TOWARDS THE PLANNING AND EXECUTION OF AN "ABSOLUTE" ASYMMETRIC SYNTHESIS OF CHIRAL DIMERS AND POLYMERS WITH QUANTITATIVE ENANTIOMERIC YIELD

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Abstract - An "absolute"asymmetric synthesis of chiral dimers and polymers has been accomplished through a process of crystallisation of an achiral monomer in a chiral crystal, followed by a topochemical photopolymerisation. Once ($2\pi + 2\pi$) photocycloadditon had been selected as a suitable reaction, we designed the chiral crystalline motifs needed for a reaction with quantitative enantiomeric yield. Unsymmetrically disubstituted dienes, translationally related in a chiral crystal, and where reaction occurs between non-equivalent double bonds, separated by 4.0Å, fit the suggested model best. The execution of the synthesis involved the following steps. By applying some empirical rules of "crystal engineering", we selected a family of chiral resolved molecules (which guarantee a chiral crystalline motif), among which R(-) or S(+) ethyl-2-cyano-3(p-sec-butyl-3'-E-propenoate)-phenyl-E-propenoate-$\underline{1}$ was found to fulfil all the stated requirements, yielding photodimers and polymers with quantitative diasterioisomeric yield. Finally, on the basis of the crystal structure of $\underline{1}$ we have designed at least two achiral molecules which pack in chiral structural motifs isomorphic with $\underline{1}$. Irradiation of crystals grown from the melt, led to polymers with high, probably quantitative optical yields. A possible model for an amplification of the generated chirality will be discussed.
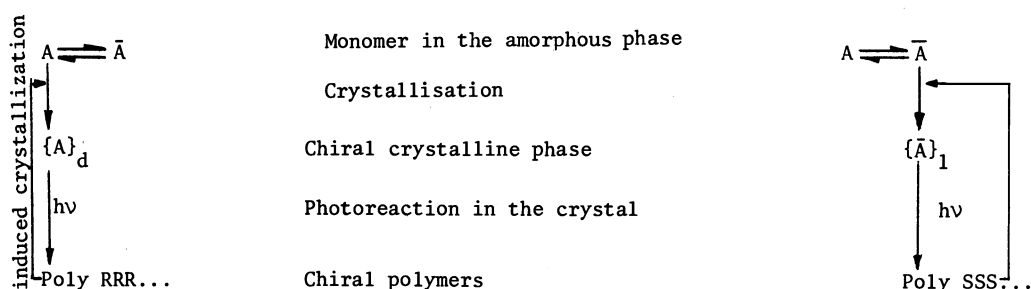
INTRODUCTION

Our interest in the systematics of the reactivity of organic solids (Refs. 1,2) has led us in recent years to test the possibilities of designing and engineering crystals of organic molecules with molecular packings suited to the achievement of specific predetermined aims. Here we describe the application of this approach to the planning of an "absolute" asymmetric synthesis with quantitative enantiomeric yield.

In classical asymmetric transformations there is always the necessity of an outside chiral agent (e.g. a chiral catalyst or chiral "handle"). By contrast, in the asymmetric syntheses of the type we are investigating the induction is affected by the chiral environment which the crystal itself provides at the reaction site.

In some systems, as in that here described in detail, it is possible to generate chiral crystals of one handedness only, starting from achiral or from chiral-racemic molecules (Refs. 3,4), and produce optically active products in these crystals (Refs. 5-10). Thus these coupled processes of crystallization and solid-state reaction provide an asymmetric synthesis in the absence of any outside chiral agent. The term "absolute" asymmetric synthesis is used to describe such processes which start with achiral materials and lead to optically active products in the absence of chiral agents. In this sense our process provides such a synthesis. It is clear that the chirality is here in fact introduced in the crystallization step; the chemical reaction then transforms the chirality of the crystal into that of the product. The purist may object to the use of the word "absolute"; however, it is accepted by chemists in this context (Refs. 11-13). It can be said that the only outside chirality is that of the observer, whose role is to detect the asymmetry of the synthesis. On the other hand in classical transformations, such as Pasteur's famous experiment, the role of the observer is to sort crystals of different handedness, and thus to introduce the chiral element. (Ref. 14).

Statement of the problem. In this lecture we describe an "absolute" asymmetric synthesis of chiral polymers, according to the process shown in Scheme 1. We also require that the product formed will have an inducing effect on the crystallization process of the starting monomer, in order to amplify the generated chirality.

<u>Scheme 1</u>

A ⇌ Ā   Monomer in the amorphous phase   A ⇌ Ā

  │   Crystallisation   │ ←───┐
  ▼   ▼   │
{A}$_d$ Chiral crystalline phase   {Ā}$_1$ │

  │ hν   Photoreaction in the crystal   │ hν │
  ▼   ▼   │
Poly RRR...   Chiral polymers   Poly SSS...

(left margin, rotated) induced crystallization

What are the requirements for generation of chiral polymers by this route? First, we need
an achiral monomer crystallizing in a chiral structure; second, the solid-state polymeriz-
ation must be such that both the initiation and propagation steps are controlled by the
crystal lattice (topochemical control); for this to be so a structure is required in which
adjacent reactant centers are at the correct distances apart and have the correct relative
orientation. The problem then becomes one of "engineering" a suitable crystal, i.e. of
selecting a monomer which will tend to crystallize in a structure which meets these
requirements. In order to describe logically the steps leading to this selection we shall
first make some remarks on chiral crystals and topochemical (2π + 2π) photodimerization and
photopolymerization reactions.

<u>Chiral crystals</u>. There are 230 distinct ways (space groups) of constructing three dimen-
sional structures from arbitrary elementary units. These space groups can be divided into
two types. One type, the chiral space groups, have only symmetry elements of the first
kind, i.e. translations, rotations, and combinations of the two. If the elementary unit is
chiral then all the symmetry elements relate it to other elementary units of the same
chirality. Space groups of the second kind, of which there are 165, contain amongst their
symmetry elements at least one mirroring element, i.e. a mirror or glide plane or a crystal-
lographic centre of inversion. Thus every chiral object in a lattice of this type is
related by symmetry to an object of opposite chirality.

