The Synthesis of Optically Active Dimers and Polymers by Reaction in Crystals of Chiral Structure

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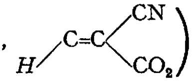
Summary The first synthesis of a chiral polymer by a topochemical reaction in a one-component chiral crystal, and the first asymmetric synthesis by reaction in a crystal of racemic composition are reported.

RECENTLY there has been a growing interest in asymmetric synthesis *via* topochemical controlled reactions in chiral crystals.[1] The feasibility of such syntheses has been demonstrated by Farina *et al.*,[2] and by our work.[3] In these reactions the sole chiral influence derives from the asymmetric environment of the molecules in the crystal. We have analysed[4] the structural requirements for enantiomeric differentiation in solid-state (2+2)-photo-dimerisation and polymerisation reactions, and an example based on this analysis has been described.[5] We now report the first successful asymmetric synthesis of a chiral dimer and polymer by reaction in a one-component system, based on an extrapolation of the previous analysis.

We have prepared a number of divinyl monomers, similar to the symmetric ones studied by Hasegawa, Nakanishi *et al.* which are known to undergo lattice-controlled polymerisation,[6] but which are unsymmetrically substituted and contain chiral 'handles,' which favour crystallisation in asymmetric structures.

Many of these monomers, on irradiation in the solid state give polymeric products. The system using monomer (**1**), synthesised from paraphthalaldehyde by successive condensations with malonic acid and ethyl cyanoacetate, followed by esterification with *R*-(+)- or *S*-(−)-s-butanol has been studied in detail. The assumed monomer-stacking and the nature of the overall reaction is shown in Figure 1.

Monomer (**1**), m.p. 103—104° (ethanol–water), has space group $P1$ with $a = 13{\cdot}17$, $b = 6{\cdot}94$, $c = 5{\cdot}25$ Å; $\alpha = 103°$, $\beta = 95{\cdot}5°$, $\gamma = 90°$, $Z = 1$. A polycrystalline sample of this material, optically pure, was irradiated with light from Westinghouse Sunlamps ($\lambda > 300$ nm) at 5°, and yielded a dimer (**2**), a low molecular weight $CHCl_3$-soluble polymer and a $CHCl_3$-insoluble polymer. The relative yields of the products vary with the wavelength of the light; $\lambda > 350$ nm (Corning Glass Filter 7380) gave only low molecular weight products with an increased amount of dimer which was separated from the polymer and monomer by preparative t.l.c. (silica gel, $CHCl_3$): mol. wt. 654; m/e 654(M), 327($M/2$), 330 (asymmetric cleavage of cyclobutane ring); n.m.r. ($CDCl_3$, rel. Me_4Si) δ 0·4—2·0(22H, Me and C-CH_2-C), 3·7—5·4 (9H, cyclobutane protons, OCH_2, OCH), 6·47 (1H, doublet, *trans*-HC=C*H*–CO, J 17Hz), 7·3—8·2 (9H, aro-

matic + *trans*-*H*C=C(H)CO_2), 8·28 (1H,  $H\!-\!C{=}C(CN)(CO_2)$).
Assignment of structure to the dimer is based on these data and topochemical considerations. The structures of (**2**) and of the *trans*-methylated molecule (**3**) are shown in Figure 2.

The dimer and low molecular weight polymer gave unambiguous optical rotations, of sign opposite to that of the monomer. Furthermore, replacement of the chiral s-butyl groups of the dimer by methyl groups enhances the optical activity. Thus, irradiation with $\lambda > 350$ nm for 14 days of the *R*(+)-monomer ($[\alpha]_D^{25} = +21°$) gave the dimer (**2**) ($[\alpha]_D^{25} = -81°$), which on transesterification with MeOH yielded the dimer (**3**)† ($[\alpha]_D^{25} = -102°$). Irradiation of this monomer in suspension in 7% aqueous ethanol gave a $CHCl_3$-soluble polymer of average mol.wt. 2400 and $[\alpha]_D^{25} = -24°$. Similarly the *S*-(−)-monomer ($[\alpha]_D^{25} = -21°$) gave (**2**) ($[\alpha]_D^{25} = +82°$), which gave (**3**) ($[\alpha]_D^{25} = +107°$). Irradiation of this monomer in the solid state with $\lambda > 310$ nm gave a soluble polymer ($[\alpha]_D^{25} = +54°$).

