Asymmetric Photopolymerisation in Chiral Crystals. An Example of a Chiral Resolved Monomer Packing in Two Quasi-enantiomeric Phases

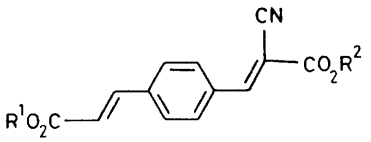
Jan van Mil, Lia Addadi, Meir Lahav, and Les Leiserowitz

Department of Structural Chemistry, Weizmann Institute of Science, Rehovot, Israel

The ability of molecules, chiral by virtue of the presence of an s-butyl group, to display conformational polymorphism has been exploited for the performance of asymmetric syntheses of either sense on the same chiral molecule; this phenomenon is illustrated for the asymmetric solid-state polymerisation of the monomer (*R*)-(−)-(**1**).

Chiral resolved enantiomers of organic molecules, chiral since they contain an s-butyl 'handle,' and their racemates, have a general tendency to pack in isostructural crystals.[1] An analysis of a number of crystal structures of such compounds has disclosed that this property stems from the ability of the s-butyl group to adopt various conformations.[2]

Comparison of the crystal structures of resolved and racemic s-butyl phthalate and *N*-s-butylphthalamide[3] showed that in



(**1**) R^1 = (*R*)-(−)- or (*S*)-(+)-Bu^s; R^2 = Pr^n
(**2**) R^1 = (*R*)-(−)- or (*S*)-(+)-Bu^s; R^2 = Et

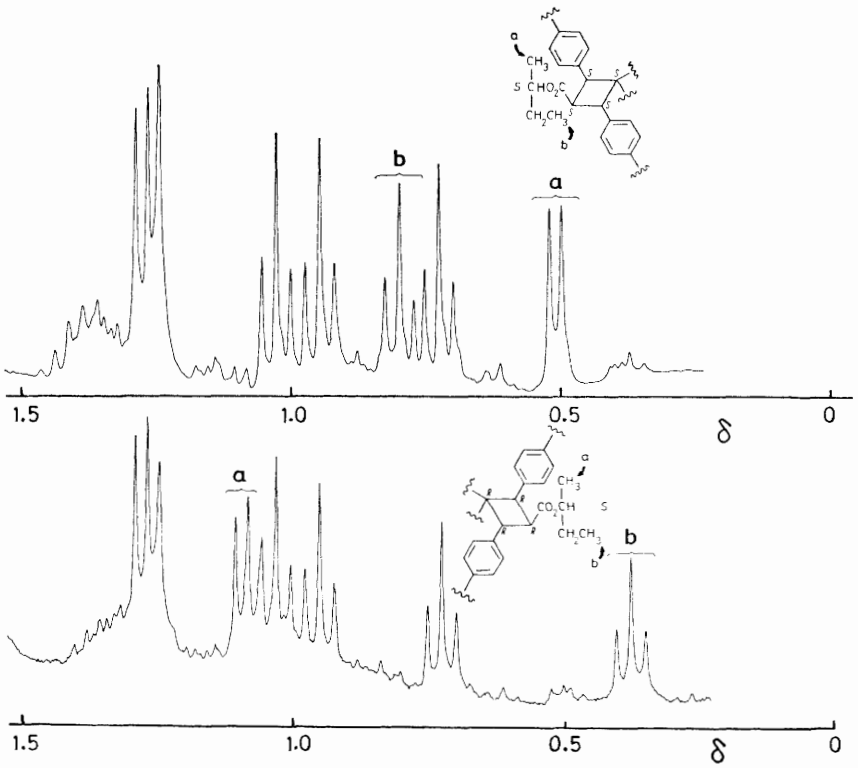
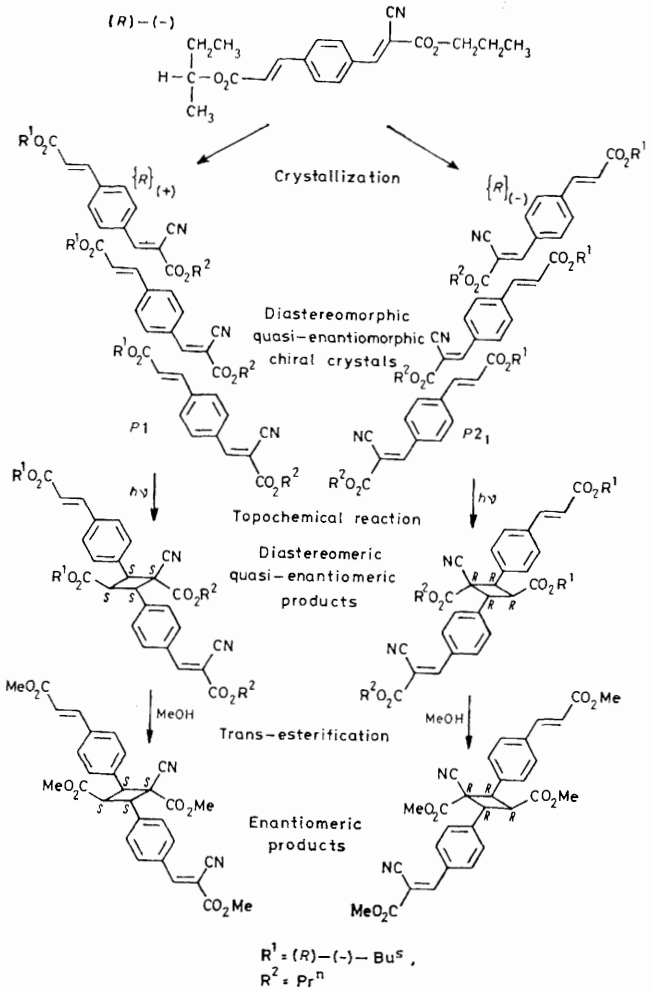


