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REVIEW COMMENTARY

INTERRELATIONSHIPS BETWEEN PHASE TRANSFORMATIONS AND ORGANIC CHEMICAL REACTIVITY IN THE SOLID STATE

EVGENYI YU. SHALAEV* AND GEORGE ZOGRAFI†
School of Pharmacy, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA

A qualitative analysis is presented of the interrelationships between phase transformations and organic chemical reactivity in the solid state, taking into consideration general thermochemical relationships and the thermodynamics of heterophase equilibrium. Two cases, where isomerization reactions depend on the solid-state solubility of the reactant and product, are considered and show that the formation of a new phase can influence both the reaction yield and rate. For example, it is shown that crystallization of a new phase from a crystalline or amorphous solid solution can supply the thermodynamic driving force for chemical transformation. Formation of a new phase may influence solid-state kinetics depending on the solubility of a reactant in the new phase and the relative rates of chemical transformation and formation of the new phase. It is further shown that even for simple monomolecular reactions, kinetic curves for the overall process can consist of up to five parts, depending on the type of phase diagram involved. These principles have been applied to some examples of solid-state isomerization in a way that allows the choice of a proper kinetic scheme and an explanation of the direction and maximum yield observed for a particular reaction.

INTRODUCTION

Solid-state organic reactions continue to attract the attention of investigators for two major reasons: (1) the use of solid-state reactions to introduce new possibilities in the exploration of the fundamental aspects of chemical reactivity; and (2) because of the practical importance of such reactions in solid-state synthesis and in the storage stability of solid chemicals, pharmaceuticals, and polymers. Solid-state reactivity can involve reactions between solids, solids and liquids and solids and gases and the transformation of a single solid material. In this paper, we shall consider only the last case because it allows us to investigate the role of phase transformations in chemical reactions without introducing complications from the diffusion of reactants through an interface, which plays a more important role in the other cases. Such reactions include isomerization, racemization, polymerization or decomposition (e.g. decarboxylation). They generally can be initiated in a single-crystal or polycrystalline form, where, in the beginning, product molecules accumulate in the crystalline lattice of the reactant, often followed by the formation of a new phase which can be amorphous (liquid or glassy), crystalline or a gas.

Most of the theories related to the reactivity of organic crystals consider only the initial single-phase (homogeneous) stage of the reaction. In such cases, the structural and mechanical properties of the parent crystal are either treated as an ideal and perfect crystal or are treated by considering the lattice to be disturbed by pre-existing defects, or by defects formed by the accumulation of product molecules. Examples of such approaches include the 'topochemical principles' of Cohen and Schmidt,[1] reaction cavity by Cohen,[2] the role of local stress by McBride *et al.*[3] and in large part the theory developed by Luty and Eckhardt.[4] Such studies allow one to consider the role of crystal structure and, in particular, the significance of defects originally present or generated as a result of the reaction. Detailed

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* Permanent address: Institute of Molecular Biology, SRC VB Vector, Kolstovo, Novosibirsk Region, 633159, Russia.
† Author for correspondence.

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descriptions of these and other relevant theories can also be found in a number of reviews.[5]

The *existence* of both homogeneous and heterogeneous stages has been reported for a number of organic solid-state reactions.[6] There also are a few theoretical descriptions of organic solid-state reactions which take into consideration both homogeneous and heterogeneous stages.[4,7,8] Paul and Curtin[7] postulated four stages: loosening of the molecules at the reaction site; molecular change due to reaction; solid-solution formation; and separation of the product(s). Dunitz[8] pointed out that in such reactions 'one cannot ignore the physics and, in particular, one must address thermodynamic considerations summed up in the Gibbs phase rule.' One of the first studies to quantitate the thermodynamic relationships between phase transformations and chemical transformations was reported by Luty and Eckhardt,[4] who attempted to predict a discontinuous phase transition on the basis of a description of thermodynamic equilibria between phases with different concentrations of perturbations.

In all of the approaches described to date for reactions leading to phase transformation, no consideration has been given to how the phase transformation can influence the chemical reaction. Moreover, such approaches have not considered how the formation of non-crystalline phases (liquid or glassy) also might influence such reactions. On the other hand, treatment of kinetic data for solid-state reactions in most cases has mainly stressed their heterogeneous nature, and not included discussion of homogeneous reactions. The kinetic curves for solid-state reactions are often sigmoid, or have even more complicated shapes, generally preceded by an induction period. Usually, the shape of such kinetic curves is considered to be a 'signature' of a solid-state reaction governed by nucleation and growth of a product phase (see Ref. 9 for a review of nucleation-based kinetics). Sigmoid-shaped kinetic curves have also been reported for chemical kinetics involving the appearance of a liquid phase. In considering a solid-state reaction with liquification, Bawn[10] described the reaction as proceeding in two phases with different rate constants. In all of these approaches where kinetic data are fitted to nucleation or two-phase models, what new phase must appear and at what stage in the reaction cannot be ascertained.

In this brief commentary, we have attempted to examine this issue more closely by considering the general relationship between solid-state reactivity and knowledge about the phase equilibria associated with products and reactants. For simplicity we have only considered reactions involving some form of isomerization: A $\longrightarrow$ B. However, conclusions derived from this analysis should also be applicable to more complex reactions. In the first part we provide a general description of the use of thermochemistry (see Ref. 11, for example) and phase diagrams[12] to determine the thermodynamic driving force for a chemical reaction in the solid state. To do this, we select phase diagrams for systems with limited solubility and complete immiscibility in the solid state. In the Appendix we provide some elementary properties of Gibbs free-energy curves which are important for our discussion. We then carry out a more detailed discussion of the influence of phase transformation on solid-state kinetics. Such analyses allow us to distinguish cases in which phase transformations and chemical reactions are coupled and uncoupled, and to establish the impact of phase transformations on a kinetic description of a particular reaction depending on the type of phase diagram for a reactant–product system. Finally, we consider a few examples from the literature of solid-state reactions, showing where this approach can prove useful.

