# SUPPLEMENTARY MATERIALS
# A Simple Model Designed to Generate New Crystal Structures Derived from a Mother Phase. Application to Molecular Compounds

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## Abstract

The basic principles of a model predicting new lattices from a known crystal structure is described. The first of the two-step procedure consists in extracting one- or two-dimensional periodic fragments (PF) from the mother structure. In the second step, symmetry operators are added to the PFs in order to generate one or several new three-dimensional lattices consistent with the 230 space groups. Most of the examples are related to polymorphism, but relationships between racemic compounds and enantiomers, twinning and lamellar epitaxy phenomena are also exemplified.

## Table of contents

## Notation

The numbering of the compounds refers to Table 3 of the publication.

# 1    Theoretical examples

## 1.1  generation of two different *Pna2₁* daughter phases from the same mother phase

Two $Pna2_1$ structures are generated starting from two different slices of a mother phase with space group $P2_1/c$ (Fig. S 1). PF1 is a slice composed of the twofold screw axis running along **b** and the translations $T_x$ and $T_y$ of the mother phase. The addition of a glide plane **a** parallel to PF1 automatically generates a glide plane **n**, leading to a daughter phase 1 with space group $Pn2_1a$ ($Pna2_1$ in the standard setting). The slice PF2 contains the glide plane **c** and the translations $T_y$ and $T_z$ of the mother phase. The addition of a twofold screw axis normal to PF2 generates also a glide plane **n**, and gives a daughter phase 2 with the same space group ($P2_1cn$; $Pna2_1$ in the standard setting). Therefore, instead of applying the glide plane **a** to PF1 or the twofold screw axis to PF2, a glide plane **n** can be applied on both PFs at different locations in order to generate the two different daughter phases.
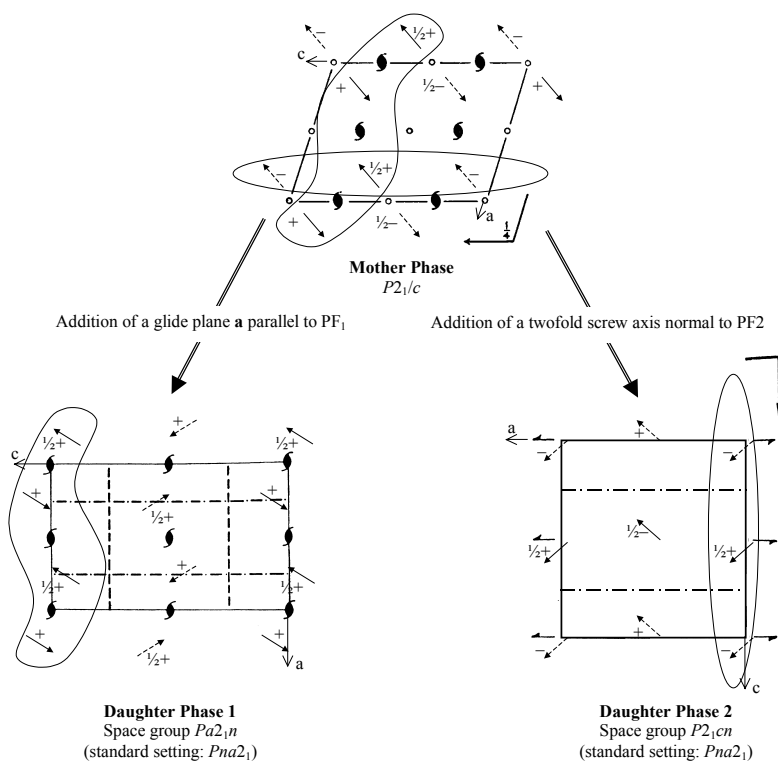


**Fig. S 1.** Construction of distinct Pna21 structures starting from different periodic fragments of a P21/c structure.

## 1.2 Considerations on the asymmetric unit value
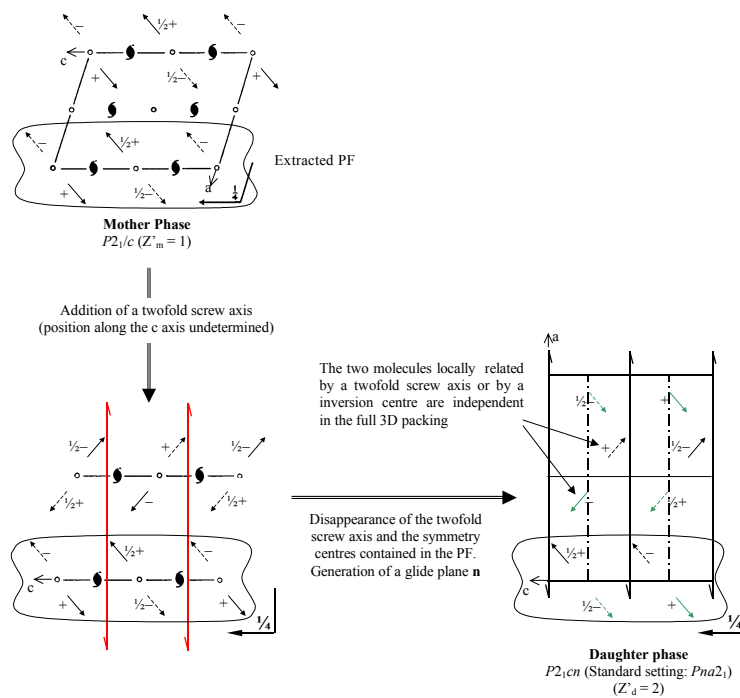


**Fig. S 2.** Generation from a mother phase with $Z'_m = 1$ of a structure with $Z'_d = 2$ in which some symmetries of the PF are not expressed in the full 3D lattice of the daughter phase.

## 2 Construction of a racemic compound for the 5-methyl-5-(4'methylphenyl)-hydantoin (71H)
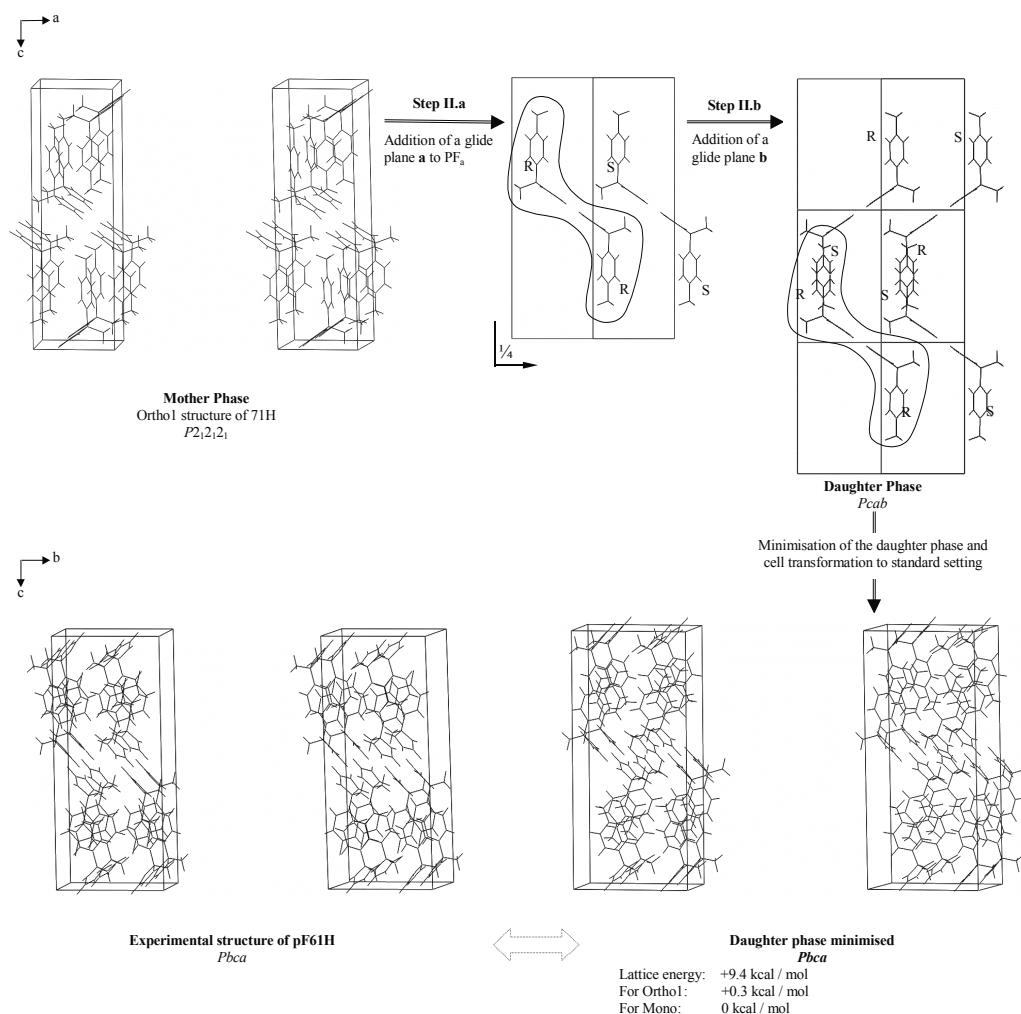


**Fig. S 3.** Construction of a racemic compound from the homochiral ribbon extracted from the Ortho1 structure of 71H. Comparison with the experimental racemic compound of pF61H (stereoviews).

