

## Mechanism of Chirality Conversion by Grinding Crystals: Ostwald Ripening vs Crystallization of Chiral Clusters

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It has been found that the simple grinding of crystals in a solution causes the conversion of the chiral structure of crystals and, in the case of organic molecules, the resultant conversion of molecular chirality. In order to clarify the mechanism of the chirality conversion, we study the change in the size distribution of chiral clusters in a Becker-Döring type model, in which chiral dimer reaction and grinding are implemented. In the absence of grinding, Ostwald ripening may cause chirality conversion if the initial size distribution is appropriate. With grinding crystals, the crystallization of chiral clusters causes an exponential amplification of the initial chiral imbalance resulting in a homochiral state. During chirality conversion, the total size distribution does not change.

KEYWORDS: chirality conversion, homochirality, crystallization, enantiomer, chiral cluster, autocatalysis,  $\text{NaClO}_3$ , racemization

The striking chirality conversion of  $\text{NaClO}_3$  crystals by grinding in a saturated solution was discovered by Viedma.<sup>1)</sup> A molecule of  $\text{NaClO}_3$  is achiral but its crystal has right (R) and left (L) types of structures.<sup>2)</sup> The material has been well known for its spontaneous chiral symmetry breaking during nucleation growth with stirring.<sup>3)</sup> The cause of the phenomenon is attributed to the predominance of the first-nucleated crystal type via secondary nucleation.<sup>4,5)</sup> The newly discovered chirality conversion of crystal structures occurs when R and L crystals coexist in a solution from the beginning, and the minority type disappears by grinding crystals for one day. The transition from a racemic (mixed) state into a homochiral state is puzzling since the two states are energetically equal. The chirality conversion of crystals has been confirmed in  $\text{NaBrO}_3$ <sup>6)</sup> and ethylenediammonium sulfate.<sup>7)</sup> Recently, Noorduyn et al. have applied the same method to an amino acid derivative and found a similar chirality conversion of crystals.<sup>8)</sup> In this system, a molecule has chirality, which can change in a solution with an added base, and the conversion of the crystal chirality implies the simultaneous conversion of molecular chirality. Thus, simple grinding converts the molecular chirality of the minority type and realizes a homochiral molecular state of all crystals in the system.

A simple reaction-type model<sup>9)</sup> has been proposed to explain the conversion of crystal chirality as well as symmetry breaking in nucleation growth. The model assumes that, in addition to achiral monomers, small chiral clusters are the growth unit of chiral crystals. It uses masses of five components (achiral monomers, two kinds of chiral clusters, and two kinds of chiral crystals of various sizes) as fundamental variables for describing time evolution, and the size distribution of crystals is neglected. Grinding produces abundant chiral clusters, whose incorporation to the crystals causes accelerated crystallization of the major crystal type. As pointed out by McBride and Tully,<sup>10)</sup> this model can be simplified

in the case of Viedma's experiment, and may also explain the molecular chirality conversion. The analysis of the model<sup>9,11)</sup> shows that it reproduces the exponential amplification of an initial chirality imbalance and some other features observed in the experiment. For chemical reactions, Saito and Hyuga<sup>12)</sup> pointed out that a nonlinear autocatalytic reaction and a back reaction to produce achiral component are essential factors for realizing a homochiral state. The proposed crystallization of chiral clusters and their decay into achiral monomers correspond to these processes.

However, the authors of ref. 8 suggest that the cause of the chirality conversion of crystals is the Ostwald ripening (OR). Two theoretical papers<sup>13,14)</sup> make the same assertion on the basis of simulation results, and a new experiment<sup>15)</sup> is used to support this viewpoint. In the experiment, starting from large and small crystals, OR produced a homochiral state *without grinding*.<sup>16)</sup> We think, however, that OR is not the essential mechanism for the chirality conversion of crystals *with grinding*. The reason is that the size distributions of R and L crystals must be almost steady during the grinding as assumed in refs. 9 and 11. The purpose of the present research is to study the change in the size distribution during grinding and clarify if OR is the essential factor for chirality conversion. We use an extended Becker-Döring model, in which cluster reaction and the grinding effect are implemented.<sup>17)</sup> We show that the size distribution is steady during grinding and that the direct crystallization of small chiral clusters and grinding are essential to the chirality conversion that leads to a homochiral state.