THEORETICAL

General description of the thermodynamic basis for solid-state reactions

Let us consider a simple reaction wherein reactant, A, converts into a product, B:

$$A \longrightarrow B \qquad (1)$$

at constant temperature, T_r, and pressure, P_r. For example, this might be a reaction involving racemization. We may express the thermodynamic driving force for this reaction in terms of the Gibbs energy change, ΔG_r where:

$$\Delta G_r = \mu_b - \mu_a = \mu_b^\circ - \mu_a^\circ + RT(\ln a_b - \ln a_a) \qquad (2)$$

and μ_b and μ_a are the chemical potentials of B and A, respectively a_b and a_a are their activities and $\mu_b^\circ = \Delta G_f^\circ(B)$ and $\mu_a^\circ = \Delta G^\circ{}_f(A)$ are the standard molar free energies of formation for compounds B and A, respectively. Further, we shall assume that

$$\Delta G_f^\circ(B) < \Delta G_f^\circ(A) \qquad (3)$$

and that both A and B are in the crystalline state at the reaction temperature, T_r, i.e. $T_r < T_{MA}$, $T_r < T_{MB}$ where T_{MA} and T_{MB} are the melting temperatures of A and B. The standard reference states of A and B are taken as pure crystalline A and B at T_r and P_r.

The general properties for Gibbs free-energy curves in binary heterophase mixtures are described in detail in Ref. 12. The Appendix gives a summary of the features which are important in this discussion.

Several cases can be considered depending on the type of phase diagram exhibited by the A + B system. Below we consider the two most common cases.

Eutectic of A and B, totally immiscible in the crystalline state

The two possible variants of the Gibbs energy diagram for such systems below the eutectic temperature can be described as in Figures 1 and 2. The curve ab_a is that for

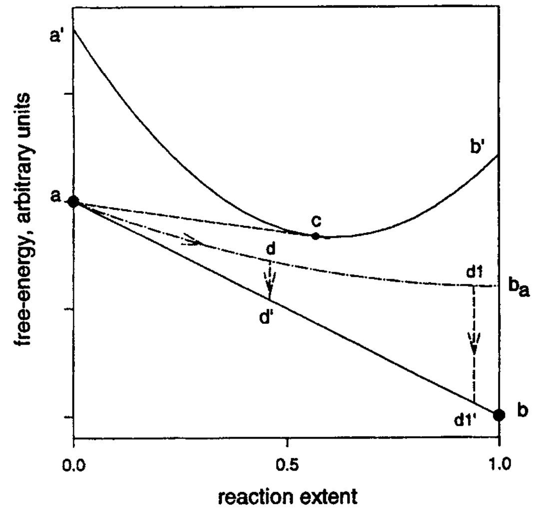

Figure 1. General appearance of the Gibbs free-energy diagram for a simple eutectic system, A–B, below the eutectic temperature. The crystalline solid solution is stable with respect to the amorphous solution. The points a, b, a′, b′ and b_a are free energies of formation of crystalline A, crystalline B, liquid A, liquid B and polymorphous unstable crystalline B, respectively. The solid curve a′cb′ is the free-energy curve for the amorphous solution, add_1ba is the free-energy curve for the solid crystalline solution and c is the composition of the amorphous solution in equilibrium with crystalline A. The chemical reaction follows along curve adb_a until ⟨B⟩ crystallizes; crystallization of ⟨B⟩ is a random event, and the lines dd′ and d_1d_1' show possible examples of ways for the crystallization of ⟨B⟩ to occur

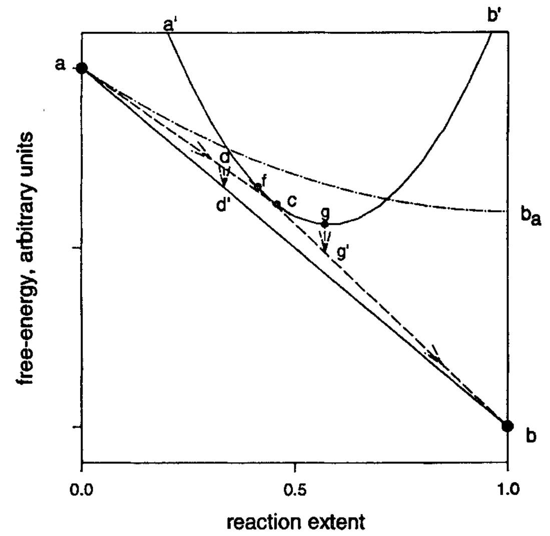

Figure 2. General appearance of the Gibbs free-energy diagram for a simple eutectic A–B system below the eutectic temperature. The amorphous solution is stable with respect to the crystalline solution; f is the composition of the amorphous solution in equilibrium with ⟨B⟩; c is the composition of the amorphous solution in equilibrium with ⟨A⟩; g is the point of a minimum on the free-energy curve for the amorphous solution corresponding to the maximum yield in the amorphous state (see text and Figure 1 for explanation of other symbols). The lines dd′ and gg′ show possible examples of ways for crystallization of ⟨B⟩ to occur

a crystalline solid solution and a′b′ is the curve of an amorphous solution. Amorphous solutions can be liquids or solids depending on the relationships between the temperature and any glass transition temperature. Both crystalline solid solutions and amorphous solutions are thermodynamically unstable with respect to a mixture of purely crystalline A and B in the system under consideration.

We consider in this discussion the case in which the free-energy curve for an amorphous solution has a minimum and for a crystalline solid solution that does not have a minimum. Other combinations can be considered by the same approach.

