chemical and photoelectron spectroscopic data support this assignment.[20]

Acknowledgment. We thank W. G. Becker and W. Schwarz for technical assistance and helpful discussion. G.J. gratefully acknowledges the support of the Division of Basic Energy Sciences of the Department of Energy to Boston University.

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[20] The oxidation potential of **2** (0.91V vs. SCE)[14] is 0.63 V lower than that of **1**[14] but its ground state lies at least 22 kcal/mol[21] and possibly as much as 27 kcal/mol[22] above that of **1**.[14] Accordingly, the energy of **5** lies ~ 14 kcal/mol above that of **3**.

[21] Kabakoff, D. S.; Bünzli, J. G.; Oth, J. M. F.; Hammond, W. B.; Berson, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1510.

[22] Wiberg, K. B.; Connon, H. A. *J. Am. Chem. Soc.* **1976**, *98*, 5411.

[23] Rogers, D. W.; Choi, L. S.; Girellini, R. S.; Holmes, T. J.; Allinger, N. L. *J. Phys. Chem.* **1980**, *84*, 1810.

Useful Impurities for Optical Resolutions. 1. On the Crystallization of Photopolymerizing Dienes in the Presence of Their Chiral Topochemical Products

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Received July 21, 1980

We report in this series a novel systematic approach to preferential crystallization of enantiomers, in the presence of tailor-made impurities, which provides a general method for resolution of conglomerates and an empirical method for the assignment of absolute configuration and which may provide a way to selectively control some physicochemical properties of crystals. Understanding of the mechanism of the impurity action came from our studies concerned with generation and amplification of optical activity in closed symmetrical systems.

A number of "absolute" asymmetric syntheses via topochemical reactions in chiral crystals have been reported from this laboratory. In one of these,[1] quantitative enantiomeric yields of dimers, trimers, and oligomers were obtained starting from achiral dienes (Scheme I). In these reactions the absolute configuration of the parent crystal determines the chirality of the product. In the absence of an outside chiral agent, the chances of crystallization of the achiral starting material in either of the two enantiomorphic phases *d* or *l* are equal, and thus, in a large number of experiments, no net chirality of product is expected. In order to preserve the chirality generated in the first successful experiment, a highly efficient mechanism of amplification is therefore needed.

In this context, Green and Heller[2] performed an elegant experiment which showed that introduction of the chiral bromination product of 4,4'-dimethylchalcone into the crystallizing melt of this chalcone caused preferential crystallization of the unwanted *d* crystal if the bromide originated from an *l* crystal and vice versa.

Scheme I

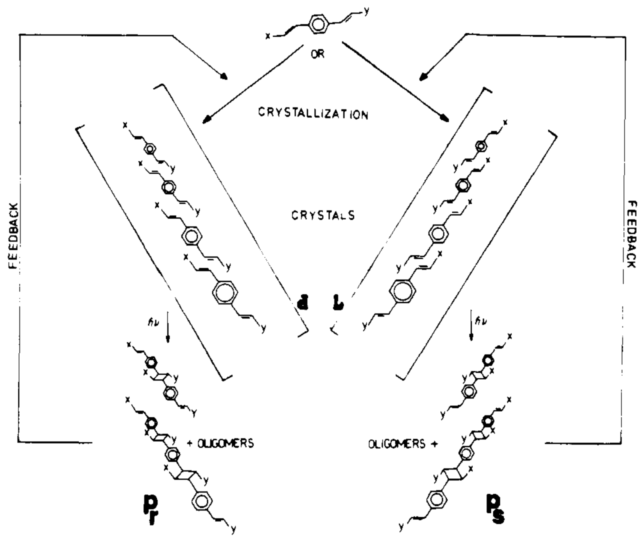
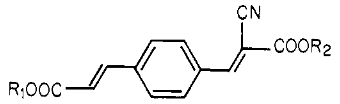


Table I. Results on Asymmetric Crystallization of Monomers 1-6 Induced by Impurity,[a] Given as Specific Rotation of Dimers[b] Obtained After Irradiation



1, R_1 = 3-pentyl; R_2 = methyl
2, R_1 = 3-pentyl; R_2 = ethyl
3, R_1 = 3-pentyl; R_2 = *n*-propyl
4, R_1 = isopropyl, 3-pentyl; R_2 = ethyl
5, R_1 = (*R*,*S*)-*sec*-butyl; R_2 = ethyl
6, R_1 = (*R*,*S*)-*sec*-butyl; R_2 = *n*-propyl