Our model is a Becker-Döring type model, which naturally describes the change on cluster size distribution in a mean field scheme and thus leads to OR.<sup>18)</sup> We assume, for simplicity, that all clusters ( $l \geq 2$ ,  $l$  is the number of molecules in a cluster) are crystals that exhibit chirality. The system is described by the number distribution of clusters  $\{n_l(t)\} = (n_1, n_2^R, n_3^R, \dots, n_{l_{\max}}^R, n_2^L, n_3^L, \dots, n_{l_{\max}}^L)$ . Grinding is assumed to set the maximum size  $l_{\max}$  of the clusters. In

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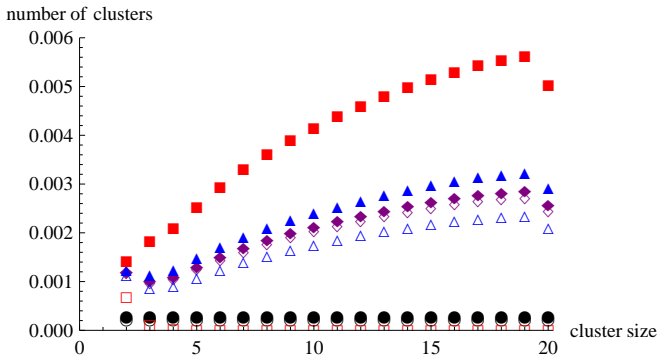
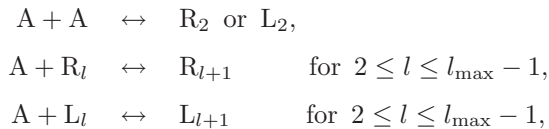
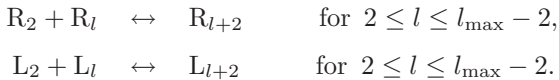


Fig. 1. Evolution of the distribution function  $n_l(t)$  at  $t=0$  (black circle),  $t=10^4$  (purple diamond),  $t=10^5$  (blue triangle),  $t=10^6$  (red square). Filled marks are R and empty marks are L.

addition to the dimer formation and the standard reactions of an achiral monomer (**A**) with a chiral cluster of size  $l$  (**R** $_l$  or **L** $_l$ ), namely,



a chiral dimer (**R** $_2$  or **L** $_2$ ) is assumed to be integrated into a chiral cluster, and a chiral dimer may be emitted from a larger chiral cluster:



A collision of a cluster with a monomer occurs with a rate proportional to the surface area of the cluster:  $\sigma_l n_1 n_l^{\text{R,L}} = a l^{2/3} n_1 n_l^{\text{R,L}}$ . The reverse process (emission of a monomer) occurs with a rate determined by the detailed balance:  $\lambda_l n_l^{\text{R,L}} = \sigma_{l-1} n_1^{\text{eq}} \exp[\bar{\alpha} l^{2/3} - \bar{\alpha} (l-1)^{2/3}] n_l^{\text{R,L}}$ , where  $\bar{\alpha}$  is a quantity proportional to the surface energy density of a cluster and  $n_1^{\text{eq}}$  the number of monomers in saturation equilibrium. The dimer reaction may occur with a similar rate,  $\sigma_l^{\text{d}} n_1 n_l^{\text{R,L}} = a^{\text{d}} l^{2/3} n_1 n_l^{\text{R,L}}$ , and a corresponding decay rate,  $\lambda_l^{\text{d}} n_l^{\text{R,L}}$ . The grinding process is modeled as follows: The largest clusters of each chirality, **R** $_{l_{\max}}$  or **L** $_{l_{\max}}$ , are destroyed at a rate of  $\lambda^{\text{gr}} n_{l_{\max}}^{\text{R,L}}$ . Simultaneously, smaller clusters of the same chirality, **R** $_l$  or **L** $_l$  ( $2 \leq l < l_{\max} - 1$ ), are produced at a size-independent rate that conserves the total number of molecules. Thus, the number of clusters of size  $l$  ( $4 \leq l \leq l_{\max} - 2$ ) obeys the equation

