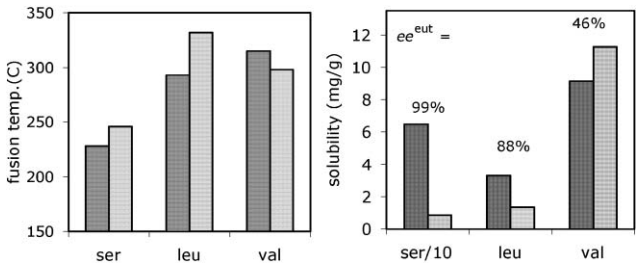

Fig. 2 Comparison of fusion temperatures (left) and solubilities (right) for L (dark bars) and DL (light bars) crystals of the amino acids serine, leucine, and valine. Eutectic *ee* values for these amino acids measured in water are taken from Ref. 7.

For a racemic compound as in Fig. 1b, the situation is different. When unequal amounts of the two enantiomers are present in the solid phase, all of the minor enantiomer will be incorporated into the DL solid, with the left-over major enantiomer forming its own enantiopure crystal from the excess. The minor enantiomer can be present in solution only *via* dissolution from the solid racemic compound, at a concentration dictated entirely by the solubility of the DL compound. The solution *ee* at equilibrium is thus controlled by the relative solubility of the racemic and enantiopure crystals, and the eutectic *ee* may fall anywhere between 0 and 100% *ee*. For serine, it happens that the solution *ee* at equilibrium is $> 99\%$ *ee* for any value of overall serine *ee*, as depicted in Fig. 1b. The solubility of the racemic crystal of serine is an order of magnitude lower than that of the pure enantiomer.

For any molecule that crystallizes as a racemic compound, heterochiral D–L interactions in the solid state must be stronger than the corresponding homochiral interactions, while clearly for conglomerates the homochiral interactions L–L or D–D are stronger than heterochiral L–D interactions. Solubilization represents a way of assessing intracrystalline forces. As shown in Fig. 2 on the right, amino acids exhibiting high eutectic *ee* values, such as serine and leucine, exhibit lower DL solubility compared to L. Fusion temperature is another property that may be used as a measure of intracrystalline force. Fig. 2 (left) shows that amino acids with high eutectics have higher melting points for DL compared to L, while amino acids with lower eutectics can exhibit the opposite behavior. In general for racemic compounds, the stronger the intercrystalline force, the higher the melting point‡, the lower the solubility, and the higher the eutectic *ee*.

Differentiation between solid and solution composition of enantiomers based on phase properties provided us with the basis of our recent model for the emergence of homochirality in solution–solid systems of amino acids.[7] High enantiopurity might be obtained in aqueous pools of amino acids even given only a small initial imbalance of amino acid enantiomers, provided that the racemic compound is much less soluble than the enantiopure compound (thus giving it a high eutectic *ee* value). Pools containing stable, highly enantioenriched amino acids could be formed, providing catalysts or building blocks

‡ We add a note of caution, however, concerning the extrapolation of solid–solution behavior from solid–liquid (melting) behavior, as discussed later in this article.

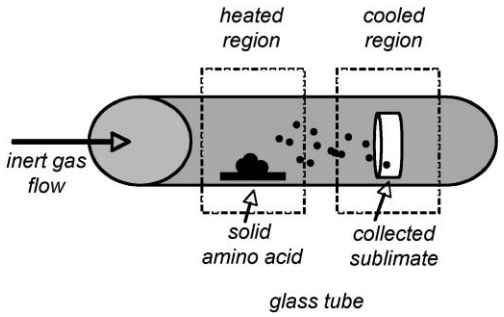

Fig. 3 Schematic of sublimation experiment as carried out in Refs. 8 and 10.

for constructing even more complex enantiopure molecules, even if it takes eons for the appropriate mix of molecules to accumulate in the pool.

Simply sublime

In the context of these phase behavior concepts, we now consider the results of Cooks and of Feringa in sublimation experiments with amino acids. Here we are dealing with gas–solid rather than solution–solid phase transfer. The experiment is described schematically in Fig. 3. Measuring the *ee* of the collected sublimate in this experiment may be considered analogous to measuring the solution *ee* in our experiments as shown in Fig. 1, although it is important to note that gas–solid equilibrium will generally not be attained in an open system as depicted in Fig. 3.