## 3 Application to polymorphism

### 3.1 Application of the model to a 3D hydrogen bond network.

The procedure presented for 5-alkyl-5-aryl-hydantoins is applied to L(+)-histidine (compound **1**), which crystallises in two space groups ($P2_12_12_1$ and $P2_1$) with a similar 3D hydrogen bond network. Three different two-dimensional slices are extracted from the orthorhombic form. Each PF contains one of the three twofold screw axis, the associated translation (*e.g.* $T_x$ for the twofold screw axis running along the a axis), and another translation of the mother phase. For each slice, a translation is added to regenerate the monoclinic form. The resulting daughter phases are minimised using the Open Force Field module of the Cerius[2] software (force field: Dreiding 2.21, with charges derived from the Charge Equilibration algorithm), and their lattice energy is

computed. The predicted structure exhibiting the lowest lattice energy (*i.e.* constructed from the twofold screw axis running along the b axis and the translations $T_y$ and $T_x$) is similar to the experimental monoclinic structure (Fig. S 4). It is noteworthy that adding a translation to this periodic fragment has regenerated the whole 3D H-bond network.
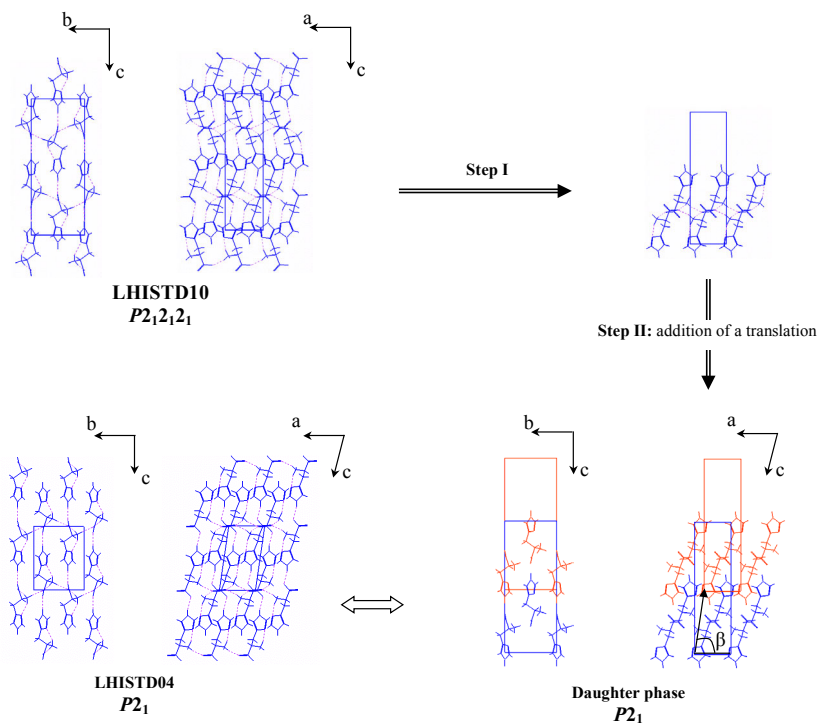


**Fig. S 4.** Construction of a $P2_1$ structure from a $P2_12_12_1$ one in case of a 3D H-Bond network (compound **1**).


### 3.2  Case of the couple $P2_1/c$ and *Pbca*

The construction of a *Pbca* structure from a two-dimensional PF of a $P2_1/c$ structure is described for CUZHUA (compound **2**, Fig. S 5). The two-dimensional PF contains inversion centres, the twofold screw axis running along the b axis, the glide plane **c**, and the associated translations, *i.e.* $T_y$ and $T_z$. The addition of a twofold screw axis normal to the PF and located at $y = \frac{1}{4}$ generates a daughter phase of space group *Pbca*.
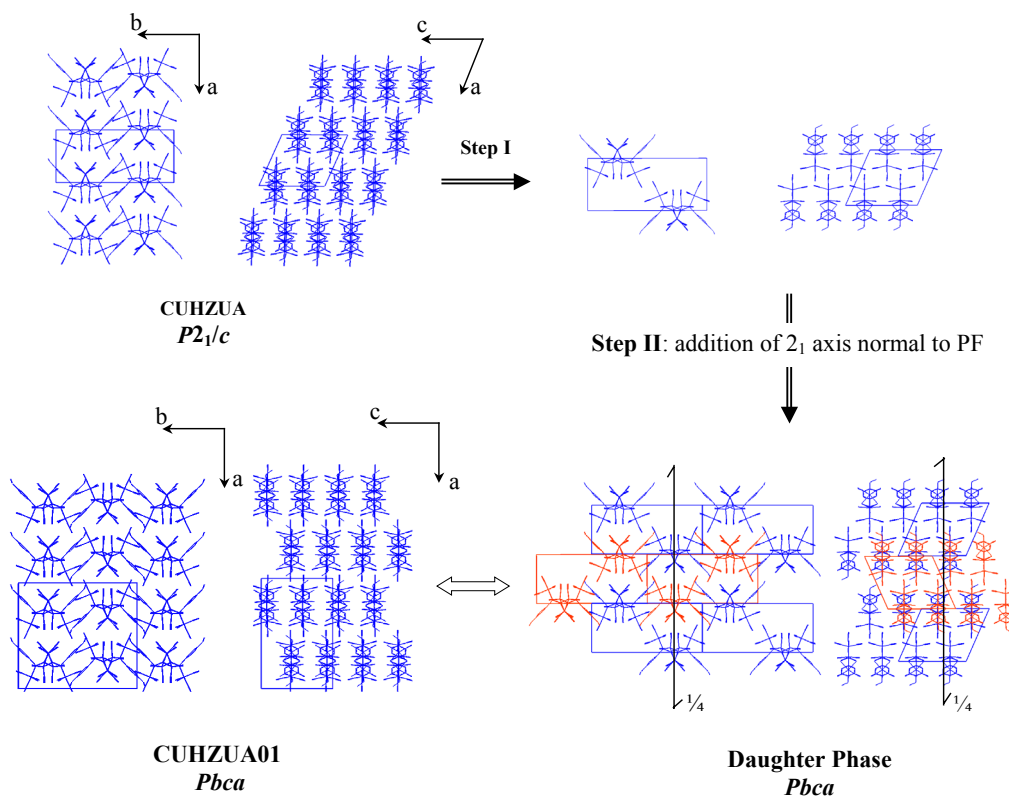
**Fig. S 5.** Construction of the *Pbca* structure starting from a two-dimensional PF of the *P2₁/c* structure (compound **2**).

### 3.3 Construction of daughter phases starting from a ribbon

The construction of a *Pbca* structure from a one-dimensional PF of a $P2_1/c$ mother phase is detailed for a typical example (Fig. S 6). The selected periodic fragment contains two equivalents of the unit cell of the $P2_1/c$ structure, linked together by the glide plane **c** ($y = ¼$), and the associated translation $T_z$. The regeneration of the three-dimensional packing is performed by adding two symmetry operators:

- **Step II-1:** The addition of a twofold screw axis normal to the PF at $y = ¼$ generates a two-dimensional slice. This slice contains as internal symmetries the glide plane **c** ($y = ¼$) which is preserved throughout the regeneration process, the added twofold screw axis and a glide plane **a** which has been automatically created.

- **Step II-2:** The addition of a twofold screw axis parallel to the 2D slice at $y = 0$ generates a daughter phase with space group *Pbca*.
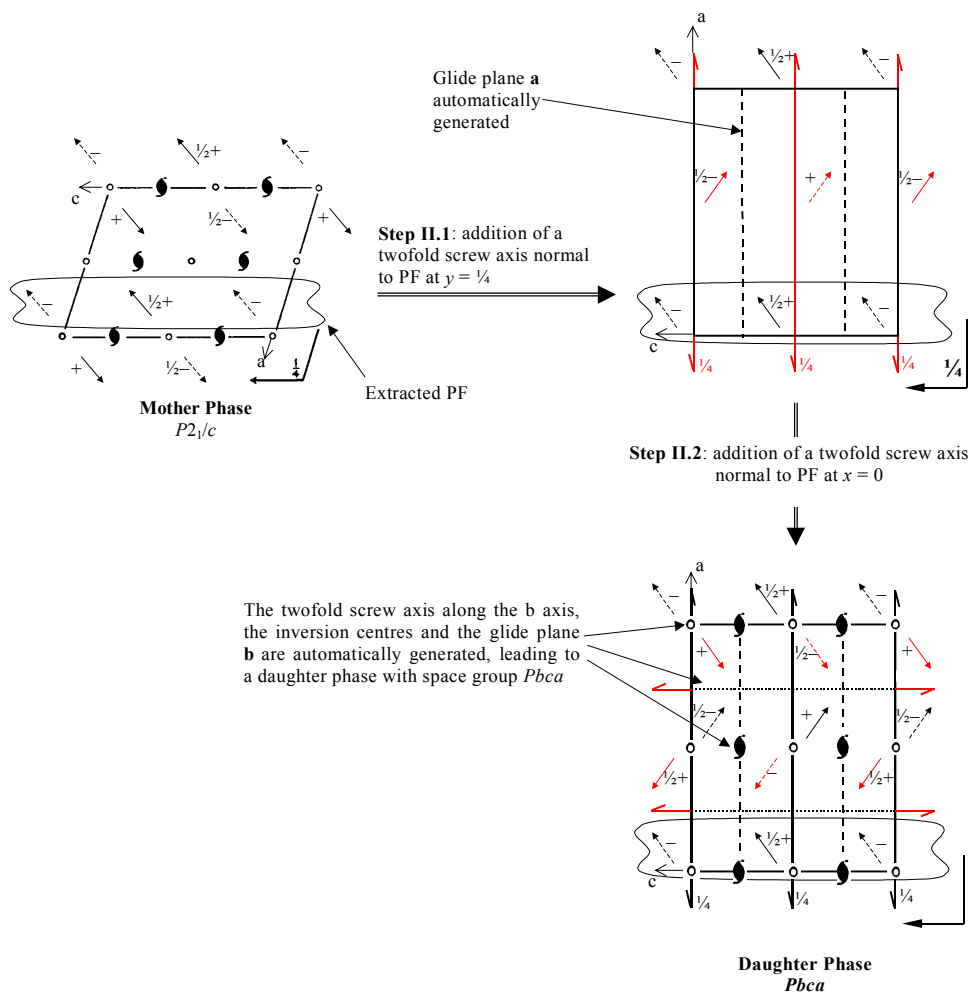
**Fig. S 6.** General example of the construction of a *Pbca* structure from a one-dimensional periodic fragment PF of a *P*2$_1$/*c* structure. (in red: new symmetry operators and the corresponding regenerated equivalents; in green: symmetry operators automatically generated.).