$$\begin{aligned} \dot{n}_l^{\text{R,L}} &= \sigma_{l-1} n_1 n_{l-1}^{\text{R,L}} - \sigma_l n_1 n_l^{\text{R,L}} \\ &+ \sigma_{l-2}^{\text{d}} n_2 n_{l-2}^{\text{R,L}} - \sigma_l^{\text{d}} n_2 n_l^{\text{R,L}} \\ &- (\lambda_l + \lambda_l^{\text{d}}) n_l^{\text{R,L}} + \lambda_{l+1} n_{l+1}^{\text{R,L}} + \lambda_{l+2}^{\text{d}} n_{l+2}^{\text{R,L}} \\ &+ (\text{term proportional to } \lambda^{\text{gr}} n_{l_{\max}}^{\text{R,L}}). \end{aligned} \quad (1)$$

A result of the numerical integration is shown in Figs. 1 and 2. The number of clusters is normalized by the total number of molecules,  $N = n_1 + N^{\text{R}} + N^{\text{L}}$ ,

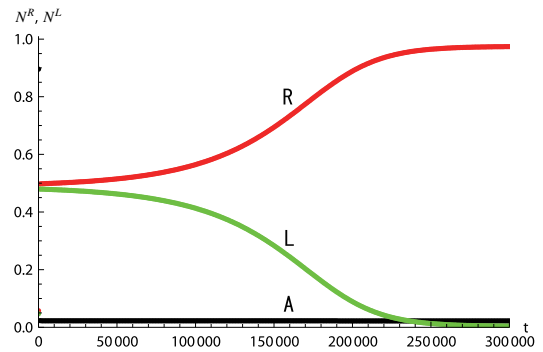


Fig. 2. Number of molecules (normalized by the total number) as achiral monomers  $n_1(t)$  (**A**, black) and in right and left chiral clusters  $N^{\text{R}}(t)$  (**R**, red),  $N^{\text{L}}(t)$  (**L**, green). The parameter values are  $n_1^{\text{eq}} = 0.001$ ,  $\lambda_{\text{grind}} = 0.1$ ,  $a = a^{\text{d}} = 1.0$ .

where  $N^{\text{R,L}} = \sum_{l=2}^{l_{\max}} l n_l^{\text{R,L}}$ , so that the total number is unity. The parameter values used are as follows:  $n_1^{\text{eq}} = 0.001$ ,  $\lambda^{\text{gr}} = 0.1$ ,  $a = a^{\text{d}} = 1.0$ , and  $l_{\max} = 20$ . The initial distribution is set slightly R-rich:  $n_l^{\text{R}} = 0.11/l_{\max}^2$ ,  $n_l^{\text{L}} = 0.9/l_{\max}^2$  (circles in Fig. 1) and  $n_1 = 1 - N^{\text{R}} - N^{\text{L}} (= 0.8955)$ ; the initial solution is strongly supersaturated. At first the cluster numbers  $n_l^{\text{R,L}}$  increase rapidly and reach a “quasi-steady” (slowly-varying) distribution with a small chirality imbalance (diamonds in Fig. 1). The enantiomeric excess (EE) defined by  $\phi = (N^{\text{R}} - N^{\text{L}})/(N^{\text{R}} + N^{\text{L}})$  represents the imbalance, and its initial time evolution is plotted in Fig. 3(a) for various dimer reaction rates  $a^{\text{d}}$ . In the initial stage, EE decreases from its initial value  $\phi = 0.1$  and then increases back to  $\phi \sim 0.02$ . After  $t \approx 2000$ , EE changes slowly and exponentially with an amplification rate  $\omega = 2.14 \times 10^{-5}$ , as shown by the circles (red) in Fig. 3. The exponential amplification of  $\phi$  continues until  $t \approx 1.7 \times 10^5$  when the saturation of EE sets in (Fig. 2). This feature is similar to that observed in the reaction model.<sup>9)</sup>