Based on the arguments involving intracrystalline forces discussed above, we may propose that for racemic compounds, lower solubility of a DL crystal might predict lower volatility of that crystal compared to the enantiopure crystal. Thus an enantioenriched sublimate should result from the sublimation of an amino acid that forms a racemic compound and is present at a composition below its eutectic *ee*. For conglomerates, D and L crystals should be equally volatile, just as they are equally soluble. And these predictions are just what Cooks' results show. A 3% *ee* serine sample sublimed with *ee* values of 68–92% *ee* at 190–205 °C, while 7% *ee* threonine sublimed at 208 °C in a nearly racemic ratio. In both cases, the sublimation values are in good agreement with solution eutectic values (99% and 0%, respectively) for these amino acids, thus showing a strong correlation between relative solubility and relative volatility of crystal types.

Cooks hypothesized that the sublimation process itself occurs *via* formation of homochiral serine octamer clusters. However, the analogy we present here between solution–solid and gas–solid phase transitions leads us to suggest that the formation of such clusters is neither a requisite for nor a necessary consequence of the phase transition. This is supported by a recent exhaustive investigation that concluded that such clusters do not exist in solution.[13] While the fascinating properties of *charged* serine clusters in the gas phase have been documented,[14] this does not provide evidence for involvement of clusters under *non-ionising* conditions.

Although Cooks rejected the idea that preferential sublimation of L-crystals in solid serine mixtures is the cause of the observed enantioenrichment, the discussion here points exactly to this explanation. Indeed, the concept of "fractional sublimation", in analogy to fractional crystallization, is one that was first suggested nearly half a century ago[15] as a means to prepare small amounts of enantioenriched material, and this concept has been revisited about once a decade since then.[11,16,17] Based on the observations presented, Occam[18] would unquestionably balk at invoking anything more complicated than simply the basic concepts of phase behavior to explain the observed amplification in *ee* in these sublimation studies.

Settling differences

Feringa's group studied sublimation of a wider range of amino acids. They concluded that the role of clusters was unproven and they pointed towards a simpler mechanism involving differences in intermolecular interactions in enantiomers and racemates. The Feringa results gave a number of notable differences compared to those of Cooks. While Cooks found no selectivity in sublimation of alanine, Feringa did. Indeed, Feringa found some degree of enantioenrichment in the sublimate for all six amino acids tested (all racemic compounds). In Cooks' work, this amplification appeared to be a special feature of serine alone.

How can we reconcile these differences? A comparison of the experimental protocol in the two studies, in conjunction with consideration of kinetics in addition to thermodynamics, leads us to a tenable explanation based on two key points: 1) in the Cooks experiment, scalemic amino acids were prepared by mixing the appropriate amounts of pure D and pure L enantiomers, while in the Feringa experiment, samples were prepared by mixing the racemic DL compound with excess pure L enantiomer; and 2) sublimation is almost always a non-equilibrium process.

How will the manner in which the scalemic sample is prepared influence its sublimate composition? To answer this question, let's return to our analogy with solid–solution phase behavior and to recent results from our group that appeared puzzling to us at the outset.[19] Scalemic samples of proline, an amino acid exhibiting a eutectic composition of 50% *ee*, were prepared at compositions of 20% and 60% *ee* (either side of the eutectic point) by physically mixing the pure solid D and L enantiomers and partially dissolving them in solvent to be in excess of the solubility limit, so that solid–solution equilibrium would eventually be attained. The solution *ee* was monitored as the system was stirred.

Now the question is: what *initial* solution composition do we expect to find, at time $t = t_o$, just as the two enantiomers begin to dissolve?

A reasonable guess might be that the 20% *ee* sample weighs in near 20% *ee*, and the 60% *ee* sample near 60% *ee*, before both start to approach the eutectic *ee* of 50%. However, what we find instead is that the initial solution *ee* is close to *zero*, no matter what the overall proline *ee* value is (Fig. 4)!