Crystals belonging to one of the chiral space groups appear in two enantiomorphous forms.
A resolved sample of a chiral material must crystallize in a chiral space group, while a
racemate generally packs in non-chiral crystals, with the two enantiomers related by sym-
metry elements of the second kind. Achiral molecules can crystallize either in chiral
or achiral structures. In the former case the chiral environment of the crystal forces
the molecule to adopt a chiral conformation. In these systems it is possible, by growing
a large single crystal, to bring the entire ensemble of molecules into one handedness:

       A ⇌ Ā   A ⇌ Ā
         │   │
         ▼   crystallization   ▼
   {A}$_d$ {Ā}$_1$
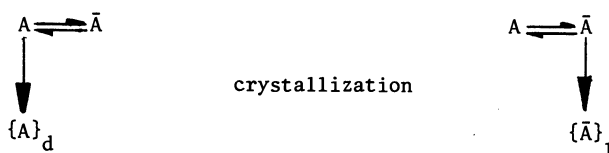
where { } designate a crystalline phase. Such a process of crystallization, which has
been termed "total asymmetric transformation", in principle spontaneously generates
optical activity starting from achiral material. Several examples of such effects have
been described (common examples are quartz, urea, sodium chlorate, and binaphthyl). (Refs.
3,4). In the absence of any outside chiral agent, the probabilities of crystallization
of these non-chiral molecules in crystals of either handedness are identical.

We have thus far discussed some of the factors associated with crystallization in chiral
structures, and pointed out that the molecules in such structures must adopt conformations
which are to some extent chiral, whether or not they do so in dispersed phases. If the
molecule takes part in a topochemically controlled solid state reaction, we can conceivably
exploit the chirality of both the molecule and its environment for the performance of
asymmetric syntheses.

Successful demonstrations for the feasibility of such processes are the heterogeneous
addition of gaseous Br_2 to single crystals of 4,4'-dimethyl-chalcone (Ref. 5) (Scheme 2),
and the selective photodimerization in mixed crystals of diaryl butadienes. (Ref. 6).

Scheme 2
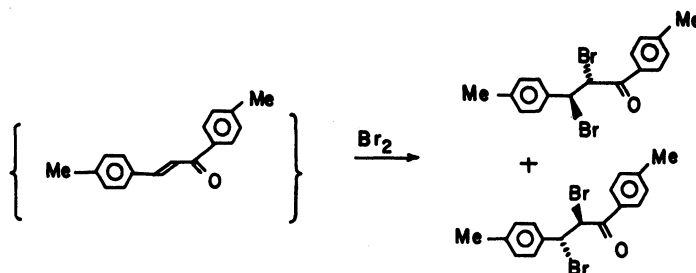
In both examples however, the optical yields were not quantitative, due to competitive pathways which allowed the formation of both enantiomers in the same chiral crystal.

Topochemical solid state photodimerizations and photopolymerizations.   Studies by G.M.J. Schmidt et al. on (2π + 2π) photocycloadditions of substituted ethylenes in the solid state (Ref. 15) have demonstrated that such reactions are strictly controlled by the packing arrangement of the molecule in each given crystal. The trans-cinnamic acids provide a clear example of the structural requirements of these reactions, and we shall. discuss them now since we need this background for the development of our main theme.

The trans-cinnamic acids are found to crystallise in three types of crystal structures, each one of which has a specific photochemical behaviour (Ref. 16). One type, designated β, has adjacent molecules translationally related by a short crystal axis of 4.0Å and reacts photochemically to give mirror-symmetric cyclobutanes (β-truxinic acids). In a second type of structure, designated α, the molecules are arranged in centrosymmetric pairs, with the distance between the (antiparallel) molecular planes being 4.0Å. Upon u.v. irradiation, materials in this structure give the centrosymmetric α-truxillic acids. (Scheme 3).
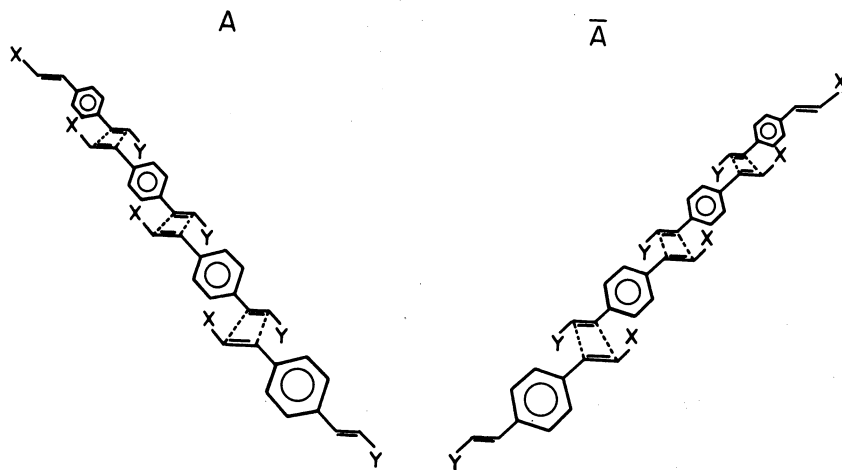
Scheme 3

β type

α type
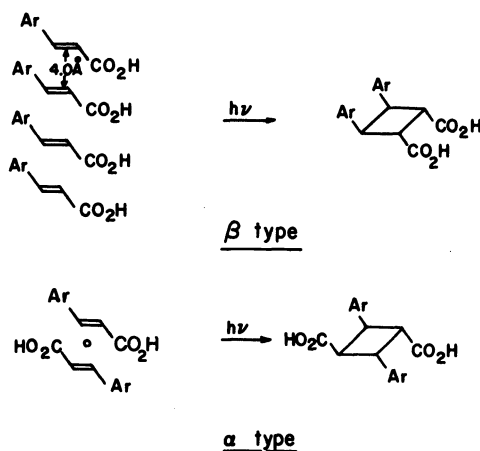
The third type of structure, designated γ, has the double bonds of adjacent molecules separated by a distance greater than 4.0Å, or their π-electrons improperly oriented for dimerization. Ethylenes of this structural type are not affected by u.v. irradiation.