Although the distributions of R and L clusters markedly change, the total size distribution  $n_l^{\text{R}}(t) + n_l^{\text{L}}(t)$  stays approximately constant during the chirality conversion of crystals. The EE changes without changing the total size distribution. If we start with a chiral-symmetric initial condition,  $n_l^{\text{R}}(0) = n_l^{\text{L}}(0)$ , the final state with grinding is symmetric and close to half of the distribution  $n_l^{\text{R}}(t) + n_l^{\text{L}}(t)$  after the quasi-steady state in Fig. 1. This symmetric (racemic) state is unstable against a small asymmetric perturbation. If the initial condition is slightly asymmetric, the distribution first approaches the unstable distribution quickly, and then the asymmetry is amplified. The final state is that in Fig. 1 (or the state with R and L exchanged), which is unique and almost homochiral with a very few small minority clusters. Because of the large degree of freedom in the cluster model, we have been unable to prove mathematically the above statement, but numerical data with various initial conditions support the scenario. The unstable symmetric distribution corresponds to the unstable racemic fixed point and the final stable distributions correspond to the stable fixed points in ref. 9.

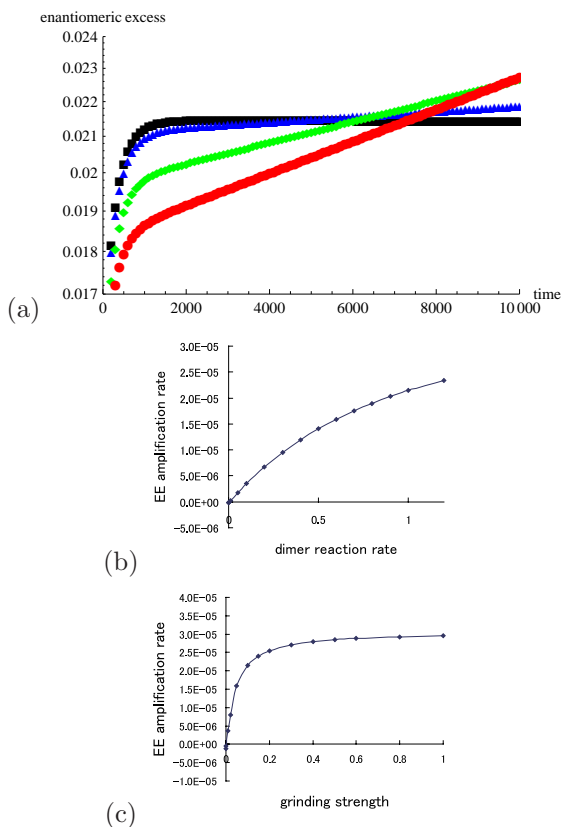


Fig. 3. (a) Change in EE (semilogarithmic plot) with the dimer reaction coefficient  $a^d$ :  $a^d = 0$  (black square), 0.1 (blue triangle), 0.5 (green diamond), 1.0 (red circle). (b) EE amplification rate  $\omega$  for various values of  $a^d$ . (c)  $\omega$  for various values of the grinding strength  $\lambda^{\text{gr}}$ .

Thus, implicit assumptions of the reaction type models<sup>9,11</sup>) that grinding produces a steady cluster size distribution is justified. From the racemic state to the homochiral state, the number of monomers changes slightly [ $n_1(10^4) = 0.02248$  and  $n_1(10^6) = 0.02205$ ], a feature also seen in refs. 9 and 11. These numbers of monomers correspond to the critical cluster sizes  $l_c = 9.826$  and  $l_c = 10.011$ , and OR apparently has no significant role.