We rationalized this behavior by considering that when the separate solid crystals of proline are added to the solvent, the kinetics of two physical processes compete: 1) solution–solid equilibration; and 2) solid–solid equilibration. Proline forms

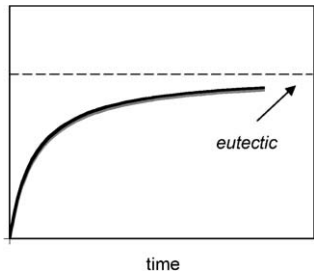

Fig. 4 Phase transition of a solid amino acid when separate L and D crystals are dissolved. The solution *ee* = 0 at the beginning of the dissolution process, regardless of the initial overall *ee* of the solid, and approaches the eutectic composition over time.

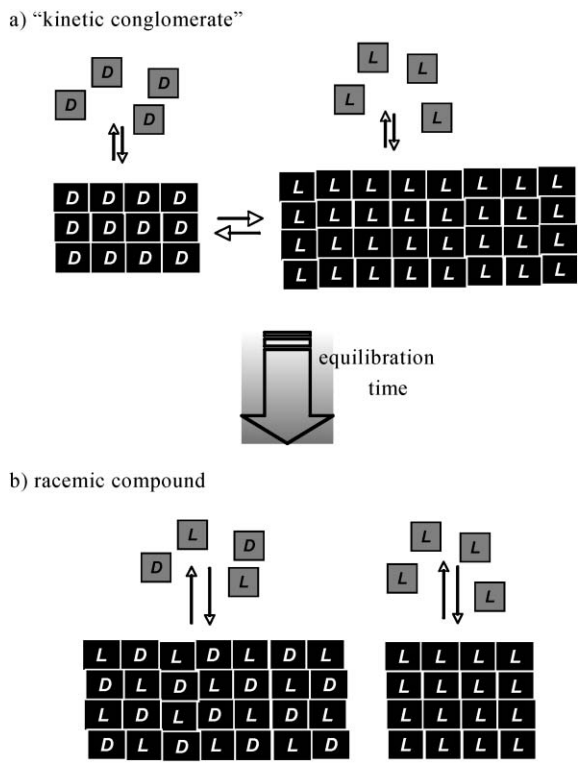

Fig. 5 Phase transition of a solid amino acid when separate L and D crystals are dissolved (or sublimed). a) Solution–solid (or gas–solid) transition occurs concurrent with solid–solid phase transition; b) solution–solid (or gas–solid) transition occurs after the solid phase equilibration between the enantiopure solid and the DL racemic compound.

an LD crystal at equilibrium, but before that equilibrium is established, the two separate crystals L and D each begin to dissolve without regard to the other. This results in behavior more like that of a conglomerate (Fig. 5a) than that of a racemic compound (Fig. 5b). Thus during the transient initial regime, a system of separate D and pure L crystals acts as a "kinetic conglomerate"[19] before solution–solid and solid–solid equilibrium are attained. If we had started this experiment with scalemic samples prepared from LD proline plus extra enantiopure proline (as in the Feringa protocol), then the solution composition at the outset would reflect a value closer to the eutectic *ee*.

Now let's consider these ideas in the context of the Cooks and Feringa sublimation experiments. Leucine, which was the amino acid studied in the most detail by Feringa, was found to sublime from 9–10% *ee* samples at temperatures lower than 179 °C to give sublimates of 72–89% *ee*, in good agreement with our measured eutectic of 88% *ee*. These samples were prepared from DL + L leucine, meaning that solid–solid equilibration had already occurred prior to sublimation. The same holds true for Feringa's alanine experiments, which showed enantioenrichment. In Cooks' experiment with alanine prepared from separate L + D crystals, it is likely that the slight depletion of *ee* observed for the sublimate occurred because the system was still struggling to emerge from its "kinetic conglomerate" state even while the sublimation process began, with sublimate *ee* following the profile shown in Fig. 4.