Figure 1. ^{1}H N.m.r. spectra (Bruker WH 270 MHz) in the range δ 0—1.5 of the two diastereomeric, quasi-enantiomeric products of the dimerisation of (**1**), showing the differences in the chemical shift of the methyl groups of the s-butyl groups in the two dimers.



Scheme 1

the crystal structure of the pure enantiomer, *e.g.* *R*, there are two independent molecules per asymmetric unit. One of them, (A), adopts exactly the same conformation as does molecule *R* in the racemate crystal, whereas the other molecule (B) adopts a conformation which is almost enantiomeric to (A), thus mimicking the conformation of molecule *S* in the racemate.[1,3]

These findings suggest that chiral resolved organic molecules containing an s-butyl group as the sole chiral 'handle' might frequently display conformational polymorphism[4] whereby the two polymorphs are almost enantiomorphic.

Such polymorphism, coupled with a topochemical asymmetric synthesis, would lead to the formation of chiral products of opposite chiralities starting from the same chiral substrate. In the course of our studies on 'spontaneous asymmetric synthesis'[5] we came across such a system, the results of a study of which are presented here.

The resolved monomer (**1**) is polymorphic. Crystallisation under different conditions from the melt or from solution (propan-1-ol, cyclohexane–ethyl acetate, hexane–methylene dichloride, or propan-2-ol) yields form α or form β without any apparent preference for either. (Occasionally a third γ-form was obtained which is crystallographically very similar to the β-form and chemically identical.) However, in a given crystallisation either phase is obtained in crystallographically pure form, *i.e.* without contamination by the second phase, as demonstrated by *X*-ray powder diffraction analysis.