*Without grinding*, the chirality conversion of an organic compound by OR has been reported recently.<sup>16</sup>) If crystals of one type is larger than those of the other, OR causes chirality conversion. We have confirmed this phenomenon in the present model without grinding ( $\lambda^{\text{gr}} = 0$  and  $l_{\text{max}} \rightarrow \infty$ ). Figure 4 shows the size distribution under the initial condition with more small L crystals and fewer large R crystals. OR brings about the amplification of EE irrespective of the existence of the dimer reaction. However, the problem posed by the grinding experiments<sup>1,8</sup>) is that whether crystals of similar size distributions produced by grinding (as the data at  $t = 10^4$  indicated by diamonds in Fig. 1) can realize the amplification of EE. Our analysis shows that, even with a steady size distribution, the crystallization of chiral clusters with grinding can make a racemic mixture dynamically unstable and produce a homochiral state.

As shown in Fig. 3, both the crystallization of chiral clusters (the dimer reaction in the present model) and grinding are necessary for the amplification of EE.

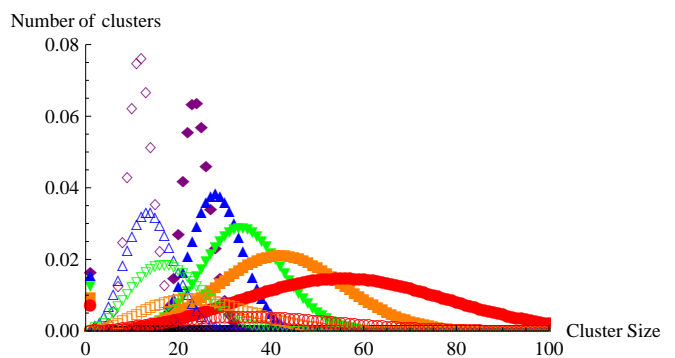
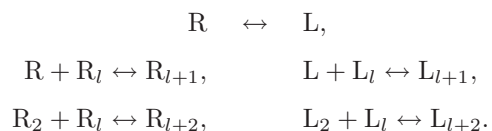


Fig. 4. Evolution of the distribution function during OR without grinding:  $n_l(t)$  at  $t = 200$  (purple diamond),  $t = 800$  (blue triangle),  $t = 1600$  (green inverted triangle),  $t = 3200$  (orange square),  $t = 6400$  (red circle). Filled marks are R and empty marks are L. The initial conditions are  $n_{10}^R(0) = 0.45/10$ ,  $n_{20}^R(0) = 0.4/20$ , and  $n_1^R(0) = 0.05$ . The parameters are  $\lambda^{\text{gr}} = 0$  and  $l_{\text{max}} \gg 100$ , other parameters are the same as those in Figs.1 and 2.

Without the dimer reaction  $a^d = 0$ , EE decreases very slowly at a rate  $\omega = -1.75 \times 10^{-7}$  (black squares in Fig. 3(a)). With increasing dimer reaction rate  $a^d$ , the EE amplification rate  $\omega$  increases from this small negative value, and becomes positive for  $a^d$  larger than 0.005 (Fig. 3(b)). Note that the critical value of  $a^d$  is rather small, and a small amount of the dimer reaction is sufficient to induce the amplification. If grinding is absent in the present model ( $\lambda^{\text{gr}} = 0$ ),  $n_l^{\text{R,L}}$  increases with  $l$  and an “equilibrium” distribution is realized since the maximum cluster size is limited to  $l_{\text{max}}$ . (In real systems,  $l_{\text{max}} \rightarrow \infty$  and infinitely large clusters will appear.) In this case, EE decreases very slowly after  $t \sim 2000$  with  $\omega = -1.21 \times 10^{-6}$ . With grinding,  $\omega$  increases with increasing grinding strength  $\lambda^{\text{gr}}$  and becomes positive for  $\lambda^{\text{gr}}$  larger than 0.002 (Fig. 3(c)). The monotonic acceleration of amplification rate with grinding strength is consistent with the experiment.<sup>1,7,15</sup>)

It is easy to extend the model to the conversion of molecular chirality. In the case of organic systems,<sup>8,16</sup>) a monomer molecule has chirality, which is converted at a constant rate  $r$  in a solution. Thus, instead of the achiral monomer **A**, we have converting chiral monomers **R** and **L**, and the reaction scheme becomes