The concept of a "kinetic conglomerate"[19] provides an alternate explanation for Cooks' finding that sublimation of serine with very high initial *ee* values gave a sublimate with decreased chiral purity, which he interpreted to be the result of racemization. If the sublimation of separate D and L crystals of serine took place (as in Fig. 5a) prior to equilibration of the solid DL compound (as in Fig. 5b), the sublimate would indeed exhibit a chiral purity lower than serine's eutectic of > 99% *ee* in the transient phase prior to solid–solid equilibration (as in Fig. 4), even in the absence of chemical racemization.

If the goal of the sublimation is to maximize enantioenrichment, then the Feringa experimental protocol, starting from the racemic compound as in Fig. 5b, is a better choice than the Cooks protocol as in Fig. 5a. However, the ideas presented here also show that Feringa's concern that "mixing of the racemate and the enantiomorph was incomplete at the molecular level" is misplaced. As long as we have crystals in a scalemic mixture, we will find that "molecular level mixing" between the enantiomorph and the racemate does not occur at all.

Good things come to those who wait

Thus the differences between the results of Cooks and those of Feringa may be rationalized by considering the physical state of the starting materials along with a strong interplay between kinetic and thermodynamic driving forces. We have made the point here that the basic laws of thermodynamic phase behavior in our studies of the evolution of homochirality in solution–solid systems can be applied just as well to the gas–solid systems of the sublimation model. In practice, however, sublimation carries several extra considerations that we address here.

By their very nature, sublimation experiments are most often open systems that may seldom be expected to reach solid–vapor equilibrium, whereas in solution–solid systems reaching the eutectic point is simply a matter of having enough time and enough material. The implication from this is that any "mistakes" that are made early on in a sublimation experiment—for example, the wrong enantiomer subliming due to kinetic effects—are unable to be corrected by re-depositing and re-subliming. Therefore sublimate *ee* values lower than the eutectic point are likely to be attained under all but the most meticulously optimized conditions.

Temperature is a parameter that plays a more important role in sublimation protocols than it does in solution–solid systems, which typically are carried out far from melting or racemization conditions. Cooks' sublimation protocols include temperatures up to the melting points of both L and DL serine. Since fractional sublimation depends on the difference in intracrystalline forces for racemic *vs.* enantiopure crystals, we should expect to observe no enantioenrichment at or near melting temperatures. Sublimation, racemization, and melting may all occur at reasonable rates within the same temperature window, making the sublimate composition dependent on all of these competing processes.§[,20] In addition, apart from the fact that most amino acids decompose upon melting, phase behavior is generally temperature-dependent and can therefore exhibit not only gradual but also principal differences between ambient and melting point temperature. This brings us back to the note of caution mentioned earlier: for example, a conglomerate can become a racemic compound and *vice versa* at different temperatures. Several such examples are known, from nineteenth century studies to more recent ones.[21,22]

Another aspect in which gas–solid and solution–solid systems may offer different practical results concerns a concept we recently developed to enhance solution phase enantioenrichment of amino acids by tuning the eutectic composition.[9,23,24] Based on our finding that incorporation of small achiral molecules into the amino acid structure *via* hydrogen bonding can be an effective method of altering solubility,[9] we discovered several cases in which this incorporation resulted in near-complete "shutdown" of the racemic compound's solubility and near-perfect solution *ee* values. For instance, the eutectic *ee* of valine was enhanced from 47% *ee* to 99% *ee* by incorporation of fumaric acid into the solid DL crystal structure.[23] In another case, incorporation of $CHCl_3$ from the solvent into proline's DL structure (Fig. 6) caused an even greater reduction in its relative solubility and enhancement of solution *ee*.[9]

The effect of $CHCl_3$ on solution *ee* for proline was first reported by Hayashi[25] and had been recognized for some time by both our groups,[26] but the rationalization we ultimately provided based on the crystal structure shown in Fig. 6[9] proved to be elusive. Our first clues that the proline DL solid from $CHCl_3$ was different from that crystallized from solvents such as EtOH or DMSO came from the observation that the crystals quickly turn opaque once taken out of solution, suggesting the loss of $CHCl_3$ through evaporation. The powder X-ray diffraction patterns confirm this assumption, as shown in Fig. 7.