Irradiation† of a polycrystalline sample of (*R*)-(−)-(**1**) of form α (space group $P2_1$, cell dimensions $a = 5.43$, $b = 28.24$, $c = 6.79$ Å, $\beta = 103.8°$, $Z = 2$), yields topochemical dimers, trimers and oligomers with new chiral centres at the cyclobutane carbon atoms with absolute configuration (*RRRR*) ($[\alpha]_D$ of the dimer: +101°). The stereochemical behaviour of this form is similar to that of the monomer (**2**), described

† Powdered crystals were irradiated at 5 °C with $\lambda > 290$ nm through Pyrex for *ca.* 2 weeks. The product dimer was isolated by preparative t.l.c. (silica gel, cyclohexane–ethyl acetate, 3:1) and dried *in vacuo*. Specific rotations were measured in $CHCl_3$.

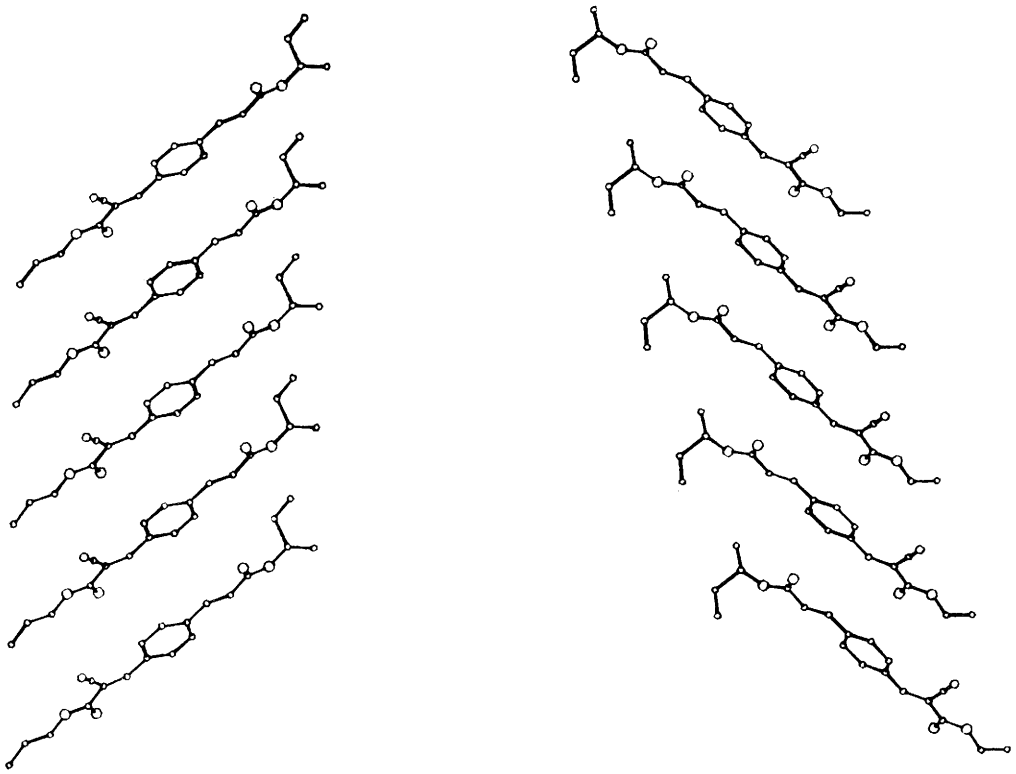


Figure 2. Crystal structures of (A), monomer (*R*)-(−)-(**1**) (β-form) and (B) (*R*)-(−)-(**2**), with enantiomeric polymerisation stacks and the (*R*)-(−)-s-butyl groups in different conformations.

previously,[6] which exists in one crystalline form; the (*R*)-enantiomer gives the (*RRRR*)-cyclobutane and the (*S*)-enantiomer the (*SSSS*)-cyclobutane. Analogously, (*S*)-(+)-(**1**) in the α-form yields compounds with (*SSSS*)-cyclobutane rings.