If the chemical reaction starts from pure A, we can assume three possible pathways: formation of crystalline B, ⟨B⟩ (along the segment ab in Figures 1 and 2); formation of a metastable crystalline solid solution (along the segment ad in Figure 1); and formation of an amorphous solution, S (along the segment ac). For all three cases $\Delta G_r < 0$, and the reaction can proceed by any of these pathways. From Figures 1 and 2, it can be seen that the most thermodynamically stable state is a mixture of crystalline A and B, hence from the beginning of the reaction the formation of ⟨B⟩ is favored. However, the formation of a new crystalline phase involves overcoming a significant energy barrier, i.e. nucleation, whereas the activation energy for the formation of both the amorphous and crystalline metastable solid solutions is essentially zero. Therefore, on the basis of kinetics we can assume that the formation of a solution is more probable. The most likely pathway of the chemical reaction, therefore, also depends on the free energy relationships between the amorphous and crystalline solid solutions in any particular case.

Figure 1 shows a case where the amorphous solution is metastable with respect to the crystalline solution. In this case the reaction involves the formation of a solid solution of B in A along line ab_a, which is metastable with respect to a mixture of pure ⟨A⟩ and ⟨B⟩. The crystallization of ⟨A⟩ + ⟨B⟩ (dd′ or d_1d_1', for example) depends on numerous factors governing its nucleation and crystal growth. Figure 2 gives a case in which the crystalline solid solution is metastable with respect to the two-phase system, ⟨A⟩ + amorphous solution of composition c, and, therefore, the formation of an amorphous solution is possible. On the reaction path ac a mixture of ⟨A⟩ and amorphous solution, c will exist. Further reaction beyond this point will depend on the crystallization of ⟨B⟩.

If crystallization of ⟨B⟩ is hindered, ⟨A⟩ will disappear when the overall chemical composition of the reacting system reaches point c. Beyond point c the system consists of only one phase (S) and the reaction now moves along the segment cg. After point g (point of minima on the a′b′ curve) the reaction cannot proceed in solution because the chemical potentials of the reactant A and product B are equal, hence $\Delta G_r = 0$ Thus the reaction can now proceed only through the formation of crystalline B. Crystallization of B from the solution causes the formation of an amorphous solution of composition f, and further reaction proceeds in an amorphous solution with composition between f and g. Crystallization of ⟨B⟩ changes the composition of the amorphous solution from right to left, supporting the thermodynamic driving force for the transformation of A in solution which changes the composition from left to right. On the other hand, B can crystallize from the supersaturated solution, c, in the beginning of the reaction (line dd′) and in this case ⟨A⟩ can be directly transformed into crystalline ⟨B⟩ on the nucleus formed. In all cases described above, this reaction leads to the production of 100% ⟨B⟩.

Limited solubility of A in B and B in A in the crystalline state

In Figure 3 we present one example of a possible free energy diagram for such a system. In this case the following phases can exist: crystalline phase 1 (crystalline A, ⟨A⟩, or a solid solution of B in A, $\langle \mathrm{SS}_1 \rangle$), crystalline phase 2 (crystalline B, ⟨B⟩, or a solid solution of A in B, $\langle \mathrm{SS}_2 \rangle$) and an amorphous solution (S). Here, we assume that the free-energy curves for crystalline solid solutions and amorphous solution both exhibit minima. In the beginning of the reaction $\langle \mathrm{SS}_1 \rangle$ forms along segment a–f, the most thermodynamically favorable pathway. After point f, a two-phase mixture of $\langle \mathrm{SS}_1 \rangle + \langle \mathrm{SS}_2 \rangle$, a more thermodynamically favorable state, exists; however, the reaction can proceed up to point g_1 in the homogeneous $\langle \mathrm{SS}_1 \rangle$ state. Beyond g_1, the transformation of A to B requires a phase change at which point $\Delta G_r < 0$. Thus at this point, in contrast to the homogeneous nature of the reaction at a lower reaction extent, the thermodynamic driving force for the reaction is now the phase transformation that can occur along the line f″c or fh.

From this diagram, therefore, we can discuss two possible reaction processes after point g_1: (1) the formation of $\langle \mathrm{SS}_2 \rangle$ with composition h; and (2) the formation of an amorphous solution with composition c. The relative driving force for these processes would be $1 > 2$, so from a thermodynamic perspective one can expect the formation of the two-phase system $\langle \mathrm{SS}_1 \rangle + \langle \mathrm{SS}_2 \rangle$ to be favored. From a kinetic perspective, however, it is possible for certain metastable phases to be preferred. For example, the formation of a new crystalline phase ($\langle \mathrm{SS}_2 \rangle$) will have a finite energy of activation, E_a, associated with such a transformation, whereas the formation of an amorphous solution will have $E_a = 0$. In this case we might expect the formation of the amorphous phase (glassy or liquid) to be the favorable pathway. However, as described for a system with complete immiscibility in the solid state (Figure 2) above, although the reaction would proceed from f to point g in this manner, at this point it would require crystallization of $\langle \mathrm{SS}_2 \rangle$ to proceed further.