Fig. 7 shows that the air-dried DL proline compound we isolated from $CHCl_3$ (Fig. 7, bottom) gave an X-ray pattern different from that calculated for DL proline (Fig. 7, middle), and it also differed from that we ultimately calculated for the DL-proline–$CHCl_3$ structure in Fig. 6 (Fig. 7, top). Air-dried samples from $CHCl_3$ also showed considerable variability depending on time of exposure to ambient air. After we were

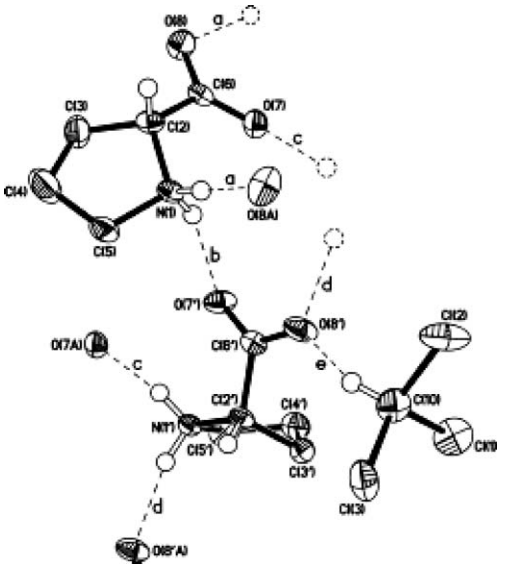

Fig. 6 Structure of DL proline crystallized from $CHCl_3$–MeOH, where one $CHCl_3$ molecule is incorporated in the structure *via* hydrogen bonding and causes a significant reduction in solubility. The letters a–e refer to five distinct hydrogen bonding interactions. The structure was obtained from a sample for which special care had been taken to prevent loss of chloroform upon isolation. (From Ref. 7, Supporting Information).

able to obtain the single crystal structure incorporating $CHCl_3$ shown in Fig. 6, however, we attributed the sample variability to the volatility of $CHCl_3$. Upon sitting under atmospheric pressure, the crystals lose $CHCl_3$, causing the structure in Fig. 6 to collapse.

This finding has implications for the viability of using additives to enhance enantioenrichment in sublimation experiments. The volatility of an additive will have less impact on co-crystal stability under solution–solid equilibrium, where incorporation in the crystal can be accomplished by mass action, than it might under sublimation conditions. While this approach has not yet been tested in fractional sublimation experiments, it is likely in many cases that the relative volatility of the additive may be too high to produce stable solvate

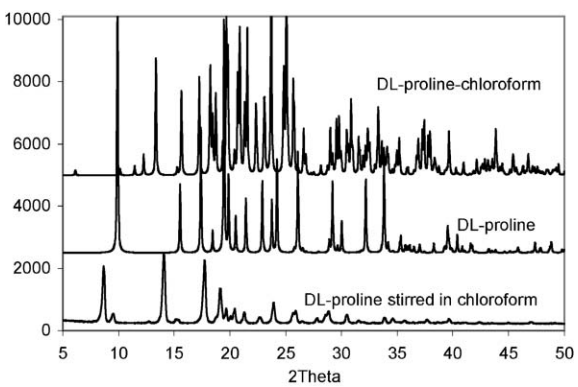

Fig. 7 X-Ray pattern calculated for the DL-proline–$CHCl_3$ structure of Fig. 6 (top) compared with that calculated for DL-proline (middle) and an experimental pattern for a sample of DL-proline stirred for 24 h in $CHCl_3$ and dried in air (bottom).

§ The "preservation of enantiomeric ratios" in sublimation discussed in Ref. 20 referred to lack of observed racemization; contrary to the interpretation by Feringa in Ref. 10, the subject of enantioenrichment during sublimation was not addressed in that work.

structures that can afford the same enhancement in chiral purity in sublimation that we find in solution–solid chemistry.