		$[\alpha]_D$, deg					
		dimer				trimer	oligomer
monomer[b]	chirality	15%[c]	15%[d]	8%[d]	3%[d]	15%[c]	8%[c]
1 ($P2_1$)	+	−70	−62	−74	−75	−92	−11
	−		+61	+89	+83	+75	+52
2 ($P1$ or $P\bar{1}$)	+	−47	0[e]	0	0	−30	
	−	+73	0	0	0		
3 ($P1$)	+	−67	−61	−40	−59	−31	−21
	−	+38	+65	+54	+58	+45	+36
4 ($P1$)	+	−42[f]	−47	−51	−40	−41	−9
	−	+46	+47	+56	+36	+30	+15
5 ($P1$)	+	−21	−12	−3	−30		
	−	+33	+8		+17		
6	+	+31	−36	−27	−54		
	−	45	42	40	+30		

[a] Reference 4. [b] $[\alpha^\circ]_D$ of 100% optically pure dimers ranges from 100 to 110° depending on the side chains. In the whole family of $[\alpha^\circ]_D$ compounds, (+)-dimers have absolute configuration *RRRR* around the cyclobutane ring. [c] Fast crystallization (~4 h). [d] Slow crystallization (~2 weeks). [e] Upon slow crystallization the stable polymorph of this monomer is obtained which has a centrosymmetric space group ($P\bar{1}$) and thus no induction is expected or obtained. [f] The reported rotation refers to the homodimer with isopropyl-isopropyl side chains.

Such a process of asymmetric crystallization induced by topochemical products on their parent phases is investigated here systematically, using systems where a strict relationship links the stereochemistry of the former with the structure of the substrate. The aim was to reach a general understanding of the effect and thence to design a system appropriate for amplification. The crystallization of monomers **1–6** was studied (Table I) in the presence of their resolved chiral products (Scheme I). These systems are suited to our purpose, since a given product molecule (say P_R) can conceivably, with only a slight deformation, take the place of a corresponding number of monomer units in the parent (*d*) crystal, while this is not true in the enantiomorphic crystal (*l*).

Monomers **1–8**[3] were melted together with variable amounts (3–15%) of resolved dimer, trimer, and oligomer of **5** (the "impurity") of either chirality,[4] in closed nitrogen-flushed vials, allowed to crystallize, either rapidly (4 h) or slowly (~2 weeks), and then crushed and subjected to irradiation (UV light, four

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[1] (a) Addadi, L.; Lahav, M. *J. Am. Chem. Soc.* **1978**, *100*, 2838. (b) *Ibid.* **1979** *101*, 2152. (c) *Stud. Phys. Theor. Chem.* **1979**, *7*, 179. (d) *Pure Appl. Chem.* **1979**, *51*, 1269.

[2] Green, B. S.; Heller, L. *Science* (*Washington, DC*) **1974**, *185*, 525.

[3] Full crystallographic information on these systems will be reported in a following publication.

[4] The reaction products of resolved **5** were used, since these are easily obtained in high optical purity from the monomer.

0002-7863/81/1503-1248$01.25/0

Table II. Some Results on Asymmetric Crystallization of Monomers 1, 3, and 4 Induced by Impurity,[a] Given as Specific Rotation of Dimers

mono-mer	impurity (dimer of 5)		solvent	$[\alpha]_D$ of product dimer,[b] deg
	chirality	%[c]		
1	+	10	CH_2Cl_2	−92, −52, −80
	+	5	CH_2Cl_2	−71
	+	10	hexane[d]	−106, −89, −101
	+	5	hexane[d]	−100
	+	10	ethyl acetate	−81, −78
3	−	10	CH_2Cl_2	+61, +53, +62
	−	10	hexane[d]	+85, +82, +70
	+	10	hexane[d]	−89, −66, −66
	−	10	ethyl acetate	+43, +43, +51
4	−	10	CH_2Cl_2	+62, +60, +50
	−	5	hexane[d]	+59, +92, +87
	−	10	ethyl acetate	+26, +31, +61

[a] Reference 4. [b] See footnote *b* of Table I. [c] % in weight of substrate. [d] With a few drops of methylene chloride to improve solubility.

Westinghouse lamps, 40 W), for 2 weeks at 5 °C. The reaction products were separated by preparative TLC (silica, cyclohexane:ethyl acetate 3:1) from unreacted monomer and impurity, and their specific rotations were used as a measure of the asymmetric induction in crystallization. Table I summarizes some typical results from monomers **1**–**6**.

The studies were extended to crystallization from solution[5] (Table II). For artifact exclusion, blanks (i.e., polycrystalline monomer samples without impurity) were run simultaneously in both series of experiments. No significant optical activity was found in any of them.