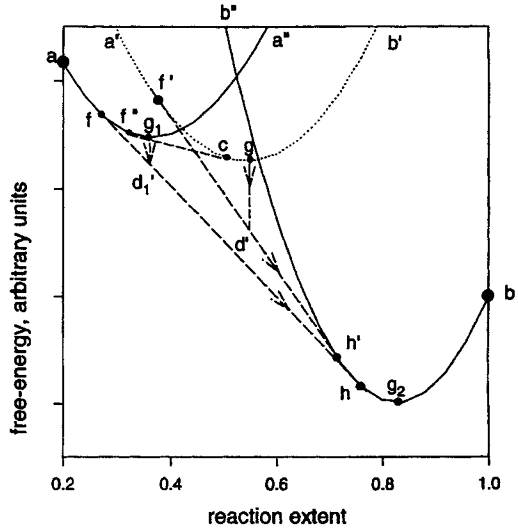

Figure 3. General appearance of the Gibbs free-energy diagram for the eutectic system with limited solubility in the solid state below the eutectic temperature (part of the diagram near A is not shown): aa″ and bb″ are part of the free-energy curves for solid solution of B in A ⟨SS1⟩ and solid solution of A in B ⟨SS2⟩, respectively; f and h are compositions of ⟨SS1⟩ and ⟨SS2⟩ in equilibrium; f″ and c are compositions of ⟨SS1⟩ and amorphous solution (S) in equilibrium; f′ and h′ are compositions for S and ⟨SS2⟩ in equilibrium; $g_1d'_1$ and gd′ are possible ways for ⟨SS2⟩ to crystallize from ⟨SS1⟩ and S, respectively; g_1, g_2 and g are points of minima on the free-energy curves for ⟨SS1⟩, ⟨SS2⟩ and the amorphous solution, respectively

Influence of phase transformations on solid-state chemical kinetics

To obtain physically meaningful parameters from kinetic studies (rate constants, activation energies), it is necessary to choose a proper kinetic model. There are many kinetic equations available for the treatment of solid-state kinetic data (see Ref. 9 for a review). Most equations are based on the nucleation and growth of a new phase, while others assume a two-phase system involving liquification.[10,13] In many cases the same set of experimental data has been shown to be described by more than one equation, so the choice of the correct kinetic model can be difficult on this basis alone. We would suggest that closer attention to the phase relationships existing in a particular system can provide some improved basis for the choice of a correct kinetic model. Minimally, such an approach helps to separate those reactions involving nucleation from those that are homogeneous or those that involve two phases. Of course, to differentiate further reactions involving different nucleation mechanisms, it is necessary to use additional criteria and observations (see Ref. 9 for a discussion of nucleation mechanisms). To illustrate this within the framework of each case provided in the previous section, we present the following situations.

Complete immiscibility in the solid state (Figures 1 and 2)

(a) With direct transformation of ⟨A⟩ to ⟨B⟩ where chemical reaction and crystallization proceed simultaneously (nucleus is crystalline B), we can expect that the kinetics of reactivity will be best described by equations involving nucleation and growth of the product phase (Avrami–Erofeev, contracting geometry, etc.).

(b) As in Figure 1, the reaction proceeds in a homogeneous phase (solid solution) up to d or d_1 so that equations for homogeneous reactions should be used. It should be noted that a homogeneous character for a reaction does not necessarily mean that the reaction will follow a simple kinetic scheme or that it can be characterized by one rate constant (first order, for example). Kinetic curves for a number of gas-phase and solution homogeneous reactions have a complex shape if this is a chain reaction or other complex reaction (e.g. autocatalysis). Then B crystallizes and the reaction now proceeds directly from ⟨A⟩ to ⟨B⟩. This stage can be described by one of the nucleation-control equations (e.g. Avrami–Erofeev). Hence it requires two different kinetic models to describe the two stages for reactions of this type.

(c) As in Figure 2, the first stage of the reaction involves the creation of an amorphous phase with composition c. Thus, the material contains ⟨A⟩ and the amorphous phase c. In this case we assume that the reaction takes place in both phases and that the transformation of A in the amorphous phase changes the composition of this phase from left to right along the segment cg creating the possibility of ⟨A⟩ dissolving in the amorphous phase. In this particular case, the reaction actually depends on the rate of the chemical transformation itself and on the rate of dissolution of A in the amorphous phase. Thus this process can be described as shown in Scheme 1, where Sc and Sg are the composition of the amorphous solution at points c and g, respectively, in Figure 2.

$\langle A\rangle \rightarrow Sc$	chemical transformation
$Sc \rightarrow Sg$	chemical transformation
$\langle A\rangle + Sg \rightarrow Sc$	dissolution

Scheme 1

The kinetics of solid-state reactions with liquification, such as these under discussion, have been described by Bawn[10] with the use of three constants, first-order rate constants for decomposition of A in the solid and liquid phases, k_s and k_a respectively, and the solubility of the initial material in the presence of liquified product, s. Thus, on the basis of Scheme 1, it is possible to specify the physical meaning of the Bawn equation as follows. If the dissolution rate is much faster than that of the chemical transformation, k_a and k_s will determine the rate of the reaction and s will correspond to the equilibrium composition c (Figure 2). Otherwise, s will correspond to some composition between c and g. In the extreme case, when dissolution of ⟨A⟩ in S is the rate-limiting step, the reaction can be treated as an interfacial reaction, and the overall kinetics can be described by one of the interfacial equations. In this case, the Bawn equation or equations for the interfacial reaction can be used in the region ac while the reaction in the region cg in the amorphous phase would be treated by homogeneous reaction kinetics. Any further reaction beyond point g will proceed with the separation of ⟨B⟩, so let us assume that crystallization of ⟨B⟩ takes place in the homogeneous area (cg) and that the material here consists of ⟨B⟩ and an amorphous phase of composition, f. This amorphous phase should be both physically and chemically unstable, so the chemical reaction changes the composition from f to g. Crystallization of ⟨B⟩ causes the liquid composition to return to f, again creating a driving force for the chemical transformation, and this process will continue until pure ⟨B⟩ is obtained. In this case, therefore, the chemical reaction proceeds only in the amorphous phase. However, in order to maintain a thermodynamic driving force for the chemical transformation, ⟨B⟩ must separate out of the amorphous phase. Thus, two processes control the chemical reaction: chemical transformation itself in the amorphous phase and crystallization of ⟨B⟩. If the rate of crystallization is high enough to maintain the composition of the amorphous phase in the f–g area ($\Delta G_r < 0$), then chemical transformation is the limiting step and the kinetic model will be the same as for a reaction in a homogeneous region. If the reaction is limited by crystallization, equations such as the Avrami–Erofeev equation can be applied.