This procedure has been applied to BAZYAC (compound **3**, Fig. S 7). The crystallographic parameters related to the PFs of the mother phase (*P*2$_1$/*c*) and of the experimental *Pbca* structure are slightly different (*i.e. c* = 12.347$\mathring{A}$ and *c'* = 12.977$\mathring{A}$ for *P*2$_1$/*c* and *Pbca* respectively). However, a well-suited minimisation procedure of the daughter phase (*Pbca*) should correct the parameters to those of the experimental structure.
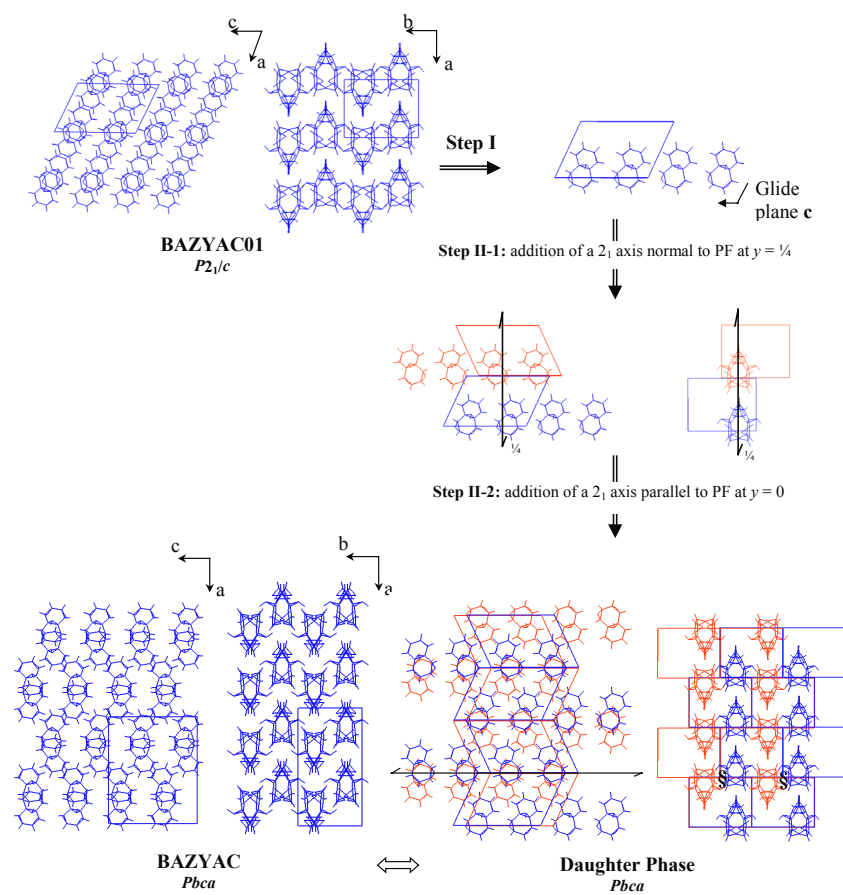
**BAZYAC01**
*P2₁/c*

**Step I**

Glide
plane **c**

**Step II-1:** addition of a 2₁ axis normal to PF at *y* = ¼

**Step II-2:** addition of a 2₁ axis parallel to PF at *y* = 0

**BAZYAC**
*Pbca*

**Daughter Phase**
*Pbca*

**Fig. S 7.** Construction of the *Pbca* structure from a mono-dimensional PF of the *P2₁/c* structure (compound **3**).
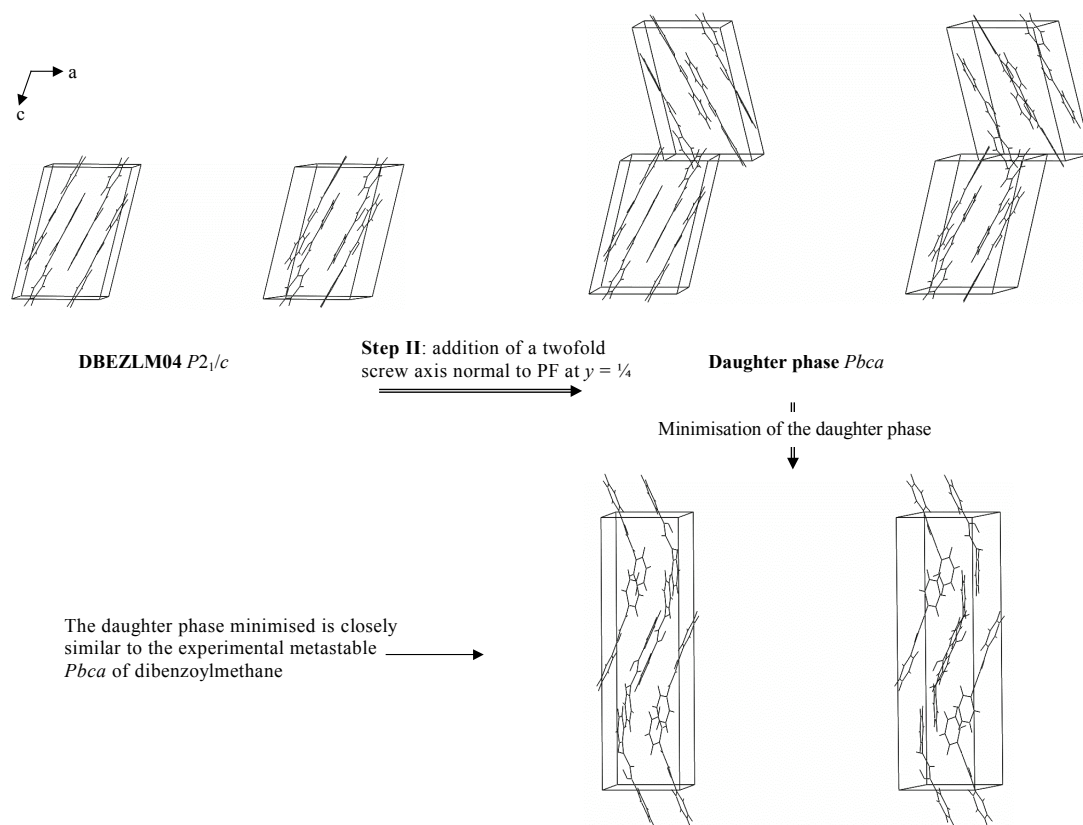
**Fig. S 8.** Construction of the *Pbca* structure of dibenzoylmethane (compound **4**) starting from a two-dimensional PF of the *P*2$_1$/*c* structure. Case of conformational polymorphism.