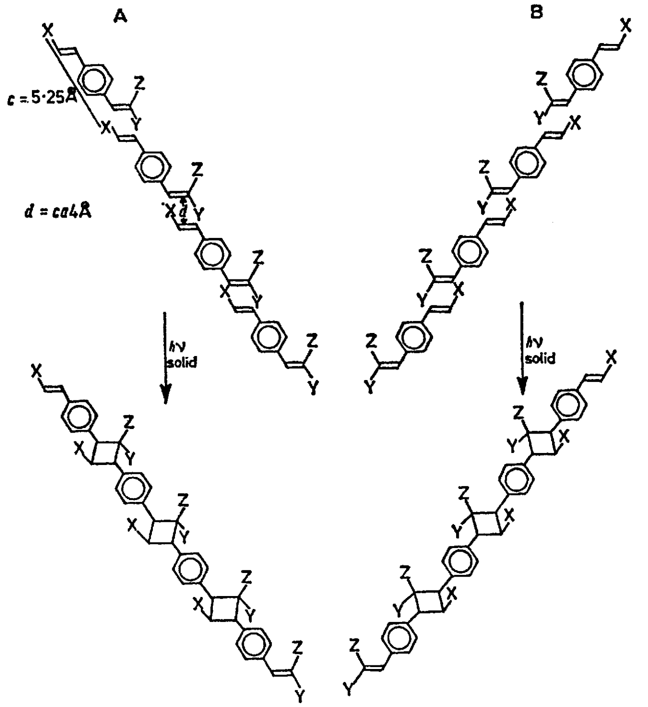
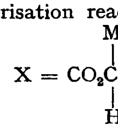


FIGURE 1. Schematic representation of the stack structures and polymerisation reactions in enantiomeric crystals [A and B] In (**1**) X =  $CO_2\overset{\displaystyle Me}{\underset{\displaystyle H}{C^*}}\text{-}Et$, Y = CO_2Et, Z = CN. The structure are compatible with the cell dimensions, where *a* and *b* are approximately in the molecular plane and along its long and short axes, respectively. The structure of the polymer is assigned by analogy to that of dimer (**2**) and to the polymers of Hasegawa and Nakanishi.[6]

Proof that the asymmetric induction results from the influence of the chiral environment at the reaction site, and not from the chiral influence of the chiral handle, is obtained from a further observation. Racemic (**1**) was crystallised from the melt or from ethanol solution in chiral space group *P*1, $a = 13{\cdot}28$, $b = 7{\cdot}02$, $c = 5{\cdot}42$ Å, $\alpha = 104°$, $\beta = 93°$, $\gamma = 92°$, $Z = 1$; m.p. 94 °C. Since the cell constants of the racemic (**1**) and its *X*-ray diffraction intensities are similar to those of pure chiral (**1**), but not identical with them, the racemate does not undergo spontaneous resolution but gives a solid solution of the two enantiomers disordered with respect to the chiral s-butyl group.[7] The wide range of mutual solid solubility of the two enantiomers is shown also by D.S.C. analysis.

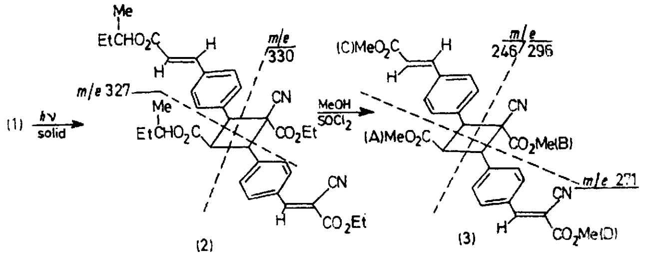


FIGURE 2

The difference in structure between crystals of optically pure monomer and of racemic composition is shown in Figure 1. In the former, all X's in a given crystal are of the same chirality, and the chiral handle imposes a preference toward crystallisation in one of the two enantiomeric structures. In the latter every enantiomeric single crystal contains equal numbers of X's of opposite chiralities. The racemate has equal probability of crystallising in each of the two enantiomeric structures [A] and [B]. A large crystal of this solid solution, part of which was shown to be optically inactive when dissolved, yielded on irradiation optically active dimers‡ and low molecular weight polymers. This mixture of products had $[\alpha]_D^{25} = -24°$, the dimers alone having $[\alpha]_D^{25} = -30°$.

Thus, both dimer and low molecular weight polymer are optically active because of the backbone configuration. The optical rotation of the insoluble fraction has not yet been determined. However, we conclude by extrapolation from the above, from the knowledge that polymerisation of Hasegawa-Nakanishi-type monomers proceeds under lattice control both in initiation and propagation stages, and from the fact that the polymer is formed by linkage of chiral lower molecular weight units, that the insoluble polymer from (**1**) also has a chiral backbone.

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† Dimer (**3**) of mol. wt. 542 gave *m/e* 542(*M*), 271(*M*/2) and, by asymmetric cleavage of the C_4 ring, 296 and 246, n.m.r. ($CDCl_3$ rel. Me_4Si) δ 3·46 [3H,Me(A)], 3·51 [3H,Me(B)], 3·84 [3H,Me(C)], 3·97 [3H,Me(D)], and 4·5—5·3 (3H, cyclobutane protons).

‡ Starting with monomers containing *R* and *S* s-butyl groups one obtains (**2**) with *R*+*R*, *R*+*S*, *S*+*R*, and *S*+*S* s-butyl groups.

The determination of the optical yields in these polymerisation reactions is in progress. On the basis of the probable structure of the monomer crystal our previous analysis predicts[4] that in crystals of one handedness these yields may be near quantitative. Also under investigation are the crystal structure of the monomer and the absolute configurations of the products.

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[7] This is one of several cases in which we have found disorder in the crystal involving enantiomeric s-butyl groups, (M. Lahav, F. Laub, L. Leiserowitz, and L. Reutman, unpublished results).