

A New Approach to the Synthesis of Chiral Molecules from Nonchiral Reactants. Asymmetric Induction by Reaction at One Surface of a Single (Nonchiral) Crystal

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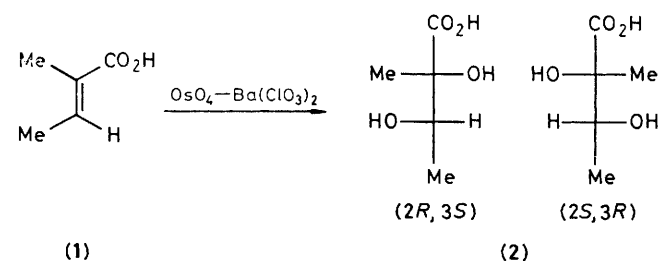
Reaction at one surface of a single achiral crystal can produce chiral products having optical purities approaching 100%.

The use of chiral crystals in chiral syntheses is well known,¹ and the concept of different chemical reactions occurring on opposite faces of a chiral crystal is becoming established.² We have recently shown³ that the stereoselectivity of a reaction can be controlled even when nonchiral crystals are involved. Specifically, it is possible to generate stereoselectively a chiral product from nonchiral reactants by using one surface of a single crystal as the chiral template, provided (i) that the projection of the crystal structure on to that surface belongs to one of the diptychiral† plane groups p1, p2, p3, p4, or p6, and (ii) that the molecules in the crystal are aligned in certain ways relative to the symmetry elements in the crystal.³

This prediction has now been confirmed by allowing a single crystal of tiglic acid (1) to react, on the $(\bar{2}10)$ or $(2\bar{1}0)$ surfaces, with osmium tetroxide, generating optically enriched *threo*-2,3-dihydroxy-2-methylbutanoic acid (2). Tiglic acid belongs to the space group $P\bar{1}$,⁴ and its projections onto the $(\bar{2}10)$ or $(2\bar{1}0)$ planes belong to the plane group p2. The π -electron density of the alkene is aligned approximately perpendicular to these planes, as shown in Figure 1.

The experiments were performed using large single crystals of tiglic acid grown from acetone. A single crystal was cut into two approximately equal portions, exposing the $(\bar{2}10)$ and $(2\bar{1}0)$ faces. Each portion was embedded in epoxy-resin so that only the freshly cut surfaces were exposed, and each was then treated separately; the exposed faces are diptychiral and produce enantiomeric products. Reactions were carried out in a small volume of stirred ice-cold aqueous solution of barium chlorate and osmium tetroxide over a period of 48 h.⁵ During this time, the crystal disappeared, leaving only the epoxy-shell; control experiments confirmed that a similar quantity of tiglic acid, even when fully exposed to the solvent did not dissolve in a comparable time.

The aqueous solutions from reactions performed as described above exhibited approximately equal optical activity, but with opposite signs of rotation. Isolation of the diol (2) was carried out as described,⁵ and gave a 40–60% yield of samples whose chemical identity was confirmed by chromatographic and spectral comparison with an authentic sample of racemic material obtained (in 70% yield), by *cis* dihydroxylation of (1) in aqueous solution.⁵ The isolated samples of (2) showed complementary o.r.d. curves in the



region 400–700 nm, showing that reaction on opposite diptychiral crystal faces produces opposite enantiomers. Comparison of the specific rotations, at 436 nm, of the two enantiomers so produced with those of *threo*-(2) produced by chemical resolution⁶ indicated that optical purities as high as 95% were obtained when good crystals were used, and were carefully mounted in the epoxy-resin. Typically, optical purities of 50–90% have been obtained in successive experiments.

All of the monoclinic and triclinic space groups, including chiral ones, have at least one projection which belongs to a diptychiral plane group. A large proportion of organic crystal structures belong to the monoclinic or triclinic crystal systems,⁷

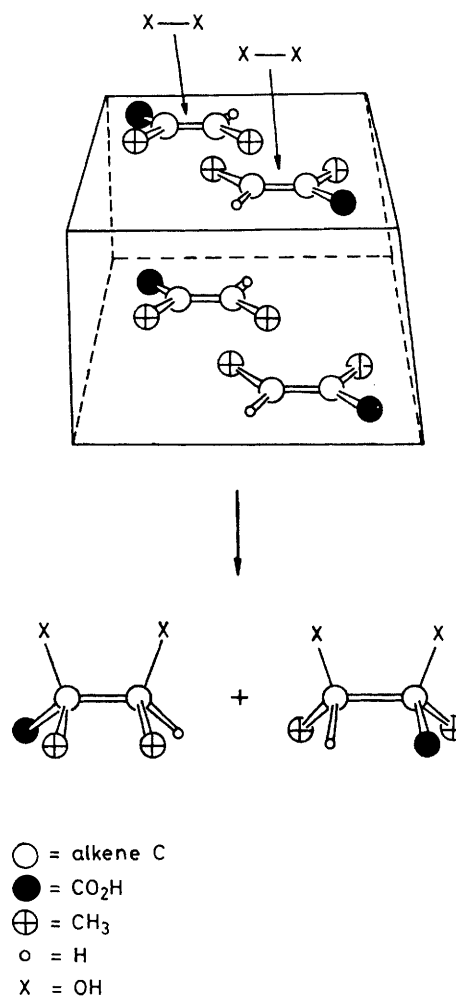


Figure 1. The BaClO_3 -catalysed reaction of tiglic acid with OsO_4 . The two molecules on the top plane $(\bar{2}10)$ are related by a centre of symmetry. The bounding planes for this view of tiglic acid are $(\bar{2}10)$, $(2\bar{1}0)$, (001) , $(00\bar{1})$, (100) , and $(\bar{1}00)$.

† Having nonsuperimposable mirror images in two dimensions.

so this method offers an unprecedented opportunity for the stereochemical control of organic reactions.

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References

- 1 B. S. Green, M. Lahav, and D. Rabinovich, *Acc. Chem. Res.*, 1979, **12**, 191.
 - 2 E. N. Duesler, R. B. Kress, C. Lin, W. Shiau, I. C. Paul, and D. Y. Curtin, *J. Am. Chem. Soc.*, 1981, **103**, 875.
 - 3 H. L. Holland and M. F. Richardson, *Mol. Cryst. Liq. Cryst.*, 1980, **58**, 311.
 - 4 R. G. Wyckoff, 'Crystal Structures,' Vol. 5, Wiley Interscience, 1966, pp. 500—501.
 - 5 D. J. Robbins and D. H. G. Crout, *J. Chem. Soc., C*, 1970, 1334.
 - 6 G. S. Myers, P. Morozovitch, W. L. Glen, R. Barber, G. Papineau-Couture, and G. A. Grant, *J. Am. Chem. Soc.*, 1955, **77**, 3348.
 - 7 G. H. Stout and L. H. Jensen, 'X-Ray Structure Determination: A Practical Guide,' Macmillan, New York, 1968, p. 135.
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