It should be stressed that the photobehaviour is controlled by the crystal structure, and not by the particular cinnamic acid molecule employed. Thus, for example, ortho-ethoxy-trans-cinnamic acid is trimorphic, crystallizing in each one of the structural types α,β

and γ. Crystals of the three structural types react differently on irradiation, according
to the rules described above (Ref. 16). This simple correlation established first for
cinnamic acids, was later shown to be valid also for cinnamides, stilbenes, fumarates,
chalcones, coumarins, nucleotides, and other olefinic systems (Ref. 15). Indeed, it is
possible to predict with a high degree of confidence, the stereochemistries of the photo-
dimers from such materials, on the basis of knowledge of the orientations of the monomer
molecules in the crystal, and vice versa. These studies have been subsequently extended by
the group of Hasegawa in Japan to the solid-state photopolymerisation of distyryl pyrazine
(Ref. 17), and other symmetrically substituted dienes (Refs. 18,19). U.V. irradiation of
these monomers brings about a series of (2π + 2π)-cyclodimerization steps leading to the
development of high molecular weight, sometimes crystalline, linear polymers. Contrary to
solid state vinylic polymerization (Refs. 20-24), in this system both the initiation steps
(dimerization) and the propagation steps (coupling of dimers and other oligomers), proceed
under the control of the crystal lattice of the monomer, and the polymer chain grows in
very well defined crystallographic directions.

Our system for asymmetric solid state polymerization. On the basis of the above knowledge,
we felt that photocycloaddition could be the appropriate reaction for our purpose. A
detailed analysis of the chemical and crystallographic conditions needed for the performance
of asymmetric polymerization by use of this reaction, yielded two model structural
motifs (Refs. 1, 25). In the first, we consider an asymmetrically substituted diene,
packing in a chiral crystal, where the molecules are related by translation and the two
different double bonds are separated by a distance of 4.0Å (Scheme 4).

<div align="center">Scheme 4.</div>

It is clear from the Scheme that, if the only reactive contacts are those within the
represented stack, a solid-state topochemical photodimerization and photopolymerization
will generate only one of the two possible enantiomeric polymeric chains.

To facilitate our search for monomer molecules crystallizing in the above structure, we
divided the problem into two steps. In order to guarantee crystallization into a chiral
space group, we built first the desired motif with chiral resolved molecules. In a second
step, we tried to use the rules of isomorphous replacement, in order to construct the
desired crystal composed of non-chiral molecules.

Scheme 6

$[\alpha]_D^{CHCl_3} = -109$ $[\alpha]_D^{CHCl_3} = -128$

* (δ = ^{1}H NMR chemical shifts)
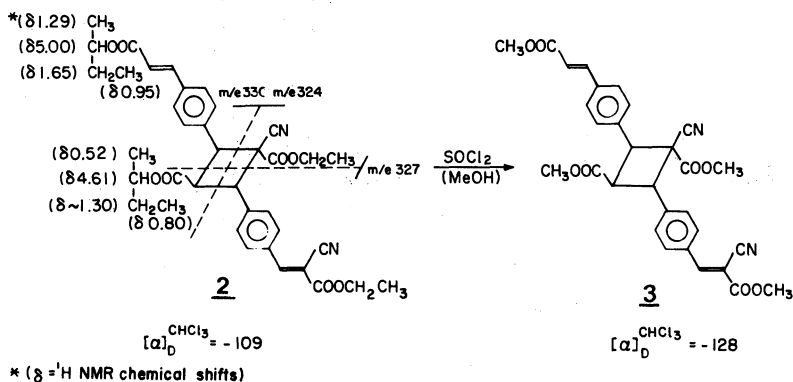
Comparative ^{1}H and ^{13}C NMR studies of the products obtained from the pure enantiomers with those of the mixture of the two possible diastereoisomers (Figs. 1,2), independently synthesized, have unambiguously demonstrated that the diastereomeric yield of the reaction is quantitative both in initiation (dimers) and in propagation (trimer and oligomers) (Ref. 31).
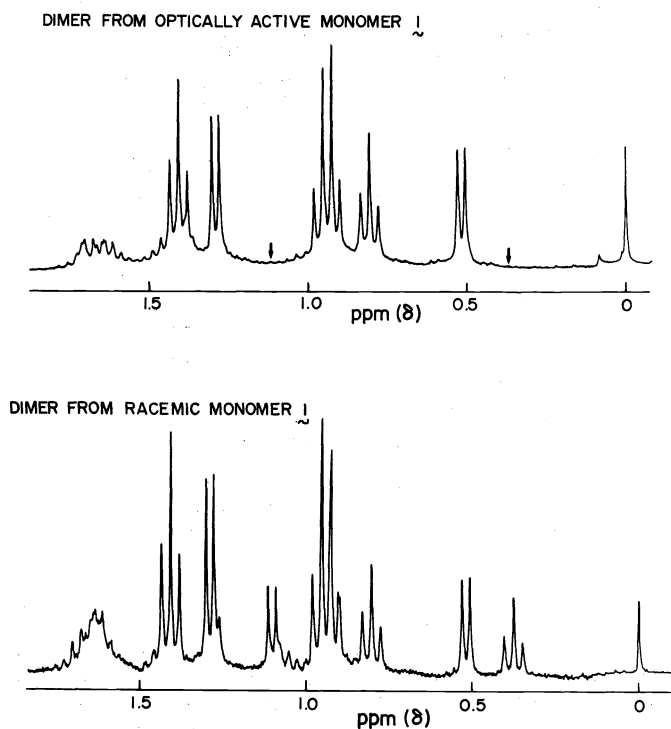

Fig. 1. ^{1}H NMR spectrum in the range 0-2 ppm of the dimer from pure S(+) 1 (upper) and of a mixture of diastereomeric dimers having opposite absolute configurations at the cyclobutane ring centres (lower).

To guide our choice of a suitable class of compounds, we applied some empirical rules:
we avoided carboxylic acids or amides, since these generally pack in centrosymmetric or
quasi-centrosymmetric structures (Refs. 26,27); we rather selected esters, because in
many crystals of these an attractive interaction between carbonyls and phenyls of adjacent
molecules (Refs. 28,29) has been observed which would juxtapose in our case the double
bonds at the correct distance of 4.0Å (Scheme 5).