## 4    Enantiomorphous / non-enantiomorphous structures

### 4.1  Case of *P*2$_1$ and *P*2$_1$/*c*

It is possible to generate non-enantiomorphous structures, starting from an enantiomorphous mother phase. The construction has been successfully performed for non-chiral compounds (KUSVID (**6**), MBZYAN (**7**) and BANGOM01 (**9**) on Fig. S 10, Fig. S 11 and Fig. S 13 respectively) as well as for the single enantiomers of ZZZBLS01 (**5**) and VALEHC11 (**8**), leading to the structures of their racemic compounds (respectively Fig. S 9 and Fig. S 12). In each case, the applied procedure is identical: starting from the *P*2$_1$ structure, a slice containing the twofold screw axis running along the b axis and two translations (including the translation associated to the twofold screw axis) is selected. For compounds **8** and **9**, one of the translation of the PF is a combination of the unit-cell translations (*e.g.* [T$_x$+T$_y$] for compound **8**). The addition of a glide plane **c** normal to PF at *y* = ¼ generates a daughter phase with space group *P*2$_1$/*c*.
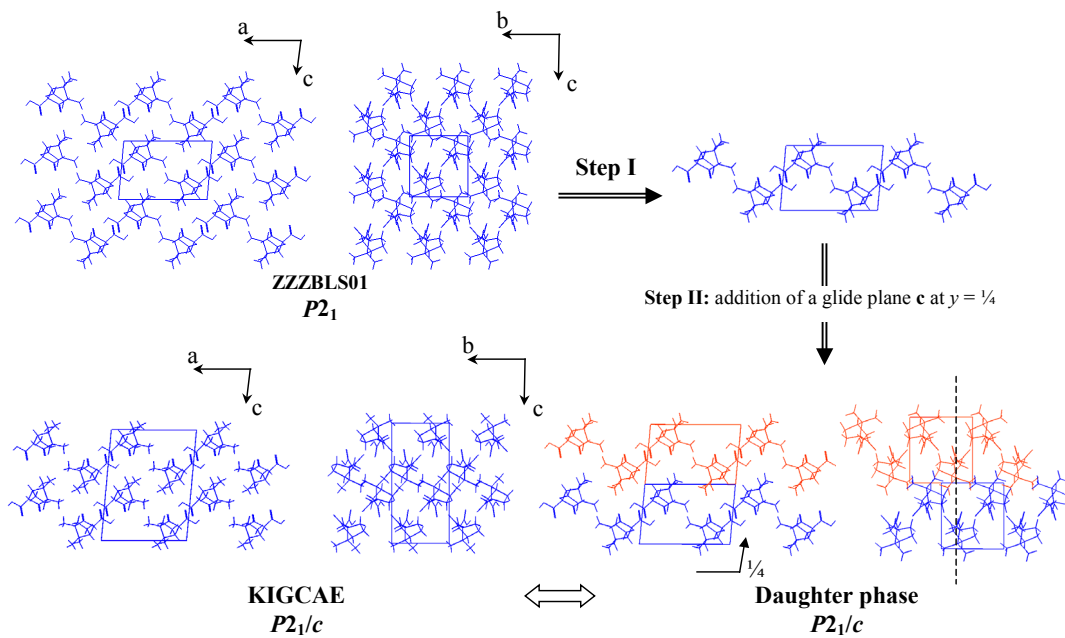
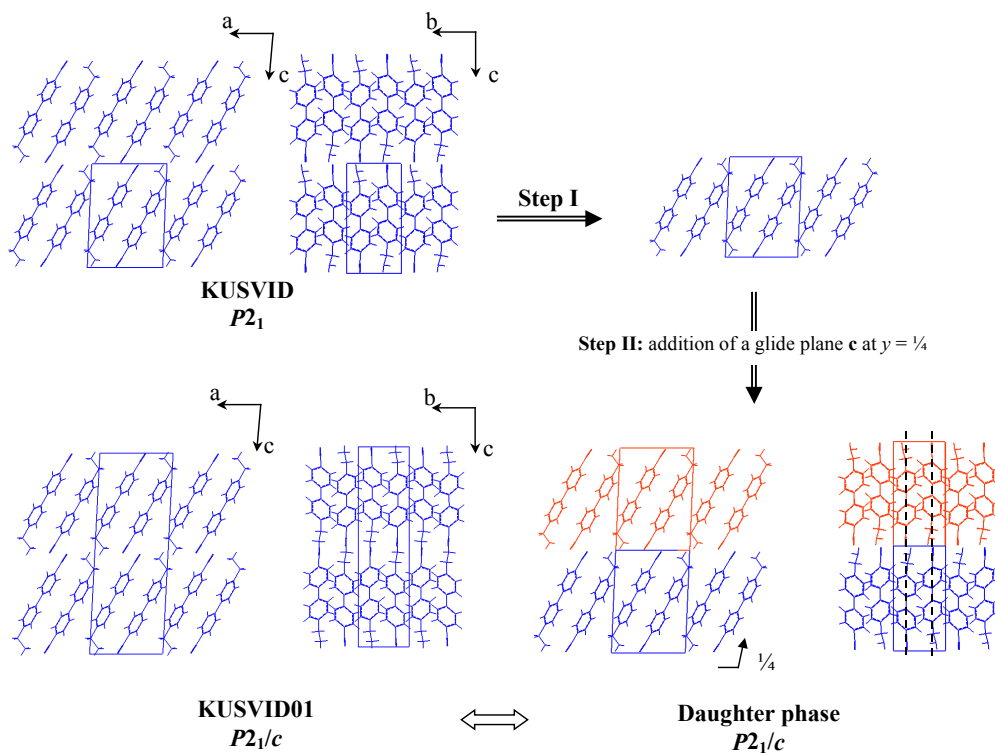**Fig. S 9.** Construction of the $P2_1/c$ structure from a two-dimensional PF of the $P2_1$ structure (compound **5**).



**Fig. S 10.** Construction of the $P2_1/c$ structure from a two-dimensional PF of the $P2_1$ structure (compound **6**).
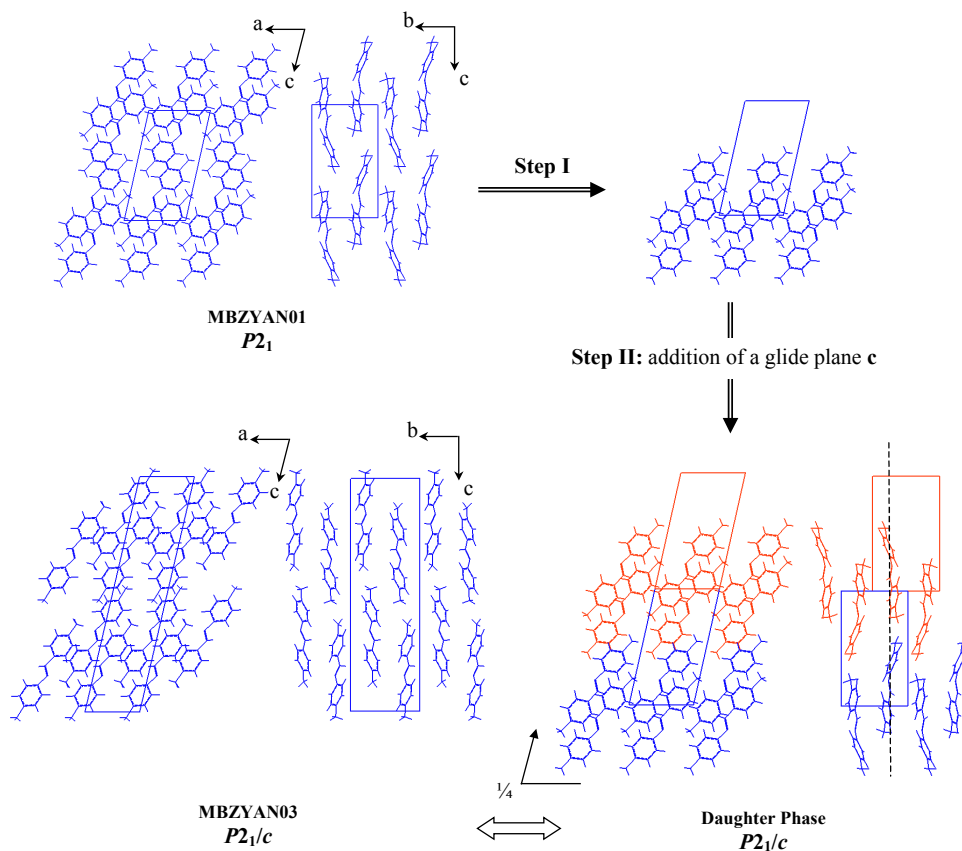
**Fig. S 11.** Construction of the $P2_1/c$ structure from a two-dimensional PF of the $P2_1$ structure (compound **7**).
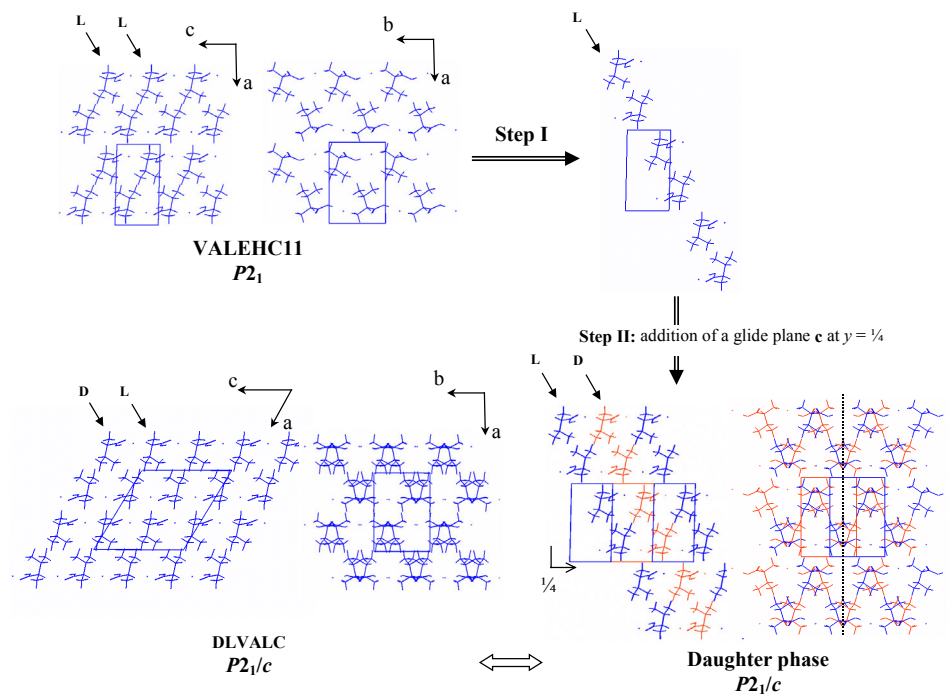


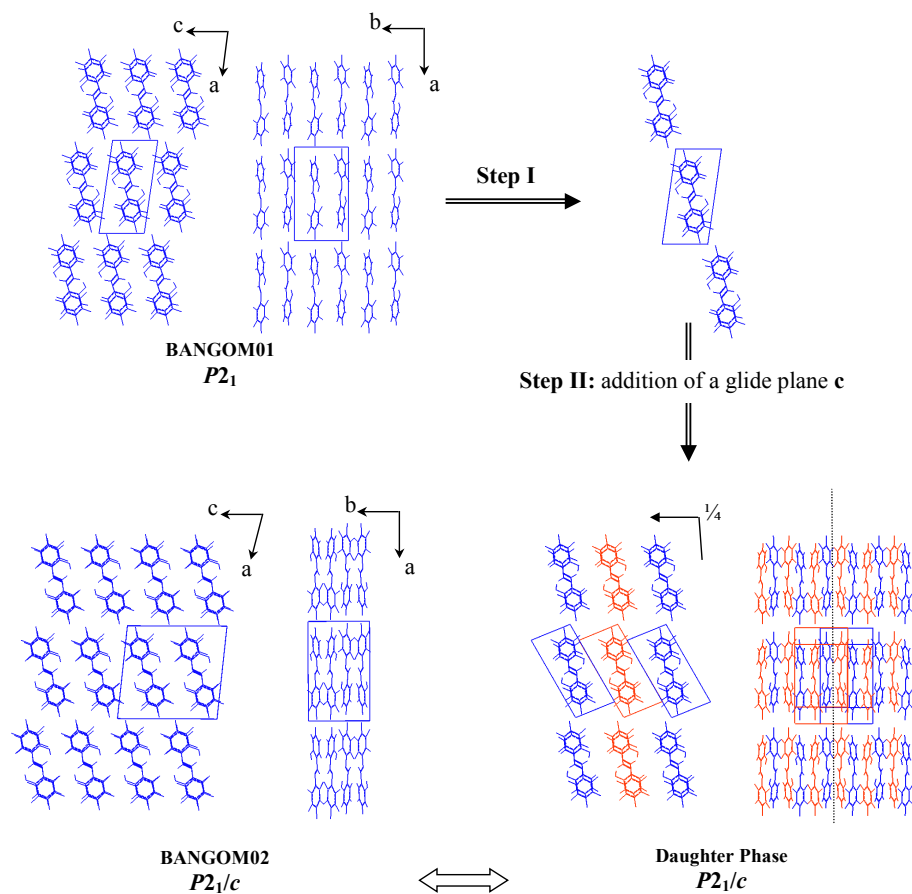**Fig. S 12.** Construction of the $P2_1/c$ structure from a two-dimensional PF of the $P2_1$ structure (compound **8**).