Prebiotic plausibility

This discussion shows that the work of our group in solution–solid systems and that of both the Cooks and Feringa groups in sublimation of amino acids may be couched together under a model for the evolution of homochirality based on enantiomer partitioning due to phase transitions. One might then ask the essentially unanswerable question: which type of phase transition makes a more plausible case for rationalizing what occurred on the prebiotic Earth? Both Cooks and Feringa imagine the early Earth being seeded with organic-rich interplanetary dust sublimed at high temperatures in space, from which enantioenriched molecules condensed in the upper atmosphere and made their way to Earth.¶ Feringa further speculates that the left-behind racemate might also be destroyed by the high temperatures of sublimation, which he suggests would allow for high *ee* to be established without destruction of the major part of the initial material. This statement may be questioned, however, as we can show that for a compound with a eutectic of $> 99\%$ *ee* that is present in overall 1% *ee*, the theoretical maximum quantity of enantiopure sublimate possible will be 1% of the total amount of material. For this reason, the term ''amplification'' of chiral purity is probably less descriptive than ''enantiomer partitioning'' or ''fractionation'' for both gas–solid and solution–solid phase transition models.

As discussed above, kinetic influences can limit the chiral efficiency of sublimation, and in this sense, the sublimation model may be considered as a ''far-from-equilibrium'' model for the evolution of homochirality.[27]

We may suggest a model that combines the sublimation and solution–solid phase phenomena. If the first enantiomeric imbalance was brought to Earth by fractionation of organic space dust *via* sublimation, further amplification could take place in terrestrial aqueous pools, where solution–solid equilibrium might be established over time through cycles of rainfall and evaporation. The presence in solution of molecules capable of hydrogen bonding with amino acids might further enhance enantioenrichment by tuning the various amino acids' eutectic points. Indeed, consideration of the additives discussed in this paper shows relevance for prebiotic chemistry, since dicarboxylic acids such as fumaric acid have been isolated from chondritic meteorite samples,[28] and $CHCl_3$ is found in non-anthropogenic sources in seawater and in gases vented from solfataric volcanoes.[29]

Conclusions

Recent studies showing that phase transitions of amino acids can lead to enantioenrichment have been discussed and compared. Gas–solid and solution–solid phase transitions both provide a partitioning or fractionation of enantiomer composition that may lead to highly enantioenriched sublimates or solutions, respectively, for some amino acids.

The fact that the topic of this article focuses on amino acids should not lead to the conclusion that the described phenomena are characteristic for this substance class only; in fact, they are general for *all* chiral substances. Wilen, Collet and Jacques gave a warning to all chemists that we feel should be repeated in this place: ''It is worthwhile emphasizing that *any* manipulation of partially resolved enantiomer mixture... is potentially selective, even just washing solid with solvent.... Such otherwise innocuous manipulations may lead to even substantial alteration of the enantiomer ratio and affect conclusions in mechanistic and asymmetric synthesis experiments.''[30] In this respect the comments of Feringa[10] concerning the experimental measurement methodology devised for probing space for extraterrestrial organics (the Mars Organic Detector, MOD) are particularly pertinent.

In the cases discussed here, an understanding of the nature of the crystal solids, along with basic thermodynamic principles and the interplay of thermodynamics and competing kinetic processes, come together to rationalize the experimental observations without invoking special effects such as magic number cluster formation. A combination of both types of phase transitions could reasonably have contributed to the evolution of homochirality on the prebiotic Earth.

Acknowledgements

Stimulating discussions with Prof. A. Armstrong and Prof. C. Viedma are gratefully acknowledged. We thank Dr A. J. P. White for X-ray crystallography. A grant from the EPSRC and funding from AstraZeneca are gratefully acknowledged. DGB holds a Royal Society Research Merit Award.