<div align="center">Scheme 5</div>
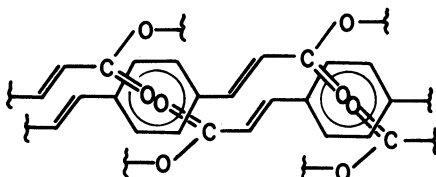
Non-equivalence between the two reactive sites was introduced by adding a nitrile group on
one of the two ethylenic double bonds, and using two different ester groups. In order to
assure a chiral space group and to avoid close contacts between the two identical double
bonds across a 4.0Å translation axis (which would lead to cyclobutanes of symmetry m),
we attached to one side of the diene a chiral sec-butyl group. We chose such a chiral
handle in which the substituents at the chiral atom have similar volumes, in order to
facilitate its isomorphous substitution with appropriate achiral moieties in the second
step.

We thus ended up with the class of compound reported below, where R is a variable

in $\underline{1}$, R= $-CH_2-CH_3$
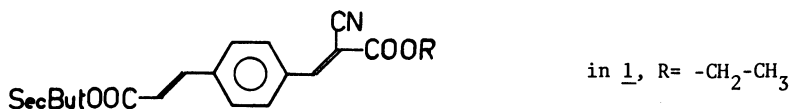
Out of a few synthesized, monomer $\underline{1}$ proved to fulfil all the stated requirements of the
chiral motif.

An asymmetric dimerisation and polymerization with quantitative diastereomeric yield. Op-
tically pure monomer $\underline{1}$ crystallizes in the chiral triclinic space group P1 with z=1. The
sole symmetry elements in this structure are the three axial translations, of lengths
a=13.17Å, b=6.94Å, c=5.25Å; the unit cell angles are α=103.1°, β=95.5° and γ=90.1°. The
unit cell axis of 6.94Å is compatible with the expected length of the polymerization axis
in a structure as in Scheme 4.

Polycrystalline samples of optically pure monomer $\underline{1}$ were irradiated at 5°C, with λ > 310 nm.
There were formed dimer, trimer and oligomers (Refs. 30,31) (ranging up to molecular weight
∿10,000).

Since these photopolymerization reactions are polyphotonic, it is possible by suitable
selection of the wavelength of the exciting light to maximize the yield of dimer and
trimer, which could be then separated from other products and used for accurate determi-
nation of the stereochemical course of the polymerization.

Irradiation of S(+) monomer $\underline{1}$, $[\alpha]_D$ (CHCl$_3$) = +22.7°, gave dimer $\underline{2}$ with the stereochemistry
shown in Scheme 6, and $[\alpha]_D$ (CHCl$_3$) = -109°. After replacement of the chiral handles by
transmethylation, $\underline{3}$ is obtained with an enhanced specific rotation $[\alpha]_D$ (CHCl$_3$) = -128°,
demonstrating that the optical activity of $\underline{2}$ is mainly due to the new chiral centers
created by reaction. Trimer and oligomers have the same stereochemistry as in $\underline{2}$ around
the cyclobutane rings, and comparable specific rotations.

OLIGOMER FROM OPTICALLY ACTIVE MONOMER 1

ppm (δ)

OLIGOMER FROM RACEMIC MONOMER 1

ppm (δ)

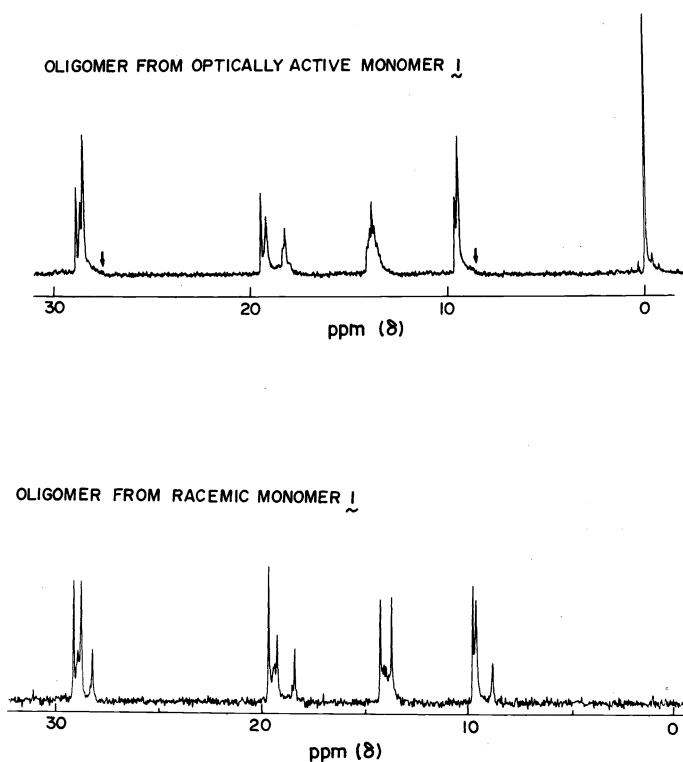Fig. 2. ^{13}C NMR spectrum in the range 0-30 ppm of the oligomers from S(+) 1 (upper) and
        of a mixture of diastereomeric oligomers having opposite absolute configurations
        at the cyclobutane rings (lower).

It is clear that the structural arrangement of the monomers must be as in only one of the
two possible diastereoisomeric motifs A and Ā of scheme 4. Reaction in each one of these
crystals would lead to the formation of cyclobutane dimer, trimer and oligomers with the
same stereochemistry around the C_4 ring, but of opposite absolute configuration.

Both in order to confirm the expected structure, and to determine the absolute configuration
of the new chiral centers, an X-ray analysis of the starting S(+) monomer has been
carried out: its packing diagram in the a b plane is shown in Fig. 3 (Ref. 32).