From these results we conclude as follows: the crystallization of monomers **1**–**6**, which pack in chiral structures as in Scheme I, is strongly affected by the presence of products which originated from the same three-dimensional motif of Scheme I. On the other hand, under the same conditions, no induced chirality was observed from similar monomer systems whose crystal structures are based on other motifs (**7**, **8**, and the second polymorph of **2**). Further, the enantiomorphic crystal with an absolute configuration opposite to that of the impurity always precipitates in excess, the enantiomeric yield ranging from 30 to 100%, depending on the monomer. Experiments were carried out also when products of different monomers **1** or **2** were used as additives, and similar results were observed, implying that the asymmetric induction is due mainly to the rigid chiral skeleton of the additive and not the *sec*-butyl groups attached to it. Finally, change of conditions, such as rate of crystallization, solvent, and temperature, affects the induction only quantitatively. Concentrations of additives from 3 to 15% lead to effects of the same order of magnitude.[6]

A possible interpretation of the results here described derives from the knowledge that, especially in inorganic systems, tiny amounts of impurities which are selectively adsorbed on specific faces of crystals may cause a dramatic decrease in the growth rates of these faces. The overall result is a habit change and a decrease in the growth rate of the affected crystals.[7] In our systems we postulate a process in which, by virtue of the stereochemical resemblance between the impurity and one of the two enantiomorphic phases, namely, the parent phase, the products selectively poison the growing surfaces of crystals of that phase, thus inhibiting their growth while not influencing the growth of the enantiomorphic crystals. This mechanism may provide a common explanation for a number of as yet unexplained results on induced crystallization by resolved impurities or additives.[2,8] In the following two papers, experimental evidence is given indicating that this mechanism is indeed correct and has important implications in the kinetic resolution of chiral materials crystallizing in the form of conglomerates.

We conclude, further, that the precipitation of the "unwanted" enantiomorph, both in the experiments of Green and Heller and in our systems, is not an unpredictable property of the specific systems but is an unavoidable and general consequence of the mechanism of the effect. The solution of the amplification problem will thus require very specially designed experiments.

Acknowledgment. We thank Professor M. D. Cohen for useful discussions; we also thank the Israel Commission for Basic Research and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support.

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(5) In this second series of experiments, the monomers were dissolved in different solvents together with a small concentration of impurity and left to crystallize to dryness (12–48 h). The workup procedure is identical with the one used in the first set.

(6) It was observed in several cases that when more than 3% impurity was used, in crystallization from the melt, some of this impurity separated in the form of an oil. Recent studies on the crystallization of **1** in the presence of 1% dimer as impurity resulted in enantiomeric excess of the same size.

(7) For the effect of impurities on crystal growth and morphology see: Brice J. C. "The Growth of Crystals from Liquids"; Wohlharth, E. P., Ed.; North Holland: Amsterdam, 1973; Chapter 3. Palm, J. H.; McGillavry, C. H. *Acta Crystallogr.* **1963**, *16*, 963.

(8) Pincock, R. E.; Perkins, R. R.; Ma, A. S.; Wilson, K. R. *Science (Washington, DC)* **1971**, *174*, 1018.

Useful Impurities for Optical Resolutions. 2. Generality and Mechanism of the Rule of Reversal

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Received July 21, 1980

We have reported studies on the preferential crystallization of one enantiomorphous form of conglomerates of photopolymerizable dienes in the presence of chiral products ("impurities") of topochemical photopolymerization within crystals of these dienes.[1] In all cases the crystal that precipitates in excess is of opposite absolute configuration to that of the chiral impurity (the "rule of reversal"). The effect can be interpreted by considering preferential adsorption of the additive at one or more of the growing surfaces of the stereochemically related parent crystal. This results in a decrease of growth rate of this crystal with respect to that of the enantiomorph. The process should then be of general applicablity to the resolution of racemic mixtures crystallizing in the form of conglomerates (Scheme I).

In order to achieve a successful resolution, the impurity *S′* needs to be "tailor-made" for each specific system.

First support for our hypothesis comes from inspection of the existing literature on induced asymmetric crystallization in the presence of resolved additives. Among all the systems investigated, there are a number for which inducing effects consistent with the pattern of Scheme I have been recorded. In these instances, a striking stereochemical resemblance indeed exists between the resolved impurity and one of the enantiomers of the racemic substrate. Thus, for example, (*R*)-glutamic acid was reported to crystallize preferentially from the racemic mixture in the presence of (*S*)-aspartic acid[2] or (*S*)-γ- methyl glutamate[3] and analogously (*R*,*R*)-sodium ammonium tartrate in the presence of (*S*)-sodium ammonium malate,[4] (+)-narwedine in the presence of (−)-galanthamine,[5] and (*R*)-Cu(Asp)$_2$ in the presence of (*S*)-alanine

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(1) van Mil, J.; Gati, E.; Addadi, L.; Lahav, M. *J. Am. Chem. Soc.* **1980**, *103*, preceding paper in this issue.

(2) Purvis, J. L. U.S. Patent 2790001, 1958.

(3) Fike, H. L. U.S. Patent 2937200, 1960.

(4) Ostromisslenski, L. *Chem. Ber.* **1908**, *41*, 3035.

(5) Barton, D. H. R.; Kirby, G. W. *J. Chem. Soc.* **1962**, 806.

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