Limited solubility in the crystalline state (Figure 3)

Initially, the reaction proceeds along the homogeneous pathway (ag_1). Then the reaction switches into a heterogeneous region with the formation of a new phase, which can be either an amorphous solution (path f″c), or a crystalline solid solution 2 (path fh). Again, Bawn-like (two-phase) kinetics can be applied in the case of the formation of an amorphous phase. For the case of the formation of solid solution 2, the Avrami–Erofeev equation (or other interface kinetic equations) can be applied if the limiting step is crystallization. Otherwise, Bawn-like kinetics can be applied when k_a is the reaction rate constant in solid solution 1 and k_s is the rate constant of the reaction in solid solution 2.

Possible types of kinetic schemes in solid-state reactions are given in Table 1. It can be seen that even if the chemical transformation itself obeys a simple law (first order, for example), the kinetic curve can consist of several parts. Besides, reactions belonging to the same kinetic scheme can exhibit different types of kinetic behavior depending on the relationships between constants for individual processes (as for the examples described above).

Induction periods

Central to most previous discussions in the literature of the kinetics of solid-state reactions is the nucleation process which involves an induction period followed by a main reaction.[9] Generally, in such cases an observed induction time is considered to be an unnecessary complication in the treatment of chemical kinetics, generally to be subtracted from any experimental data. In such cases, therefore, the nature of any chemical processes taking place during this period is often neglected and considered to primarily involve the formation of a 'germ nucleus.' This is certainly understandable when considering reactions involving explosives, since the most critical part of the reaction lies beyond the induction period. However, in other cases, such as during the assessment of storage stability for pharmaceuticals, this earlier period in the reaction could represent the most important part.[14]

On the basis of the considerations given above, it is possible to think of at least three types of induction period associated with solid state reactions. First is an induction period due to nucleation of a new crystalline phase. These can include direct conversion of $\langle A\rangle$ to $\langle B\rangle$ or, after some reaction, crystallization of $\langle B\rangle$ from an amorphous phase or from a solid solution as in Figures 1 and 2, or crystallization of SS_2 from SS_1 or from the amorphous state, as shown in Figure 3. In the former case the induction period is seen from the very beginning of the reaction, whereas in the latter case the initial reaction proceeds in a homogeneous phase and attains a certain level of conversion before nucleation and crystal growth. Figure 4 gives a hypothetical plot for the latter case wherein two parts of the kinetic curve are separated by an induction period.

A second type of induction period is one that arises due to an acceleration of the reaction in the liquid phase.

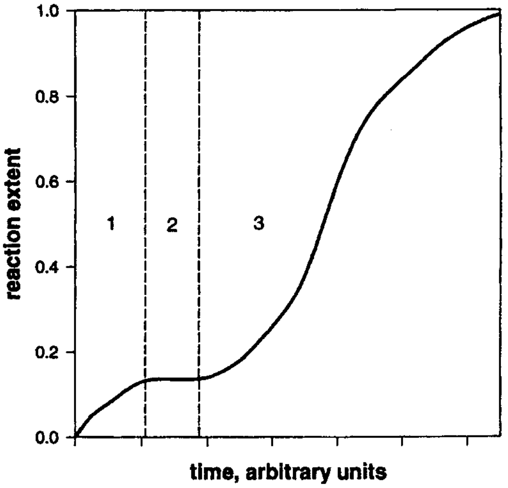

Figure 4. Hypothetical kinetic curve for the reaction in Figure 3, following the reaction pathway $\mathrm{afg_1d'_1hg_2}$. 1, Homogeneous reaction in $\langle SS1\rangle$; 2, induction period for crystallization of $\langle SS2\rangle$; 3, reaction in $\langle SS1\rangle + \langle SS2\rangle$

Table 1. Main types of kinetic schemes for solid-state reactions depending on the type of phase diagram

No.		Kinetic scheme[a]	Number of stages in the kinetic curve
1		Complete immiscibility in the solid state	
	(a)	$\langle A\rangle \rightarrow \langle B\rangle$	1
	(b)	$\langle A\rangle \rightarrow \langle SS1\rangle_m \rightarrow \langle A\rangle + \langle B\rangle \rightarrow \langle B\rangle$	2
	(c)	$\langle A\rangle \rightarrow \langle A\rangle + S_m \rightarrow \langle A\rangle + \langle B\rangle \rightarrow \langle B\rangle$	2
	(d)	$\langle A\rangle \rightarrow \langle A\rangle + S_m S_m \rightarrow \langle B\rangle + S_m \langle B\rangle$	3
2		Partial solubility in the solid state	
	(a)	$\langle A\rangle \rightarrow \langle SS1\rangle \rightarrow \langle SS1\rangle_m \rightarrow \langle SS1\rangle + \langle SS2\rangle \rightarrow \langle SS2\rangle$	3
	(b)	$\langle A\rangle \rightarrow \langle SS1\rangle \rightarrow \langle SS1\rangle_m \rightarrow \quad \rightarrow \langle SS1\rangle + \langle SS2\rangle \rightarrow \langle SS2\rangle$	4
	(c)	$\langle A\rangle\langle SS1\rangle\langle SS1\rangle_m + S_m \rightarrow S_m \rightarrow S_m + \langle SS2\rangle \rightarrow \langle SS2\rangle$	5
	(d)	$\langle A\rangle \rightarrow \langle SS1\rangle \rightarrow \langle SS1\rangle_m + S_m S \rightarrow \quad \rightarrow \langle SS1\rangle + \langle SS2\rangle \rightarrow \langle SS2\rangle$	5

[a] $\langle A\rangle$ and $\langle B\rangle$ are pure crystalline A and B, $\langle SS1\rangle$ and $\langle SS2\rangle$ are crystalline solid solutions of B in A and A in B and S is an amorphous solution. The subscript m indicates a metastable phase (it is assumed that the reaction temperature is lower than solidus temperature).