From this picture, we see that the packing of the monomer is in complete agreement
with the schematic model suggested for this synthesis. Adjacent and partially overlapped
molecules related by translation have the two different double bonds separated by a distance
of 4.04Å, leading to products with the stereochemistries reported above. The absolute confi-
gurations of the products, starting from enantiomerically pure S(+) monomer are expected
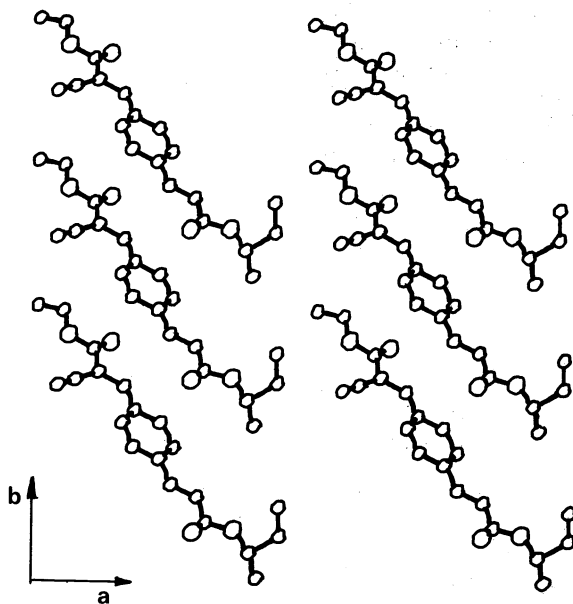to be S, S, S and S as in Scheme 4, motif A.

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Fig. 3. Packing arrangement of S(+) $\underline{1}$ in the a b plane: b is the polymerization axis.

"Absolute" asymmetric synthesis of chiral polymers. Once we have prepared the appropriate chiral crystalline phase, suitable for our asymmetric photopolymerization, we move towards the second step of our synthesis, i.e. the design of an isomorphous crystalline phase, composed of non-optically active compounds.

One possible solution to our problem came from the observation that many crystals of molecules containing the chiral sec-butyl group have a tendency to chiral disordering, resulting in the formation of isomorphic crystals between the resolved enantiomer and the racemic mixtures (Refs. 33,34). The same behaviour may be expected for racemic $\underline{1}$. Therefore crystals of racemic $\underline{1}$ have been prepared and their cell constants measured (see Table 1).

From the similarity but lack of absolute identity of cell dimensions between the racemate and the pure enantiomer, it can be deduced that racemic $\underline{1}$ crystallizes in the form of a solid-solution of the two enantiomers. The overall process may be summarized as follows:

$$
\begin{array}{cccccc}
R & \text{or} & S & R \rightleftharpoons S & \text{and} & R \rightleftharpoons S \\
\downarrow & & \downarrow & \downarrow & & \downarrow \\
\{R\}_d & & \{S\}_1 & \{RS\}_d & & \{SR\}_1
\end{array}
$$

Crystallization of the pure   Crystallisation of the racemate
        enantiomer

In other words, it might be possible to crystallize the racemate in the form of enantiomorphous crystals, but of racemic composition, where the polymerizing chromophores are alligned exactly as in the enantiomeric crystal; the difference between the two structures will be that in the latter all sec-butyls are of the same chirality, whereas in the former they are of both chiralities. Whilst in the pure enantiomer the chirality of the sec-butyl handle imposes preferential crystallization in one out of the two possible diastereomeric structures of Scheme 4, in the racemate the two structures are enantiomeric, and will therefore appear with equal probability. This implies that the success of our experiment depends on the possibility of growing a large homochiral crystal of 5OR and 5OS composition.

TABLE 1. Space groups and cell dimensions of monomers

R_1	R_2	Monomer	a (Å)	b (Å)	c (Å)	β (°)	Space group	z
sec-Butyl	Ethyl	S(+) 1	13.17	6.94	5.25	103.1 95.5 90.1	P1	1
sec-Butyl	Ethyl	Racemic 1 (from melt)	13.35	7.03	5.41	104 93 92	P1	1
iso-Propyl	Ethyl	4 (from melt)	12.56	9.90	7.52	102 91 92	P$\bar{1}$	2
3-Pentyl	Ethyl	5 (from melt)	14.88	13.66	5.28	97 91 114	P$\bar{1}$	2
50% iso-Propyl +50% 3-Pentyl	Ethyl	50% 4 + 50% 5 (from melt)	13.53	6.90	5.28	102 104 94	P1	1
iso-Propyl	n-Propyl	6 (from melt)	12.60	9.77	7.86	94 107 91	P$\bar{1}$	2
3-Pentyl	Methyl	7 (from melt)	7.01	25.50	5.37	104	P2_1	2

Since we have demonstrated (Ref. 31) that the asymmetric induction on polymerization is only due to the chiral environment in the solid matrix, and not to the chirality of the handle, reaction in such a homochiral crystal will proceed with the same quantitative asymmetric induction already found for the isomorphous pure enantiomer.

An accurate determination of the phase diagram between S(+) and R(-) 1, in equilibrium conditions, revealed however the presence of an immiscibility gap in the range 60:40 to 40:60 (Ref. 35). Therefore crystallization of a large batch of racemic 1 under thermo-dinamically controlled conditions will be associated with the precipitation of equal amounts of crystals of both chiralities, with a constant internal composition, defined by the boundaries of the eutectic.   The situation is intermediate between spontaneous resolution and the formation of a continuous solid solution (Scheme 7).

Scheme 7

Spontaneous resolution   Eutectic   formation   Continuous solid solution

amount of d=1   d=1, m ≠ n   d ≠ 1   m=n
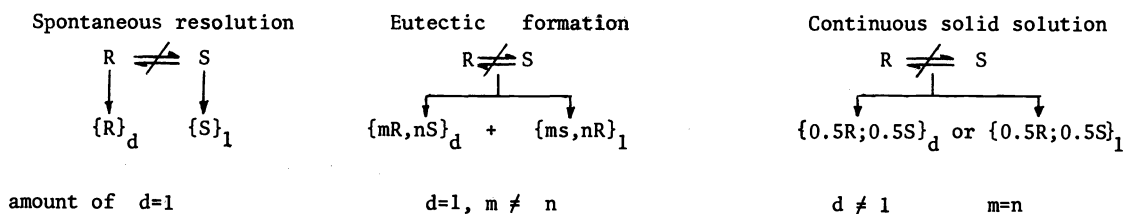
Only in the range of solid solubility are we dealing with homochiral phases, of a chirality determined by the enantiomer present in excess.