The number of  $n_1^{\text{R,L}}$  changes at a rate  $r(n_1^{\text{L,R}} - n_1^{\text{R,L}})$ . The time evolution with  $r = 0.1$  is shown in Fig. 5(a) (other parameters are the same as those in Fig. 2). The changes in R and L are very similar to those in Fig. 2, but the exponential amplification rate decreases with decreasing  $r$  (Fig. 5(b)). These features are already observed in the simple reaction model,<sup>19</sup>) and are in qualitative agreement with the experiment.<sup>15</sup>)

There are two simulation models that propose OR as the key mechanism of the chirality conversion.<sup>13,14</sup>) These simulations follow the stochastic change in the size

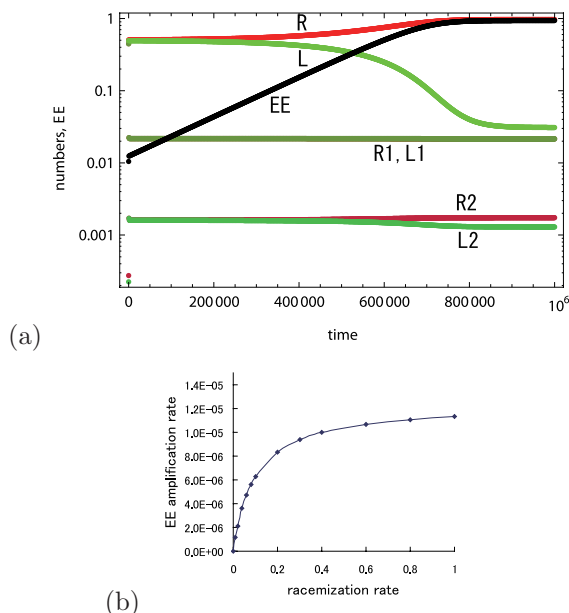


Fig. 5. (a) Time evolution of total numbers of R and L molecules (R,L), monomers (R1,L1), dimers (R2,L2), and EE. (b) Amplification rates of EE for various molecular conversion rates  $r$ .

of each cluster. In ref. 13, the decay of the smallest cluster (corresponding to the decay of a dimer in the present model) is inadequately called OR. In ref. 14, OR is imitated by the direct mass exchange between clusters, and, by assuming a faster mass exchange between clusters of the same chirality, an exponential chirality conversion is reproduced for the amino acid derivative case. One possible reason for this result is that, with a fast equilibration of clusters of each kind, in this simulation, the average cluster sizes of R and L become different and the exponential amplification of EE is realized by the mass transfer from small clusters to large clusters. If mass exchange rate is independent of the chirality of clusters, however, the exponential amplification of EE disappears.<sup>14</sup> Homochirality is realized in small systems as a result of the stochastic selection, which should not work in large real systems. Since OR is not a direct mass exchange between clusters as modeled in ref. 14, we have performed a similar Monte Carlo simulation including mass exchange with monomer and dimer reservoirs. Preliminary results show that, for small systems, homochirality is realized by the stochastic effect, as in ref. 14. For large systems, the exponential amplification of EE and homochirality occur only with the dimer reaction.

We have analyzed the simple models showing the complete chirality conversion of crystals as well as that of racemizing molecules. The steady size distribution during the chirality conversion of crystals supports the implicit assumption in the reaction type models.<sup>9,11</sup> Without grinding, OR can cause the chirality conversion if the initial sizes of crystals of the two species are different. With grinding, starting from similar crystal sizes

for R and L, chirality conversion occurs with the crystallization of chiral clusters.<sup>20</sup> In real systems, if a direct crystallization of chiral clusters occurs, it must occur irrespective of grinding. Therefore, we think that chirality conversion with grinding is an indication that the growth

units of crystallization in such a system are, in addition to usual monomers, chiral clusters.

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M. U. thanks Prof. Masato Kitamura for the informative conversation on organic chemistry.

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