However, irradiation of the same monomer (*R*)-(−)-(**1**) in the form β (space group *P*1, $a = 4.821$, $b = 7.257$, $c = 13.993$ Å, $\alpha = 76.55$, $\beta = 77.81$, $\gamma = 76.11°$, $Z = 1$) yields the same topochemical dimers, trimers, and oligomers but with opposite absolute configuration at the cyclobutane carbon atoms, (*SSSS*) ($[\alpha]_D$ of the dimer: −112°). (*S*)-(+)-(**1**) in the form β yields an (*RRRR*)-cyclobutane ring.

The structure assignment is based on the following analyses of the respective dimers. The mass spectra indicated identical molecular weights (682) and very similar fractionation patterns. The n.m.r. spectra (Figure 1) are identical for both dimers, with the exception of the signals for the s-butyl groups attached to the cyclobutane ring, which are differently shielded by the phenyl rings.

Following a previous analysis,[6] we attribute the doublet at δ 0.51 and the triplet at δ 0.79 to the dimer obtained from form α, and the triplet at δ 0.38 and the doublet at δ 1.08 to the dimer of form β. As can be seen from the spectra, the products are obtained in a practically pure diastereomeric form.‡ Furthermore, transesterification of the two diastereomeric dimers§ to give the tetramethyl esters, yields enantiomeric dimers with opposite specific rotations and identical n.m.r. spectra ($[\alpha]_D$ of the tetramethyl dimers: +128° and −128°); see Scheme 1.¶

The crystal structure of form β was solved;[7] that of form α has not yet been obtained owing to a lack of appropriate crystals. However, as just pointed out, the structure and stereochemical behaviour of the photopolymerising stack of (**2**) is very similar to that of (**1**) in the α form, and therefore (**2**) may be compared with the structure of form β to obtain some insight into the structural differences between the α- and β-forms with respect to the s-butyl 'handle' (see Figure 2).

The arrangement of the polymerising chromophores in the two structures is enantiomeric, being stabilised by the same interactions, whereas the same chiral s-butyl groups (*R*) pack into two conformations which are different from each other, as would be expected from the above analysis.

A quantitative analysis of the conformational and configurational properties of the s-butyl groups will be presented in a full paper.[2]

‡ Since the materials were synthesized using chiral s-butyl alcohol of 90% optical purity only, some of the second diastereoisomer will always be present. However, after transesterification we obtain in both cases cyclobutanes free from s-butyl groups, with an optical rotation of 128°. This corresponds to an almost quantitative enantiomeric yield. See ref. 5.

§ The dimer (100 mg) was refluxed for 24 h in methanol (25 ml) containing a few drops of thionyl chloride. The tetramethyl ester was separated by t.l.c.

¶ We point out that this experiment provides definite proof that the asymmetric induction is due only to the chiral environment of the crystal and not to the chirality of the s-butyl group.

We thank the donors of the Petroleum Research Fund administered by the American Chemical Society for financial support.

Received, 11th November 1981; Com. 1320

References

1 L. Addadi, S. Ariel, M. Lahav, L. Leiserowitz, R. Popovitz-Biro, and C. P. Tang, in 'Chemical Physics of Solids and Their Surfaces' (Specialist Periodical Report), eds. M. W. Roberts and J. M. Thomas, The Chemical Society, 1980, vol. 7, p. 202.
2 S. Ariel, L. Addadi, M. Lahav, and L. Leiserowitz, unpublished work.
3 S. Ariel, Ph.D. Thesis, Weizmann Institute, 1982.
4 For definition and other examples of comformational polymorphism see: J. Bernstein and A. T. Hagler, *J. Am. Chem. Soc.*, 1978, **100**, 673.
5 L. Addadi, J. van Mil, and M. Lahav, *J. Am. Chem. Soc.*, in the press.
6 (a) L. Addadi and M. Lahav, *J. Am. Chem. Soc.*, 1978, **100**, 2838; (b) for the crystal structure of (**2**) see Z. Berkovitch-Yellin, *Acta Crystallogr., Sect. B*, 1980, **36**, 2440.
7 We thank Dr Felix Frolow of this Department for the crystal structure analysis of form β of (**1**). The full analysis will be published elsewhere.