It might be seen with a situation that is shown in Figure 3, where a slow reaction in the SS_1 solid-solution phase switches to a 'fast' reaction in the liquid phase (see Figure 3, for the transition from the homogeneous pathway ag to the pathway f″c). Finally, a third apparent induction period can arise because of the more complex homogeneous reactions such as with chain reactions.[15]

With these thoughts in mind, it would appear that those initiating a study of solid-state chemical kinetics should first address the following two questions: is this a complex homogeneous reaction and if not, are there any phase changes taking place during the reaction? If the answer is 'yes,' at which stage of the reaction do they take place?

EXPERIMENTAL CASE STUDIES

In this final section we have chosen to analyse, in the context of the previous discussion, a number of studies in the literature that provide sufficient data for such an analysis. They each represent one of the two major cases presented above.

Complete immiscibility in the crystalline state

Very detailed studies of the *cis* to *trans*-azobenzene isomerization have been carried out by Cammenga and co workers[16,17] This is eutectic system ($T_e = 41\cdot 4\,°C$) with complete immiscibility in the solid state, or at least with very restricted solubility (according to the phase diagram in Ref. 16 the solubility in mole fraction of the *trans* isomer in the *cis* isomer is $<0\cdot 02$, and that of the *cis* in the *trans* isomer $<0\cdot 1$). Conversion in the melt and below the eutectic temperature was shown to be close to 100%. Direct microscopic observation of a nucleus for the reaction at 40 °C and the sigmoidal shape of the kinetic curves allow us to assume that this reaction follows kinetic scheme 1a (Table 1), i.e. direct $\langle A\rangle \longrightarrow \langle B\rangle$ transformation (line ab, Figures 1 and 2). Hence the rate constants obtained from the treatment of experimental data by one of the nucleation/growth equations (as was done in the original paper) can be physically meaningful.

However, this is not the case for the rate constants obtained for the reaction at temperatures between the eutectic temperature and the melting point of the *cis*-isomer (54·2–65·3 °C). The kinetic curves, also having a sigmoidal shape, were described well by the Prout–Tompkins equation;[17] however, we consider this to have limited physical meaning in this particular system. Indeed, in this case the reaction scheme can be represented better as

$$\langle A\rangle \longrightarrow \langle A\rangle + S \longrightarrow S \longrightarrow \langle B\rangle + S \longrightarrow \langle B\rangle.$$

This scheme is formally the same as the 1d in Table 1, with the exception that S in the former case is a stable phase whereas in the 1d S is the metastable phase. The kinetic curves must consist of three parts, with a majority of the experimental points (from Ref. 17) lying in the two-phase $\langle A\rangle + S$ region. Thus, in this case, a two-phase kinetic expression, e.g. Bawn equation,[10,13] is more appropriate:

$$x = (k_s\Gamma)[\exp(\Gamma t) - 1] \qquad (1)$$

where t is time, x is the fraction reacted, Γ is $k_s + k_s s - k_a$), s is the fractional solubility of the reactant in the liquid phase (in moles of reactant per mole of product) and k_s and k_a are the rate constants in the solid and liquid phases, respectively.

We have treated experimental data from Ref. 17 (Figure 4 from Ref. 17) as follows. The values of $s = (1 - x)/x$ (where x is the molar fraction of the *trans*-isomer) were determined from the liquidus line for the *cis*-isomer,[16] and the data were fitted to equation (1) with two adjustable parameters, k_s and k_a and the aid of Sigma Plot software. Figure 5 gives the Arrhenius plots for k_a and k_s. To estimate the reliability of the rate constants obtained from this procedure, we compared k_a with rate constants for the melt[17] extrapolated from higher temperatures. Figure 5 also gives the rate constants for isomerization in the melt (the part of the solid line marked by arrows). Here, it can be seen that the values of k_a are lower than the extrapolated values, and the difference increases as the temperature decreases. Note that the determination of s from the phase diagram assumes that at all times there is an equilibrium composition of the liquid phase. In other words, we assumed

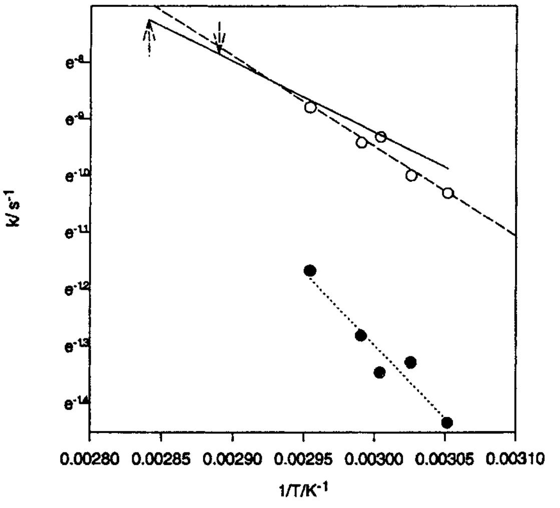

Figure 5. Arrhenius presentation of the rate constants for *cis–trans* isomerization of azobenzene in the two-phase region:[17] k_a and k_s from the Bawn equation are represented by open circles and filled circles, respectively; the solid line fits $k = {}^{12\cdot 2}\exp(-103\cdot 4/RT)$;[17] the broken line is a linear fit for k_aa; the dotted line is a linear fit for k_s