**Fig. S 13.** Construction of the $P2_1/c$ structure from a two-dimensional PF of the $P2_1$ structure (compound **9**).

### 4.2 Case of **C2** and **C2/c**

For TITNEP01 (**10**), a 2D periodic fragment is extracted from the mother phase with space group $C2$ (Fig. S 14). It contains a twofold axis and a twofold screw axis both running along the b direction, as well as the translations $T_z$ and $[T_x+T_z]$. A glide plane **c** normal to the PF and located at $y = 0$ generates a daughter phase with space group $C2/c$. Comparison with the experimental $C2/c$ highlights a slight difference in the $\beta$ angle value and in the orientation of the phenyl groups.
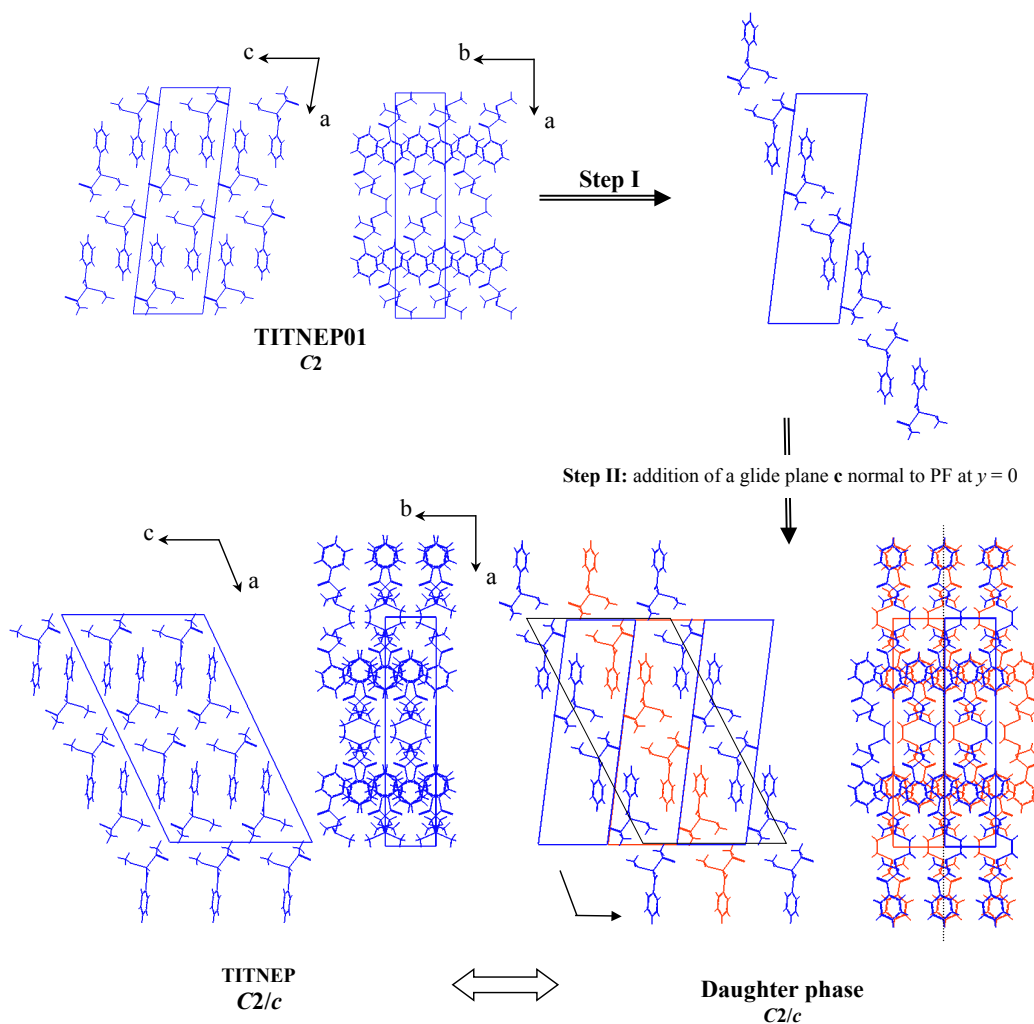
**Fig. S 14.** Construction of the $C2/c$ structure from a two-dimensional PF of the $C2$ structure (compound **10**).

### 4.3 Case of $P2_1$ and $Pna2_1$

Starting from a 2D slice of the $P2_1$ form of DFBPAC (**11**), a $Pna2_1$ structure is generated (Fig. S 15). The PF contains the twofold screw axis running along the b axis and the translations $T_y$ and $T_x$. The addition of a glide plane **c** normal to the PF at $x = ¼$ generates automatically a glide plane **n** normal to the c axis, leading to a daughter phase with space group $Pc2_1n$ (standard setting: $Pna2_1$).
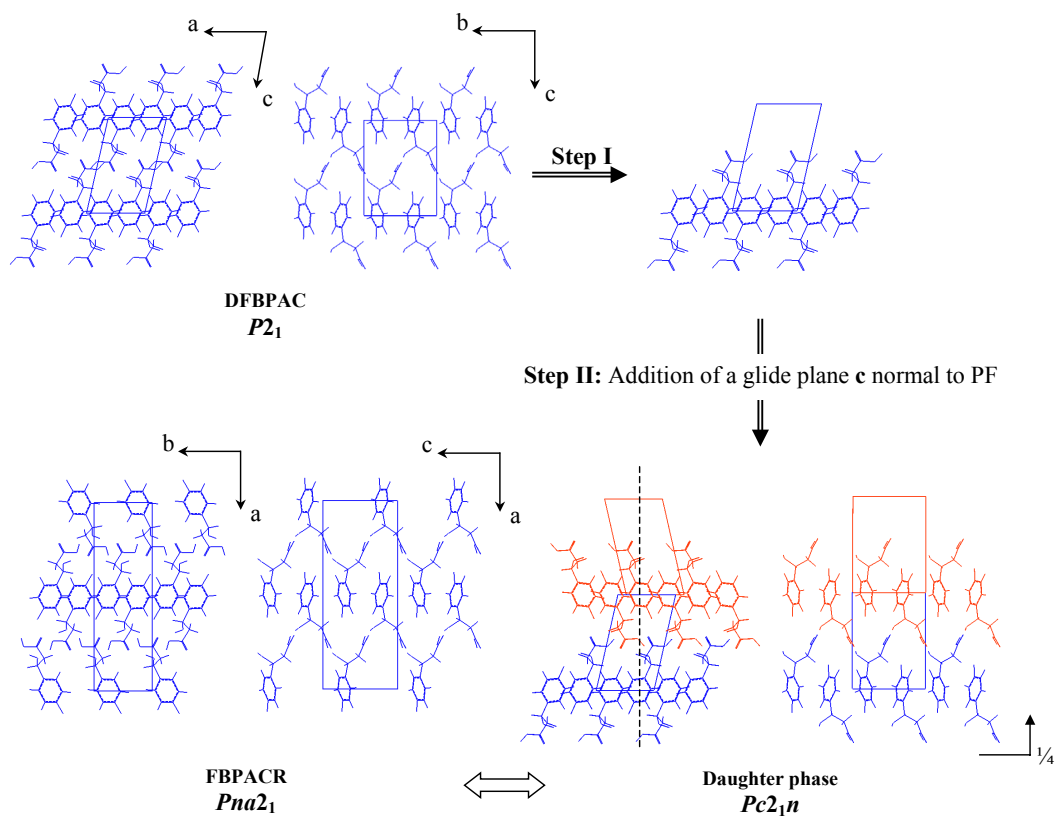
**Fig. S 15.** Construction of $Pna2_1$ structure from a two-dimensional PF of a $P2_1$ structure (compound **11**).