Notes and references

1 P. Ball, Giving Life a Hand, *Chem. World*, 2007(March), 30–31.
2 F. C. Frank, *Biochim. Biophys. Acta*, 1953, **11**, 459.
3 M. Calvin, *Molecular Evolution*, Oxford University Press, Oxford, 1969.
4 D. L. Kondepudi, *Science*, 1990, **250**, 975.
5 K. Soai, T. Shibata, H. Morioka and K. Choji, *Nature*, 1995, **378**, 767.
6 (*a*) C. Viedma, *Phys. Rev. Lett.*, 2005, **94**, 065504; (*b*) D. G. Blackmond, *Chem.–Eur. J.*, 2007, **13**, 3290–3295; (*c*) C. Viedma, *Astrobiology*, 2007, **7**, 312–319.
7 M. Klussmann, H. Iwamura, S. P. Mathew, D. H. Wells, Jr., U. Pandya, A. Armstrong and D. G. Blackmond, *Nature*, 2006, **441**, 621–623.
8 R. H. Perry, W. Chunping, M. Nefliu and R. G. Cooks, *Chem. Commun.*, 2007, 1071–1073.
9 M. Klussmann, A. J. P. White, A. Armstrong and D. G. Blackmond, *Angew. Chem., Int. Ed.*, 2006, **47**, 7985–7989.
10 S. P. Fletcher, R. B. C. Jagt and B. Feringa, *Chem. Commun.*, 2007, 2578–2580.
11 J. Jacques, A. Collet and S. H. Wilen, *Enantiomers, Racemates and Resolution*, Krieger Publishing Company, Florida, 1991 and references therein.
12 W. Meyerhoffer, *Ber.*, 1904, **37**, 2604–2610.
13 S. Vandenbussche, G. Vandenbussche, J. Reisse and K. Bartik, *Eur. J. Org. Chem.*, 2006, 3069–3073.
14 S. C. Nanita and R. G. Cooks, *Angew. Chem., Int. Ed.*, 2006, **45**, 554–569.
15 G. Pracejus, *Justus Liebigs Ann. Chem.*, 1959, **622**, 10.
16 H. Kwart and D. P. Hoster, *J. Org. Chem.*, 1967, **32**, 1867–1870.

¶ However, as pointed out in Ref. 13, serine, the amino acid giving the highest enantioenrichment in sublimation, has not been observed in organic material from meteorites or in space.

17 D. L. Garin, D. C. Cooke Greco and L. Kelley, *J. Org. Chem.*, 1977, **42**, 1249–1251.
18 "*Entia non sunt multiplicanda praeter necessitatem*", attributed to William of Ockham (1285?–1349?).
19 M. Klussmann, S. P. Mathew, H. Iwamura, D. H. Wells, Jr., A. Armstrong and D. G. Blackmond, *Angew. Chem., Int. Ed.*, 2006, **47**, 7989–7993.
20 D. P. Glavin and J. L. Bada, *Anal. Chem.*, 1998, **70**, 3119–3122.
21 H. W. B. Roozeboom, *Z. Phys. Chem., Stoechiom. Verwandtschaftsl.*, 1899, **28**, 494–517.
22 T. Shiraiwa, M. Ohkubo, H. Miyazaki, M. Kubo, H. Nishigawa, T. Tsujimoto and H. Kurokawa, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 735–739.
23 M. Klussmann, T. Izumi, A. J. P. White, A. Armstrong and D. G. Blackmond, *J. Am. Chem. Soc.*, 2007, **129**, 7657–7660.
24 D. G. Blackmond and M. Klussmann, *AIChE J.*, 2007, **53**, 1.
25 Y. Hayashi, M. Matsuzawa, J. Yamaguchi, S. Yonehara, Y. Matsumoto, M. Shoji, D. Hashizume and H. Koshino, *Angew. Chem., Int. Ed.*, 2006, **45**, 4593–4597.
26 R. M. Kellogg, *Angew. Chem., Int. Ed.*, 2007, **46**, 494–497.
27 D. G. Blackmond, *Proc. Natl. Acad. Sci. U. S. A.*, 2004, **101**, 5732.
28 A. Shimoyama and R. Shigematsu, *Chem. Lett.*, 1994, **23**, 523–526.
29 V. A. Isidorov, I. G. Zenkevich and I. O. Ioffe, *J. Atmos. Chem.*, 1990, **10**, 329–340.
30 S. H. Wilen, A. Collet and J. Jacques, *Tetrahedron*, 1977, **33**, 2725–2736.