On the basis of this analysis, asymmetric syntheses of chiral dimers and oligomers with quantitative optical yield were obtained starting from samples of low optical purity, down to 22%. The dependence of optical purity of the dimers upon the initial monomer's composition is shown in Fig. 4. (Ref. 35).
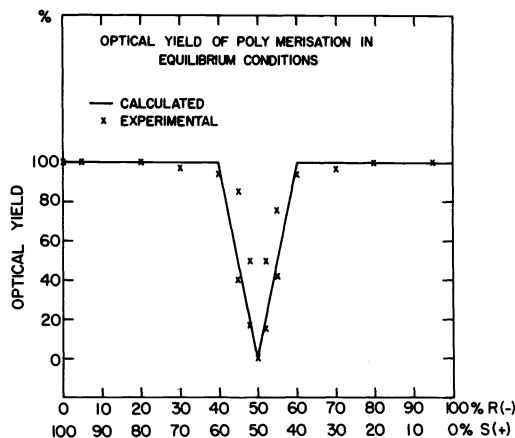
Fig. 4. Expected and measured dependence of optical purity of dimers of 1 upon
          composition of the initial monomer.

It is clear however that the presence of an immiscibility gap interferes with the require-
ments of our "absolute" asymmetric synthesis from racemic 1. On the other hand, fast
cooling induces precipitation of a metastable phase, where m=n in each crystal, and thus
the amount of 1 phase is independent of the amount of d (Scheme 7). Two independent
demonstrations of the existence and nature of this phase could be obtained by Differential
Scanning Calorimetry and by NMR analysis of the diastereomeric ratio of the dimers obtained
from the stable and metastable phases, which reflects directly the microcomposition of
each crystal (Fig. 5) (ref. 35).

The metastable phase is indeed the one we need for our experiment. Due to its metastability
however, it is difficult to grow it under the conditions of slow cooling needed for the
preparation of large homochiral crystals. Nevertheless, growth under intermediate
conditions allowed us to prepare crystals enriched in one of the two enantiomorphous forms
d or l; by irradiation of these crystals, we obtained optically active dimers and polymers.

We have conducted about 20 experiments; the 8 successful ones gave specific rotations as
high as 35° of both signs, both on the entire irradiation mixture (with an average molecular
weight of ∿4000) and on the isolated dimers. No net rotation was detected in any of
these experiments, either on the part of the crystal dissolved before irradiation or of the
monomer recovered from the irradiation mixture. (Ref. 35).

It is apparent from the results obtained, that in order to perform an "absolute" asymmetric
synthesis with quantitative enantiomeric yield in racemic 1, it is necessary to find a way
of stabilizing the metastable phase by removal of the interactions giving rise to eutectic
formation. This requires first an understanding of the structure of the disordered phase.

The relative amounts of topochemical homodimers RR,SS and heterodimers RS obtained by
irradiation of racemic 1, are directly   related to the number of nearest neighbour
contacts in the polymerization direction. (Refs. 36-38) This one-to-one correspondence
allowed us to establish by chemical means the microdistribution of the enantiomers along
the stack of translationally related molecules. Since it has been demonstrated that
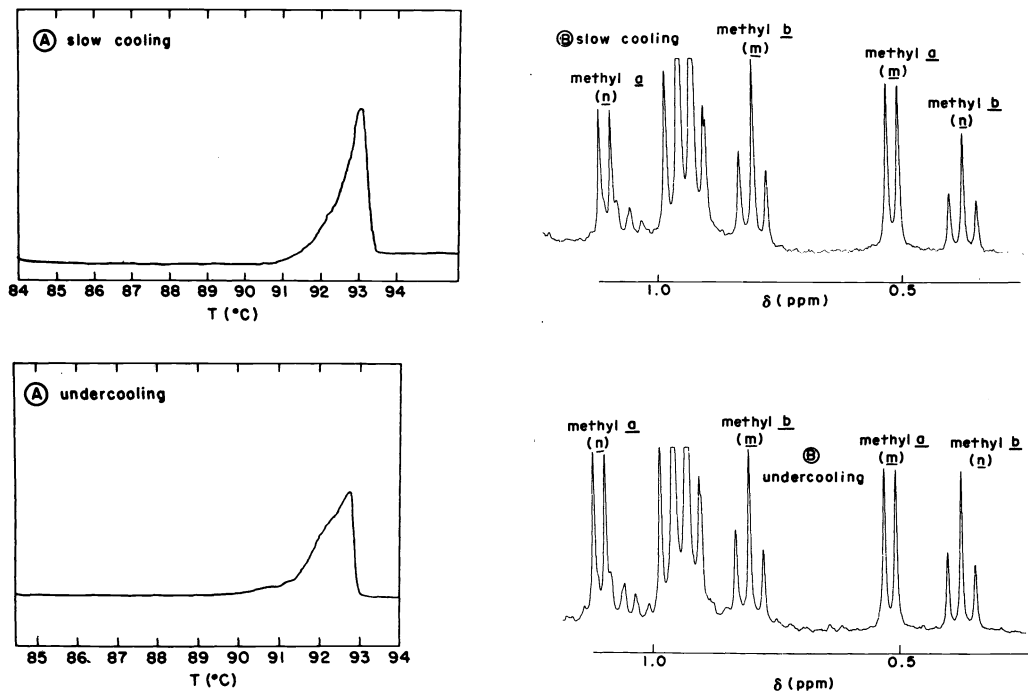RS/(RR+SS) = 1, the antipodes are randomly distributed within the monomer's structure
(Ref. 38).

Fig. 5. A: DSC curves of samples of racemic 1 crystallized slowly and quickly.
         B: ^{1}H NMR spectra of dimers from the same samples of racemic 1, in the
             slowly cooled sample, m/n = 60/40, while in the undercooled m ≃ n.

We hence formulated a working hypothesis, namely that the forces generating the
immiscibility gap are due to diastereomeric interactions between the heterochiral sec-
butyl groups in the chiral crystal.

In Fig. 6 the packing arrangement of pure S(+) 1 in the b c plane is recorded. Molecules
lying along the diagonal of this plane make short contacts of 4.19Å between sec-butyl
groups aligned and pointing towards each other.