### 4.4 Case of $P2_12_12_1$ and $P2_1/c$

For NIYQUH (**12**), a 1D ribbon is extracted from the $P2_12_12_1$ structure (Fig. S 16). The PF contains the twofold screw axis running along the c axis as well as the associated translation $T_z$. Firstly, a glide plane **a** located at $z = 0$ is added to the ribbon, generating a two-dimensional slice (step II-1). Then, the third dimension is generated by adding a translation (step II-2). The daughter phase belongs to the space group $P2_1/a$ (standard setting: $P2_1/c$).
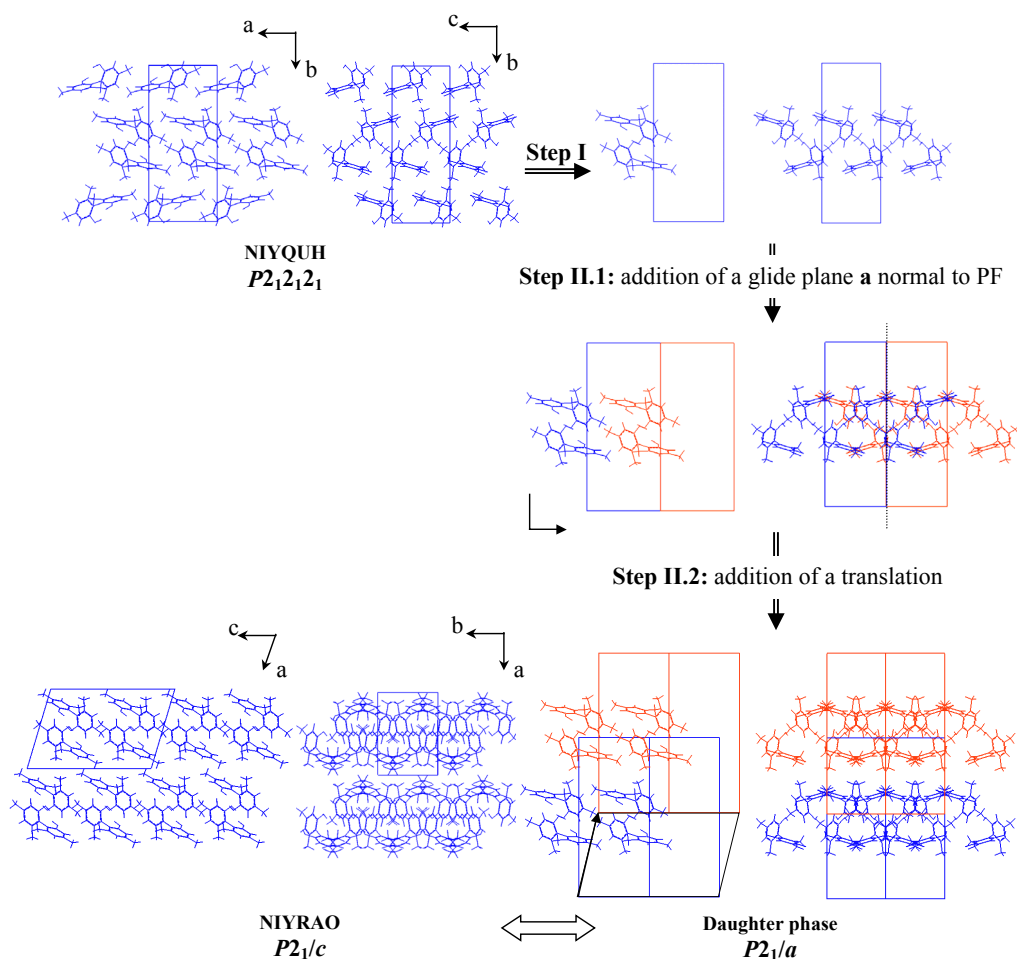
**Fig. S 16.** Construction of a $P2_1/c$ structure from a $P2_12_12_1$ structure (compound **12**).

## 5 Application of the model to structures with Z' ≠ 1

### 5.1 Daughter phase and mother phase with Z' = ½

LAZHID (**13**) crystallises as a salt ($A^{2+}$, $2B^-$) in two polymorphic forms ($P2_1/c$ and *Pbca*). In each case, the inversion centre contained in the cation $A^{2+}$ is in coincidence with an inversion centre of the lattice, leading to an asymmetric unit value Z' = ½, *i.e.* composed of one molecule of the anion and a half molecule of the cation ($\frac{1}{2}A^{2+}$, $B^-$). A 2D PF containing the glide plane **c**, the inversion centres and the translations $T_y$ and $T_z$, is extracted from the mother phase (Fig. S 17). This PF contains the whole cation ($A^{2+}$) and the two anions ($B^-$). The addition of a twofold screw axis normal to the PF and located at $y = \frac{1}{4}$ is sufficient to generate a daughter phase with space group *Pbca*. The comparison of the daughter phase with the experimental *Pbca* indicates that the anions are slightly differently located in the two structures.
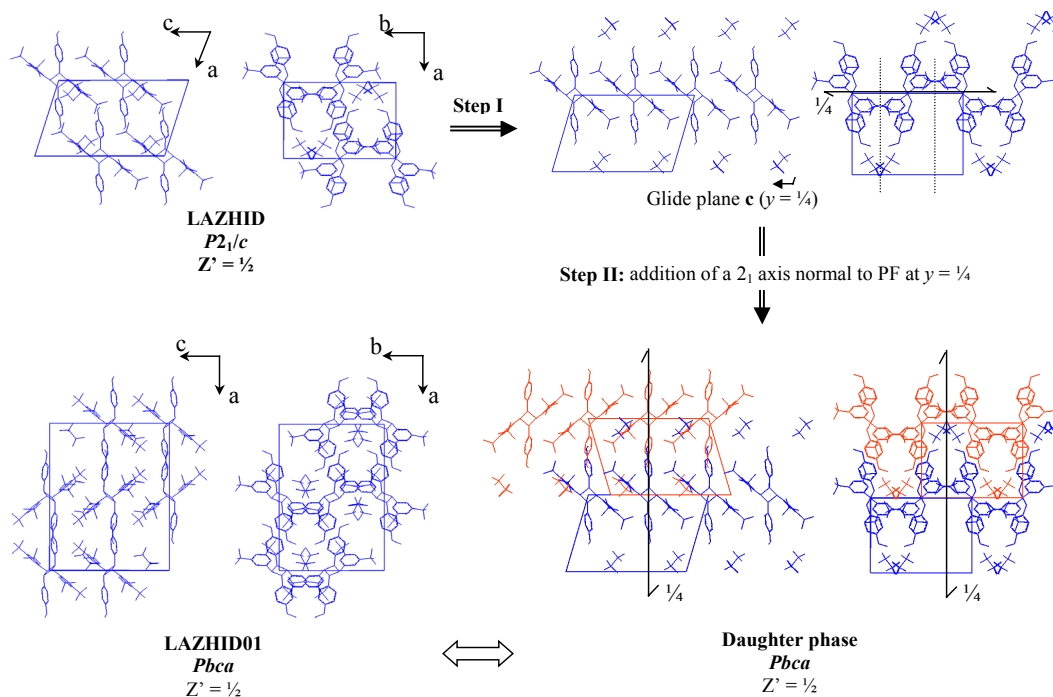
**Fig. S 17.** Construction of the *Pbca* structure from two-dimensional PF of the $P2_1/c$ structure (compound **13**). Case of Z' = ½.

### 5.2 Daughter phase and mother phase with different Z'

NIYRES (**14**) crystallises in two space groups with a different asymmetric unit, *i.e.* Z' = 2 and Z' = 1 for $P2_12_12_1$ and $P2_1/c$ respectively. The two molecules which constitute the asymmetric unit of the orthorhombic form are slightly different in their conformation and are related by a pseudo twofold screw axis (without this difference in conformation, the structure would belong to the space group $P2_12_12_1$ with Z' = 1). The PF chosen to build the monoclinic packing contains one of these two molecules with the twofold screw axis running along the a axis and the translations $T_x$ and $T_y$ (Fig. S 18). A glide plane **c** normal to the PF and located at $x = 0$ generates a daughter phase with space group $P2_1/c$ and Z' = 1. As the conformational difference between the two molecules is small, the daughter phases constructed from one or the other molecule of the asymmetric unit lead to the same crystal structure after minimisation.
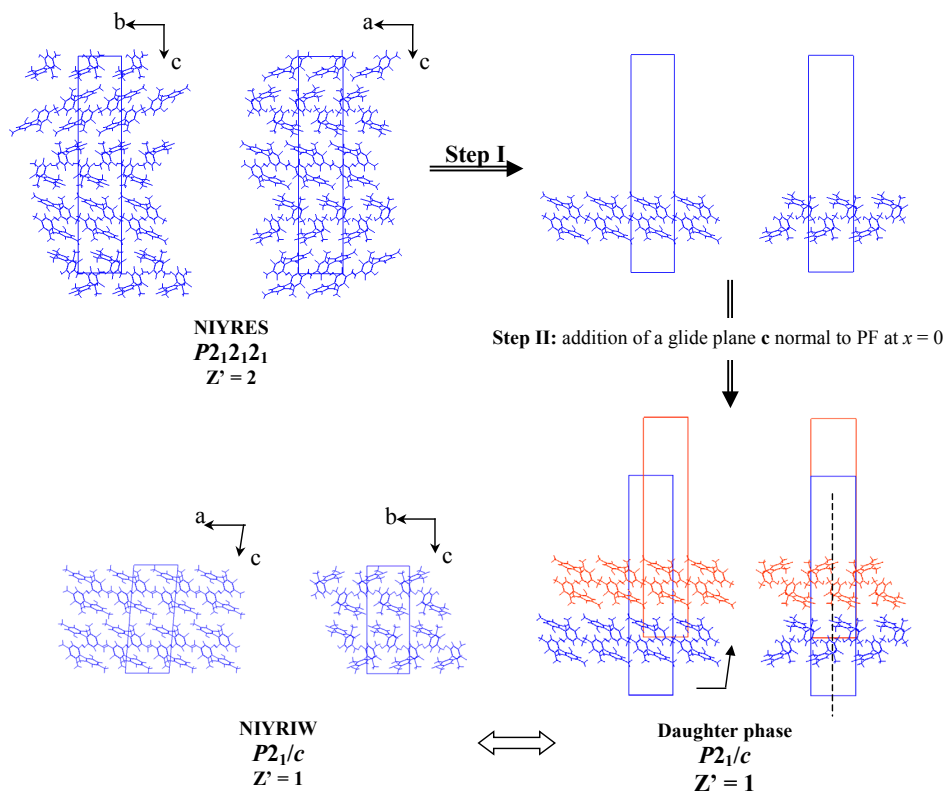
**Fig. S 18.** Construction of a $P2_1/c$ structure (with Z' = 1) from a $P2_12_12_1$ structure with Z' = 2 (compound **14**).