Table 2. Solubility of the reactant in the liquid phase, s, for the *cis–trans* isomerization of azobenzene[16,17] as a parameter of the Bawn equation

Temperature (K)	s from the phase diagrams	s as fitting parameter with fixed k_a
338·5	5·99	5·24
334·4	3·51	2·56
332·9	3·15	3·03
330·5	2·48	1·56
327·7	1·99	1·27

that the rate of dissolution of A in the liquid phase is much greater than the rate of the chemical transformation. However, it is possible that the dissolution rate is comparable, and in this case the concentration of A in the liquid phase will be lower than that estimated from the phase diagram. To evaluate the possibility that the dissolution rate is a factor here, we repeated the fitting procedure using a fixed k_a (from data taken in the melt and the Arrhenius equation), with k_s and s as adjustable parameters. We find in this case that the values of k_s are essentially the same as obtained in the first fit, but that the s values are lower than those estimated from the phase diagram (see Table 2). Based on this analysis, we conclude that the treatment of these data in terms of two-phase kinetics provides physically meaningful rate constants for the reaction which cannot be obtained from the treatment using the Prout–Tompkins equation.

Limited solubility in the crystalline state

An example of a chemical reaction in the solid state involving limited solubility is found in the work of Sukenik *et al.*[18] on a thermally induced molecular rearrangement in methyl-*p*-dimethylaminobenzene sulfonate below and above the melting temperature of the reactant (91 °C). Here, at least three crystalline phases were detected by x-ray powder diffraction when the reaction had been carried out at ambient temperature. Unfortunately, the authors did not indicate the temperature of the reaction, but it would appear to correspond to the 'ambient' temperature mentioned in Table II of Ref. 18. Moreover, there are no x-ray data available for the reaction at 81 and 88 °C.

In Ref. 18, it was claimed that three crystalline phases existed: the reactant (MSE), called the α-phase, the product (ZWT), called the β-phase, and an intermediate, called the γ-phase. Analysis of the system by x-ray diffraction (Table V in Ref. 18) indicated that after 2 and 6 days a binary crystalline mixture of $\alpha + \gamma$ was produced. Since the authors identified only MSE and ZWT to be present in this mixture, we can conclude that γ was not a new chemical intermediate. The x-ray pattern after 8 days (49·4% conversion) appears to be similar to that of the recrystallized ZWT, which indicates that the β-phase might be a solid solution of the reactant in the product. There are three possible forms of the γ phase: a molecular compound of ZWT and MSE with congruent or incongruent melting, or a solid solution (phase diagram with intermediate solid solution, Figure 6). Let us consider the last case as an example, and think of the possible scheme at ambient temperature where the x-ray diffraction data were obtained (scheme 2) in Table 1 with additional solid solution):

$$\langle \mathrm{MSE} \rangle \rightarrow \langle \mathrm{SS}\,\alpha \rangle \rightarrow \langle \mathrm{SS}\,\alpha \rangle + \langle \mathrm{SS}\,\gamma \rangle \rightarrow \langle \mathrm{SS}\,\gamma \rangle + \langle \mathrm{SS}\,\beta \rangle \rightarrow \langle \mathrm{SS}\,\beta \rangle$$

Scheme 2

From Scheme 2, we can see that the kinetic curve at ambient temperature will consist of five parts even though the chemical reaction itself is a simple first-order process. Of course, it is possible that the kinetic pictures at 81 and 88 °C will be different. For example, since these temperatures are close to the melting temperature of the reactant (90–91 °C), the formation of product might lower the melting temperature enough (see Figure 6), so that part of the reaction, at least, might take place in the liquid phase.

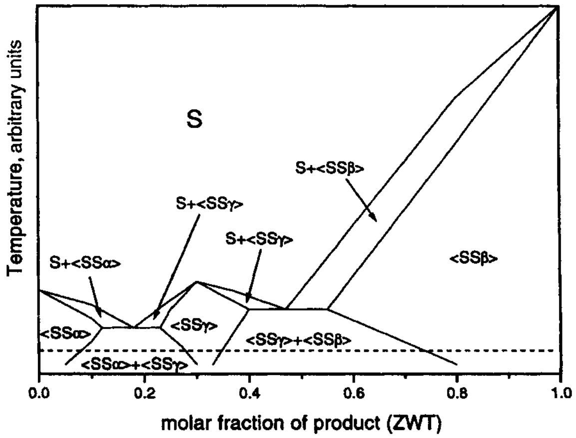

Figure 6. Hypothetical phase diagram for the MSE–ZWT system described in Ref. 18 (and in the text). The broken line shows the system at ambient temperature. SSα is a solid solution of ZWT in MSE; SSβ is a solid solution of MSE in ZWT; SSγ, is an intermediate solid solution; S is a liquid solution

It should be pointed out that the same reaction has been studied by laser Raman spectroscopy[19] and at a point where 40% conversion of MSE occurred, two crystalline phases, pure MSE, and pure ZWT, appear to exist. This is in contradiction to the earlier described x-ray diffraction studies that claim the presence of a γ intermediate form. Unfortunately, the exact conditions of this latter experiment were not detailed.