Independent determination of the structure of compounds containing disordered sec-butyl
handles (Ref. 33) have shown that the two antipodes can occupy the same crystallographic
site, by use of a mechanism which implies interchange of the methyl and ethyl group of
the sec-butyl in an extended conformation. Application of this same mechanism in the
case of racemic 1 would conceivably cause steric hindrance at the RS contacts along
the diagonal of the b c plane (Scheme 8).

In order to remove these unfavourable interactions, we intercalated into the system of
racemic 1, the achiral isopropyl homologue 4, (see Table 1). Introduction of 20% 4 in the
P1 structure of racemic 1 already caused a drastic reduction of the eutectic range,
indicating that the contacts within the eutectic phase can be modified, and the solid
solubility between enantiomers can be enhanced, by reducing the overall volume occupied
by the side groups.

Due to limited solid solubility of 4 in 1 however, this approach did not lead to complete
removal of the eutectic , and therefore did not provide us with the appropriate system
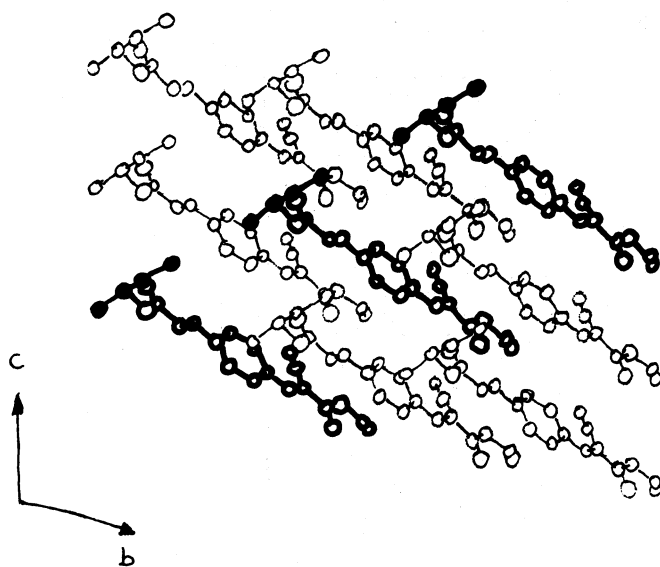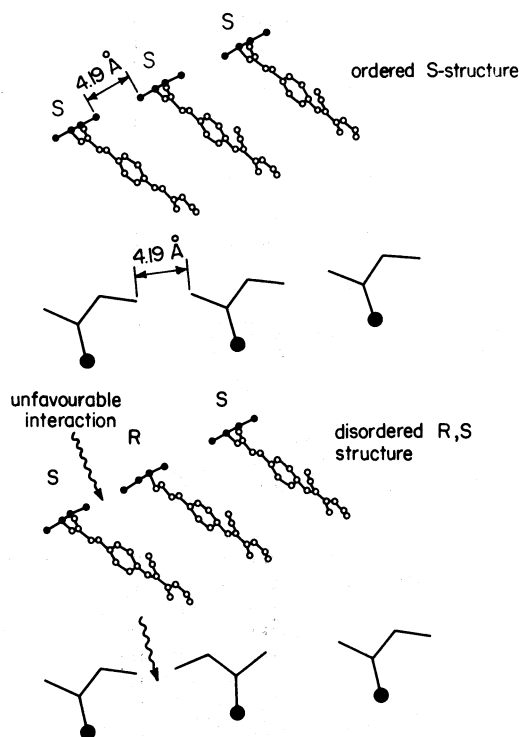for our synthesis.

Fig. 6.   Packing arrangement of S(+) <u>1</u> in the b c plane.

Scheme 8

In a second approach we tried to construct a crystalline phase isomorphic with 1, but composed of non-chiral molecules. The rules of isomorphism (Ref. 39) state that iso-morphic phases can be built from two similar systems if the overall volume occupied by the different group is the same and the interactions are not changed.

A simple transfer of one methyl group between alternate neighbouring sec-butyl groups along the diagonal of the b c plane, as schematically represented below, would replace the chiral handles with non chiral isopropyl and 3-pentyl side chains, leaving the backbone of the molecule unchanged. The overall occupied volume would be maintained. (Scheme 9).

<div align="center">Scheme   9</div>
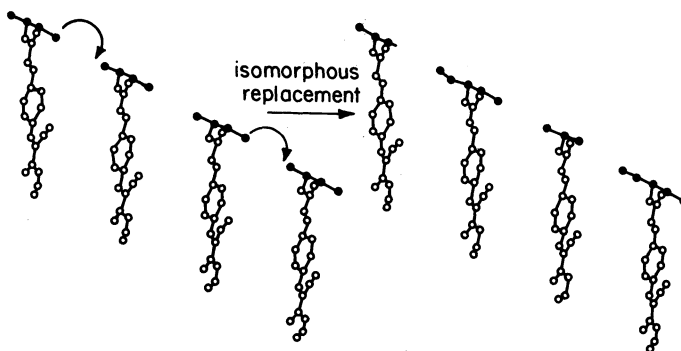
In Fig. 7 the phase diagram between monomers 4 and 5. is recorded (Table 1). Three distinct ranges can be detected. Whereas A and C represent solid solutions in the centrosymmetric triclinic structures of the pure monomers, range B clearly indicates the formation of a new crystalline phase. The cell constants of the 1:1 mixture of 4 and 5 were measured (Table 1), and confirmed that this phase is perfectly isomorphous with racemic and enantiomeric 1, thus confirming the validity of our model.
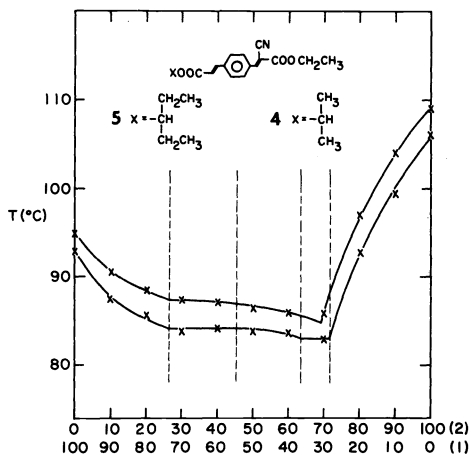
Fig. 7. Phase diagram between monomers 4 and 5

Two other possible model motifs were envisaged in an analogous way. Fig. 8 illustrates the contacts (3.889Å and 3.808Å respectively) of the sec-butyl group of a molecule sitting in the origin (0,0,0)   with the ethyl ester groups of the two neighbouring molecules at(1, 2, 1)and(1, 1, 1).