## 6 A case study: α-methyl-benzylamine mandelate

In Fig. S 18, Fig. S 19 and Fig. S 20 are respectively depicted the construction of PEAMAN01 from WIKJEF, PEAMAN from PEAMAN01, and YOWWOW from PEAMAN (compound **15**).
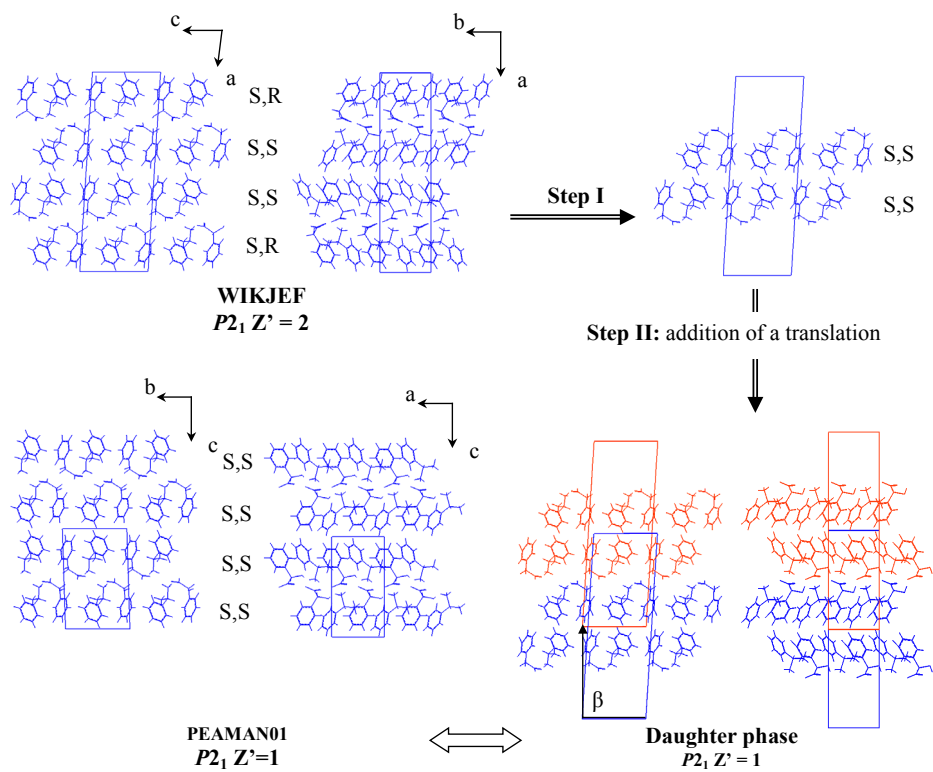
**Fig. S 19.** Construction of a $P2_1$ structure with Z' = 1 starting from a $P2_1$ structure with Z' = 2 (compound **15**).
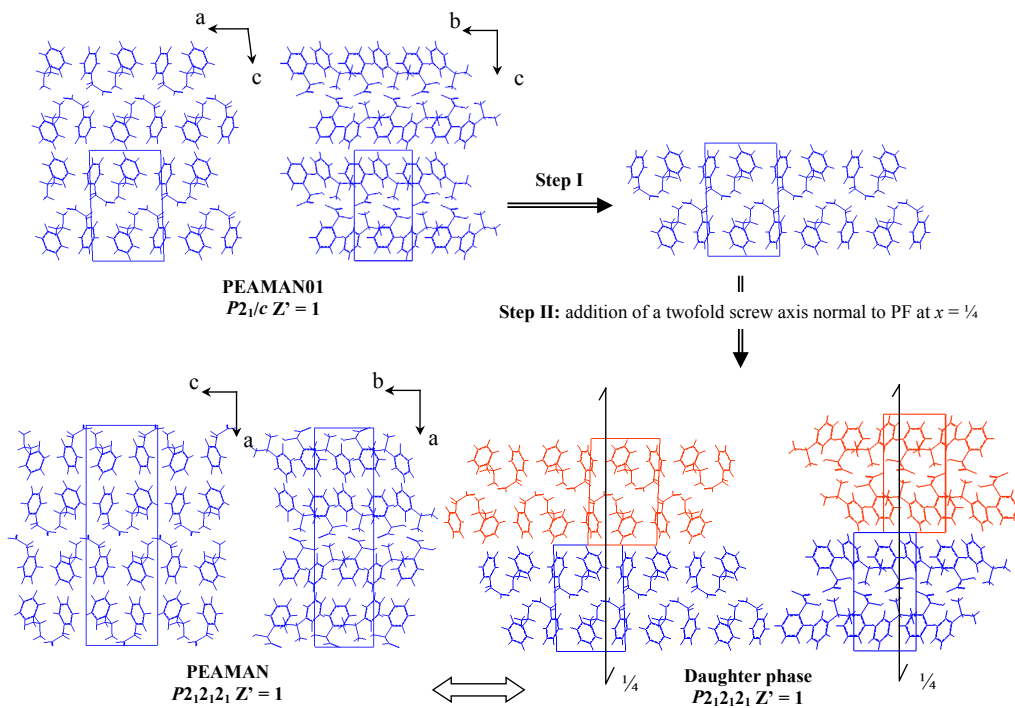


**Fig. S 20.** Construction of a $P2_12_12_1$ structure starting from a $P2_1$ one (compound **15**).
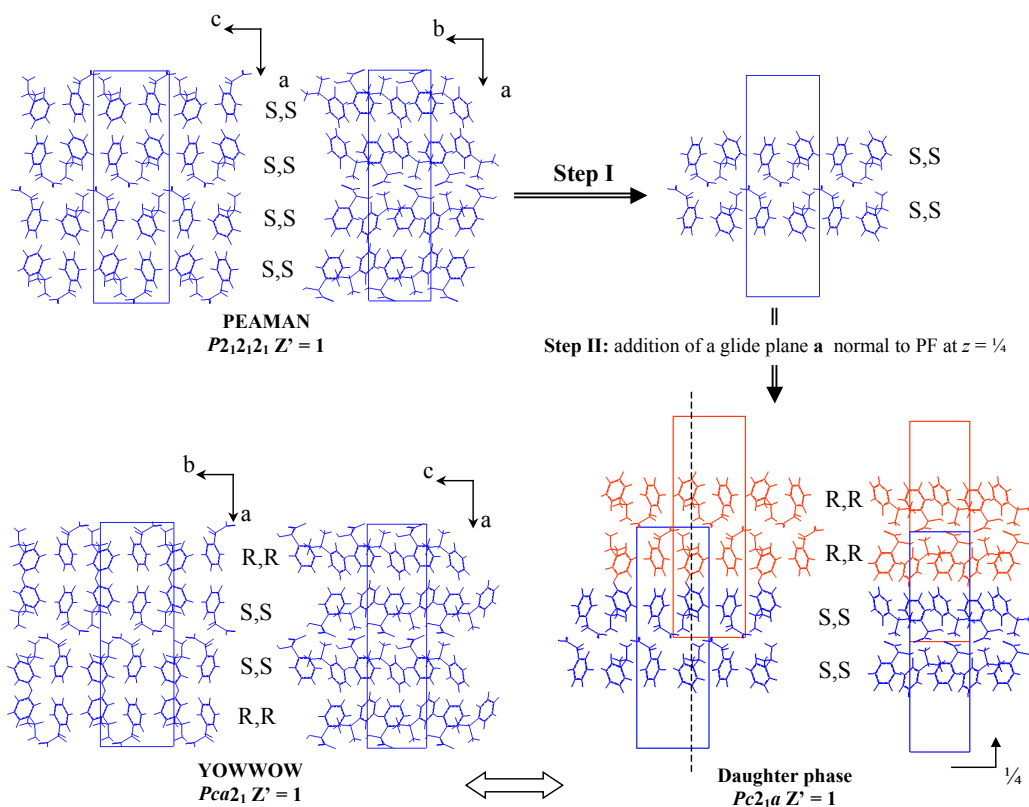
**Fig. S 21.** Construction of a $Pna2_1$ structure starting from a $P2_12_12_1$ one (compound **15**).

## 7  Application of the DCP model to diastereomers

The DCP model has been applied to the diastereomers RRS and SSS of compound **16**, for which refcodes of their crystal structures in the CSD are respectively SECNIX ($P2_1$) and SECNET ($P2_1/c$). As shown in Fig. S 22, the application of a glide plane **c** normal to the PF extracted from SECNIX leads to a daughter phase of space group $P2_1/c$, which closely corresponds to SECNET, the structure of the other diastereomer.