Another reported study where limited solubility may be involved in a solid-state chemical reaction is the apparent uni-directional $\beta-\alpha$ isomerization of the cobaloxime complex with different ligands.[20] In this solid-state reaction, with an increase in the time of irradiation the $\alpha:\beta$ ratio increased and approached a certain value asymptotically. Hence we can assume that the final $\alpha:\beta$ ratio corresponds to the minimum free energy of the solution of α in β. However, the reverse process, $\alpha \longrightarrow \beta$, does not occur, with no apparent reasons given by the authors for such unidirectional photoisomerization. We assume that this can be explained with two assumptions: (1) this system exhibits limited solid-state solubility, and either β is not soluble in α at all, or the amount dissolved is below the limits of the assay sensitivity; and (2) under the conditions of these experiments there was not enough time for the stable crystal phase to crystallize. Hypothetical Gibbs energy relations for this system are shown in Figure 7 (we assumed the case of complete immiscibility of β in α since arguments for restricted solubility are identical). There are two possible cases: (1) when the α form (point b_1 in Figure 7) is more stable than the solid solution with a composition corresponding to point g in Figure 7. In this case the solid solution obtained after irradiation is metastable with respect to pure $\langle\alpha\rangle$. In such a case the process $\alpha \longrightarrow \beta$ is prohibited thermodynamically. (2) In the second case, if the solid solution is more stable than α (point b_2 in Figure 7), the reverse reaction $(\alpha \longrightarrow \beta)$ can take place but it requires that an activation energy for crystallization of the solid solution be overcome. It may be possible that the conditions of these experiments did not allow enough time for a stable phase to crystallize.

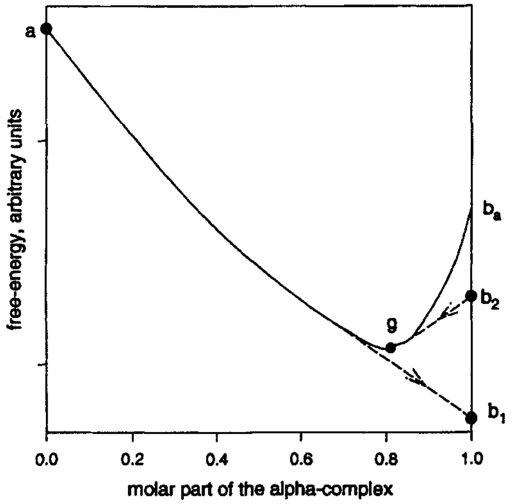

Figure 7. Hypothetical Gibbs free-energy diagram for (β,α-substituted ethyl)bis(disubstituted glyoximato)(pyridine)cobalt(III):[20] g is the point of maximum yield for the homogeneous transformation; b_1, b_2 are two possible cases for the free-energy of formation of crystalline $\langle\alpha\rangle$; b_a is the free energy of formation of the unstable polymorph of $\langle\alpha\rangle$

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APPENDIX

General properties of Gibbs free-energy curves in binary heterophase mixtures[12]

1. A two-component system below the solidus temperature can be homogeneous (one-phase solution) or heterogeneous (physical mixture of two phases).

2. The free-energy for the physical mixture is described by a straight line connecting the free-energy points for the corresponding phases.

Example: a mixture of pure crystalline ⟨A⟩ and ⟨B⟩, on the line ab (Figure A1).

The formation of a solution is possible if the solution free energy is less than the free energy of the physical mixture with the same composition.

Example: a crystalline solid solution of B in A, ⟨SS1⟩, on the curve afa' (Figure A1).

3. In order to determine the composition of two phases in equilibrium, it is necessary to construct a common tangent line.

Example: the equilibrium between ⟨SS1⟩ and ⟨B⟩, on the line fb, with a composition of ⟨SS1⟩corresponding to point f.

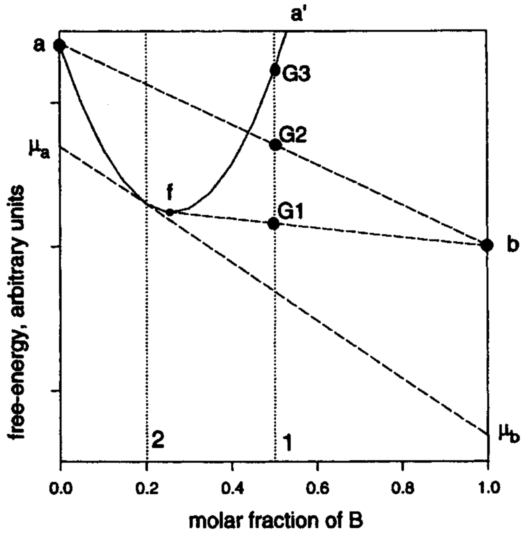

Figure A1. General appearance of the Gibbs free-energy curve for a binary system: points a and b are the standard free-energies of formation of crystalline A (⟨A⟩) and B (⟨B⟩), respectively. Segment afa' is the Gibbs free-energy curve for a solid solution of B in A (⟨SS1⟩), segments ab and fb represent the free-energy of the physical mixture of ⟨A⟩ + ⟨B⟩ and ⟨SS1⟩ + ⟨B⟩, respectively; μ_a and μ_b are chemical potentials of A and B in a solution of composition 2 (0·2 parts of B). G3, G2 and G1 are different free-energies for the system of composition 1 (0·5 parts of B): ⟨SS1⟩, a physical mixture of ⟨A⟩ + ⟨B⟩, and a physical mixture of ⟨SS1⟩ with composition f + ⟨B⟩, respectively.

4. The thermodynamically stable form will be the one with a minimal free-energy value.

Example: for composition 1 there are three possible states: homogeneous ⟨SS1⟩ (the free-energy value is at G3, Figure A1); a mechanical mixture of ⟨A⟩ + ⟨B⟩ (the free energy value is at G2); and a physical mixture of ⟨SS1⟩ + ⟨B⟩ (the free-energy is at G1). The last state is the most thermodynamically stable.

5. Chemical potentials, μ_a and μ_b, for A and B in solution of given composition can be determined at the intersection of the tangent line to the free-energy curve at a given point with the ordinate.

Example: μ_a and μ_b for composition 2 in Figure A1.