A transfer of one methyl group across these contacts might generate either of two possible isomorphous structures. Path a would generate compound 6 with R_1 = isopropyl and R_2 = n-propyl, and path b compound 7 (with R_1 = 3-pentyl and R_2 = methyl)(Table 1). Both compounds have been synthesized. While 6 packs in a racemic structure, 7 crystallizes in a chiral structure of space group $P2_1$,z=2(cell constants in Table 1). In spite of the difference in space group with respect to the original Pl, there is a clear correlation between the two structures; the two axes of lengths 7. and 5 Å are almost identical, whereas the third axis is doubled, thus doubling the number of molecules in the unit cell. Since the 7Å axis is the polymerization axis, this means that the stack of translational related molecules, held together by the dipole-induced dipole interaction, is left unchanged in the polymerization direction, while the van der Waals interstack contacts are slightly modified.
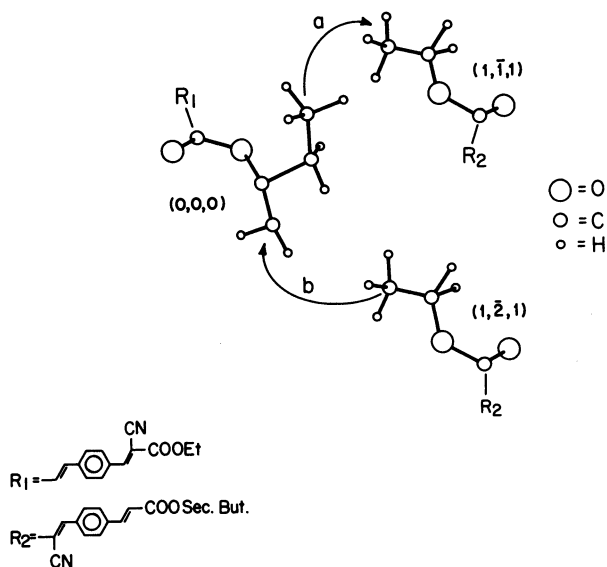
Fig. 8. Relative orientation of the sec-butyl group of the molecule in (0,0,0) with
         respect to the ethyl ester residues of the molecules in (1,$\bar{2}$,1) and (1,$\bar{1}$,1).

The above observations indicate that both the crystals of the 1:1 mixture of 4 and 5 on
one hand, and of 7 on the other, are suitable for the performance of an "absolute"
asymmetric synthesis.

Single crystals of both systems have been grown from the melt, using the modified Bridgman
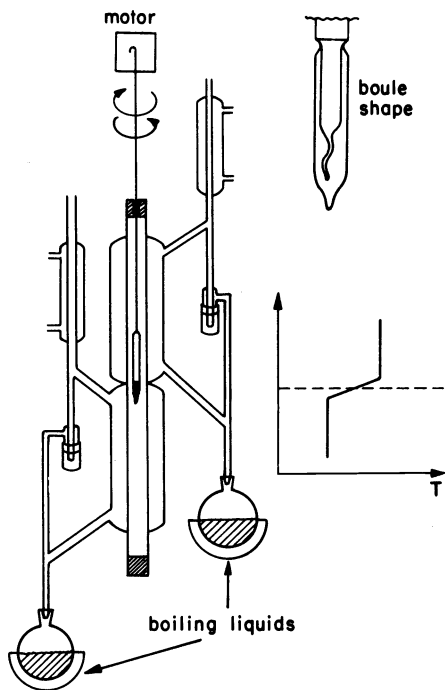apparatus designed by Sherwood, shown in Fig. 9 (Ref. 40).

Fig. 9. Apparatus for growth of single
crystals of organic compounds from the
melt. The boule containing the molten
compound is lowered slowly through a
sharp gradient ΔT (∿10°/cm) established
by the vapours of two boiling liquids.
The motor is operated at variable
lowering and spinning speeds.

Irradiation of large crystals of both systems led to the formation of optically active dimers and polymers, with the same stereochemistry as those from $\underline{1}$.

Since 7 has a tendency for better crystallization, we focused on this system for the achievment of a reaction with quantitative enantiomeric yield.

In a number of experiments performed, values of $[\alpha]_D$ of the whole irradiation mixture ranging from 0 to +64° have been observed, depending on the perfection of the crystal.

The largest specific rotation measured for the isolated dimer was 106°. ($[\alpha]_D$ of dimers with the same stereochemistry and different side groups, range from 102°-116°). The exact determination of the enantiomeric excess of dimer and polymers must await an independent determination of the specific rotation of the optically pure dimer, currently under investigation.

CONCLUDING REMARKS

In conclusion we feel that we were able to demonstrate the feasibility of the planning and construction of crystalline phases with predefined characteristics, by exploitation of empirical knowledge on intermolecular interactions. The preparation of such a phase allowed us to generate optically active polymers from non-chiral monomers, by a process of crystallization and topochemical solid state reaction, in a closed initially symmetrical system. However, the chances for the starting monomer to crystallize in either of the antipodal crystals are equal, implying equal chances of obtaining chiral polymers of opposite chiralities in a large number of experiments. In order to conserve the net chirality, generated in one successful experiment, an efficient mechanism of amplification is therefore required. One possibility, recently suggested by Green and Heller (Ref. 41), is to investigate the inducing effect of the reaction products on the crystallization of the reactant. Our system has an additional advantage in this regard, because of the remarkable similarity between the geometry of the products and of the parent phases. The utilization of this approach requires an understanding of the mechanism of crystallization of the monomers, in the presence of appropriate chiral additives.

We hope that studies using this style of approach,   may lead to the solution of a number of pending problems in material research, such as the synthesis of large chiral single crystal of conjugated polymers, organic semiconductors, etc. Studies along these lines are currently under investigation.

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