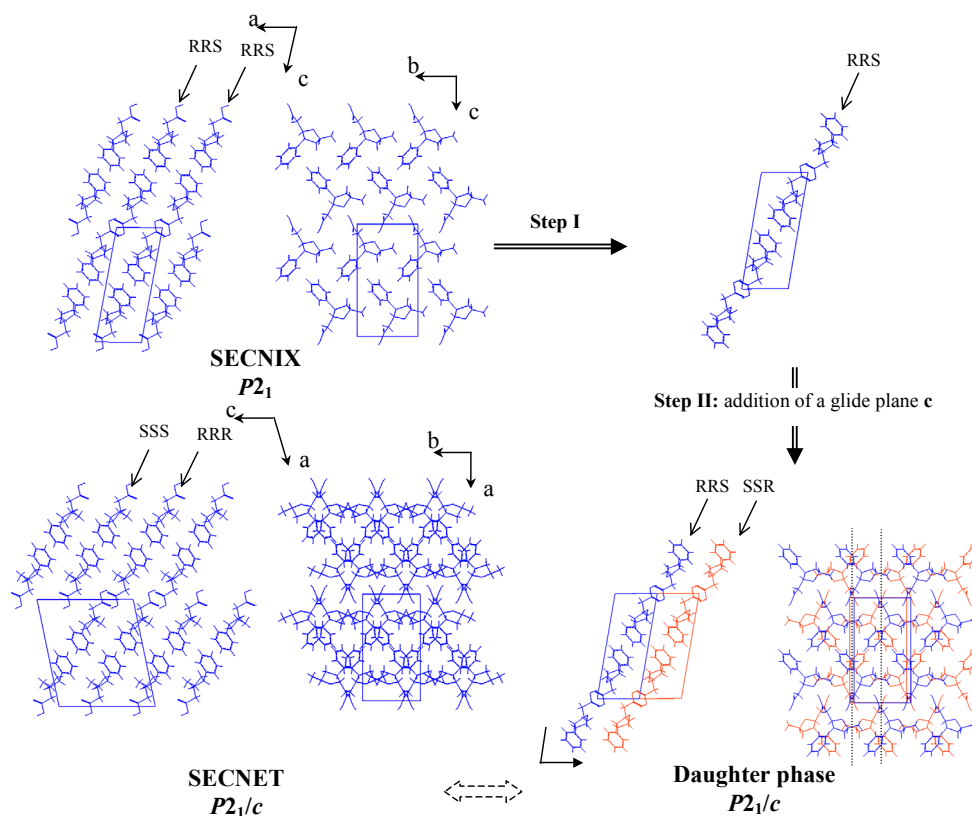**Fig. S 22.** Example of the construction of a $P2_1/c$ structure from a two-dimensional PF extracted from the $P2_1$ structure of the diastereoisomer RRS (compound **16**). This daughter phase corresponds to the experimental structure of the diastereoisomers RRR and SSS.

## 8    Expression of structural similarities by forming twins and epitaxies

### 8.1  Example of twinning

Trinitrotoluene (**17**) can crystallise either in the stable monoclinic form ($P2_1/c$) or in the metastable orthorhombic one ($Pb2_1a$). In the two structures, the asymmetric unit is composed of two molecules A and B (*i.e.* Z' = 2), with similar conformations. Gallagher *et al* (1996, 1997), analysed carefully the two structures and showed that the molecular stacking sequence is AABBAABB… in the monoclinic form, whereas that of the orthorhombic one is ABABAB…. Moreover, the two polymorphs are composed of identical molecular layers composed of the two molecules A and B. These layers are related each other by a glide plane in the orthorhombic structure, and a pseudo-glide plane in the monoclinic one. The pseudo-glide plane is due to the close similarity between the two conformations A and B, and emphasises the correspondence between the two polymorphs. Indeed, replacing the pseudo-glide plane by a real one leads to the structure of the orthorhombic form. The authors also highlighted that the monoclinic form shows extensive twinning. They determined by means of X-ray and full-crystal Laue

topography that these twins are arranged in lamellae of various thickness parallel to the {100} planes. Moreover, it appears that in certain conditions, the two forms crystallise simultaneously, *i.e.* as concomitant polymorphs (Bernstein *et al.*, 1999). These two phenomena (concomitant polymorphism and twinning) are a direct consequence of the similarities between the two structures, and it is not surprising that the DCP model demonstrates the structural relationships between them (Fig. S 23). The extracted periodic fragment of the monoclinic form contains the two molecules A and B, the glide plane **b** and the translations $T_y$ and $T_z$. The addition of a twofold screw axis normal to the PF at $z = ¼$ generates a daughter phase of space group $P2_1ab$ (standard setting: $Pca2_1$) with a packing similar to the experimental orthorhombic form.
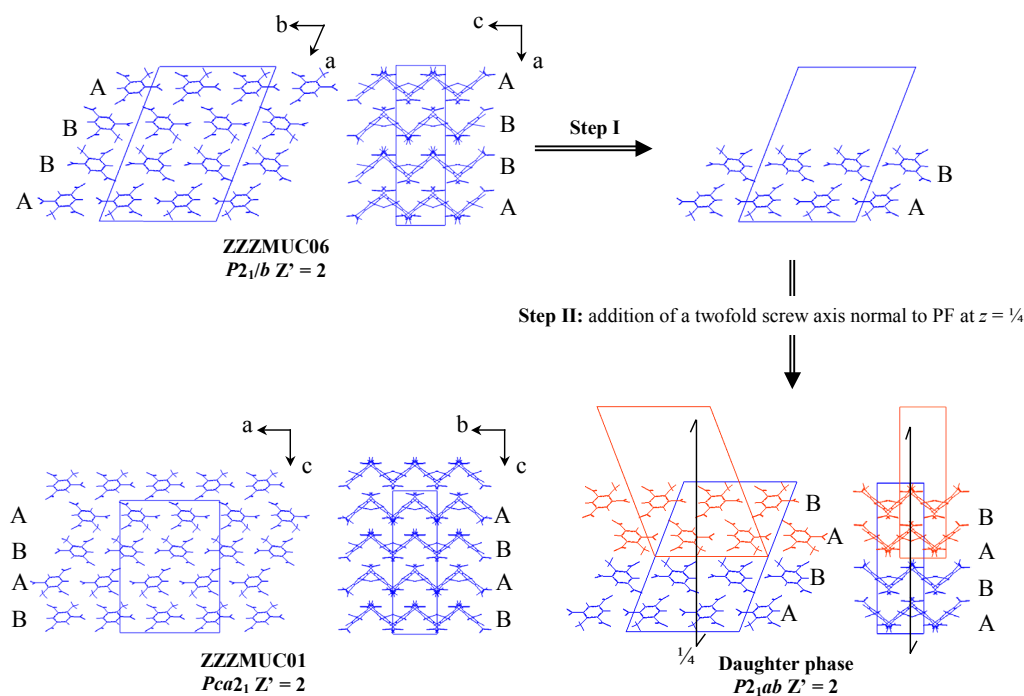


**Fig. S 23.** Construction of a $Pca2_1$ structure starting from a $P2_1/b$ one (compound **17**). It is noteworthy that the monoclinic form is often twinned when grown in specific solvents.

### 8.2 Example of epitaxy between two enantiomers

(R,S)-Alanine (**18**) crystallises from water in the space group $Pna2_1$, whereas the pure enantiomer crystallises in the space group $P2_12_12_1$. In order to resolve this racemic compound, Weissbuch *et al.* (1994) introduced several optically pure α-amino acids which should inhibit the nucleation of the racemic as well as the enantiomorphous crystals. The addition of a chiral auxiliary R' should bind the {R,S} and {R} nuclei, prevent their further growth, and thus allow the selective growth of {S} nuclei. Surprisingly, although this method was shown to be successful for other compounds (Weissbuch *et al.*, 1987), this approach, when applied to (R,S)-alanine, resulted in 'twinned' racemic crystals exhibiting a morphological symmetry 222, instead of the expected achiral

morphological symmetry mm2. The authors explained this result as follows: since the (R,S) crystals (which are thermodynamically stable) cannot nucleate and grow because of the chiral auxiliary R', they epitaxially grow on the {S} nuclei which are not (or at a less extent) inhibited by R'. The resulting 'twinned' crystals are composed of two (R,S) parts separated by a central twinned zone containing the starting {S} nucleus. Therefore, it seems that the epitaxy between the $Pna2_1$ and the $P2_12_12_1$ structures is rather easy to be performed and does not provide a high excess of energy.

The DCP model is applied as follows: the two structures have a 2D slice in common, which is thus chosen as periodic fragment (Fig. S 24). In the chiral structure of alanine (*i.e.* $P2_12_12_1$), the PF contains the twofold screw axis running along the c axis, its associated translation $T_z$ and the translation $T_x$. The applied symmetry operator is a glide plane **b** normal to the PF (*i.e.* in the direction a). The generated daughter phase belongs to the $Pbn2_1$ space group (standard setting $Pna2_1$), and corresponds to the experimental $Pna2_1$ structure.
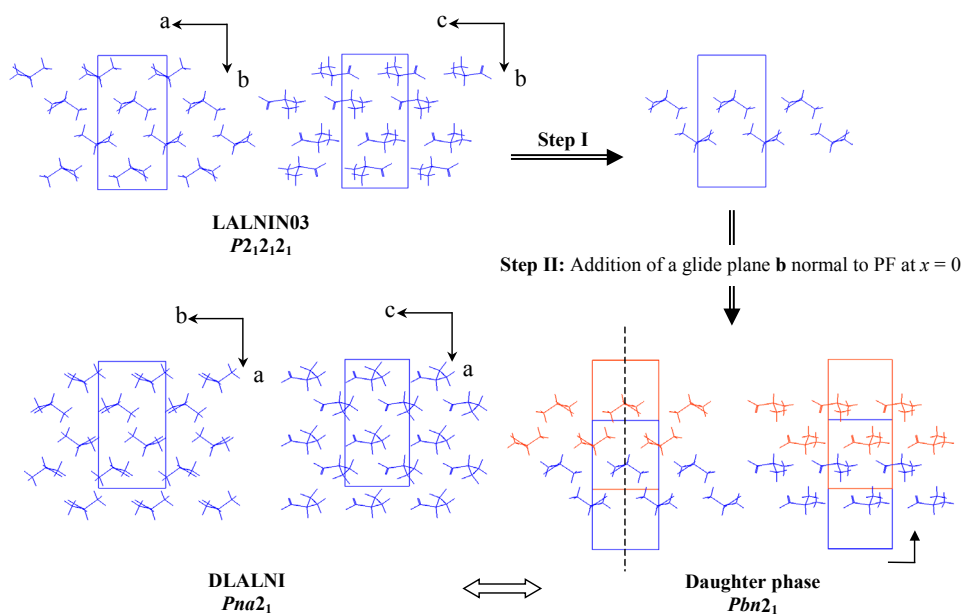


**Fig. S 24.** Construction of a $Pna2_1$ structure starting from a $P2_12_12_1$ structure (compound **18**). The enantiomorphous structure shows epitaxy between the two enantiomers.

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