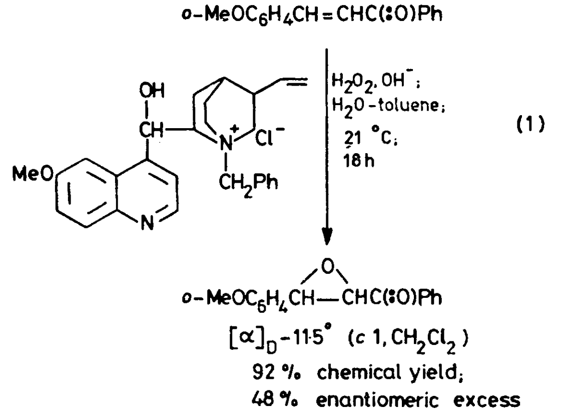
Solvent Effects in Homogeneous Asymmetric Catalysis

By HANS WYNBERG* and BEN GREIJDANUS
(*Department of Organic Chemistry, The University, Groningen, The Netherlands*)

Summary In a number of 1,4-addition reactions yielding chiral products through asymmetric catalysis the enantiomeric yield of products was found to be inversely proportional to the dielectric constant of the solvent.

IN our continuing study[1] on practical methods to obtain chiral compounds by homogeneous asymmetric catalysis we have come across a remarkable solvent effect. The effect was systematically studied in the phase-transfer[2] chiral epoxidation shown in equation (1) but appears to apply to other 1,4-addition reactions run under single-phase conditions[3,4] [equations (2) and (3)].

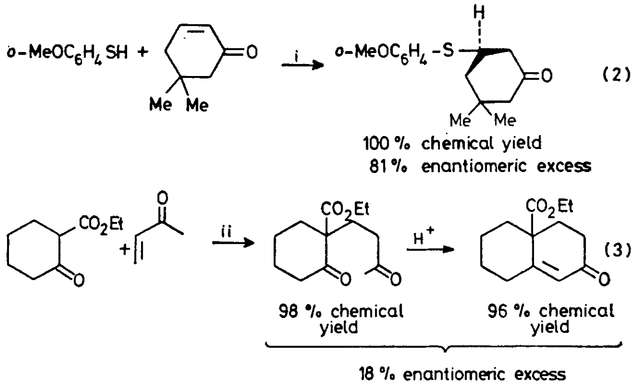


The Table lists the solvents used for the epoxidation [equation (1)], the dielectric constants (D), and the enantiomeric yield of the reaction determined as described previously.[2] All experiments were repeated many times and attempts were made to keep all other reaction parameters as constant as possible. The inverse relationship between the dielectric constant and the enantiomeric yield is even more apparent from the Figure. This relationship is presumably related to the fact that the force between two charged species is inversely related to the dielectric constant.

TABLE. Relationship between enantiomeric yield and dielectric constant in epoxidations [equation (1)]

Solvent	Dielectric[a] constant (D)	$1/D$	Enantiomeric excess (%)	Yield ratio (+):(−)
(1) $PhNO_2$	34·8	0·03	10	55:45
(2) CH_2Cl_2	9·1	0·11	28	64:36
(3) PhCl	5·71	0·18	34	67:33
(4) o-$Me_2C_6H_4$	2·6	0·39	38	69:31
(5) PhMe	2·44	0·41	48	74:26
(6) C_6H_6	2·28	0·44	54	78:22

[a] Values from A. A. Maryott and E. R. Smith, 'Table of Dielectric Constants of Pure Liquids,' National Bureau of Standards, Circular 514 (1951).



Reagents: i, cinchonidine, toluene, 21 °C, 18 h; ii, N-methylquininium hydroxide, CCl_4, 25 °C, 1 h.

The discontinuity in the plot in the Figure is interesting, and may be related to the fact that solvents 1, 2, and 3 have large dipole moments. This fact means, *inter alia*, that the dielectric constant of the first three solvents is temperature dependent while that of solvents 4, 5, and 6 is nearly temperature independent.

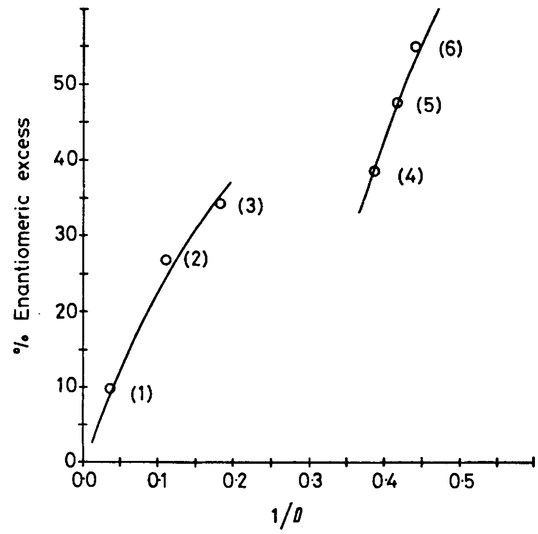


FIGURE. Effect of solvent on asymmetric induction; plot of enantiomeric excess against reciprocal of dielectric constant. Numbers pertain to the solvents in the Table.

Furthermore, we note that we have omitted solvents which can either hydrogen-bond with reactants or catalyst, or which can influence such hydrogen bonding (alcohols and ethers). Complex additional parameters would be introduced since hydroxylic solvents enhance reaction rates (in our reactions) while some ethers will compete with the carbonyl oxygen for the hydrogen bond of the hydroxy-group of the quinine salt.

It is evident that enantiomeric yield data provide a new and sensitive tool to investigate the role of the solvent in, and thus the mechanism of, certain ionic reactions. Since the change in $\Delta G^{\ddagger}$ between reactions proceeding with e.e.s. of 10 and 50% is 530 cal[5] 'minor' variables (conformations, orientations, solvents) are amenable to these probes.[6]

(*Received*, 13*th February* 1978; *Com.* 148.)

[1] J. C. Hummelen and H. Wynberg, *Tetrahedron Letters*, in the press.
[2] R. Helder, J. C. Hummelen, R. W. P. M. Laane, J. S. Wiering, and H. Wynberg, *Tetrahedron Letters*, **1976**, 1831; B. Greijdanus and H. Wynberg, in preparation.
[3] R. Helder, R. Arends, W. Bolt, H. Hiemstra, and H. Wynberg, *Tetrahedron Letters*, **1977**, 2181; H. Hiemstra and H. Wynberg, unpublished result.
[4] H. Wynberg and R. Helder, *Tetrahedron Letters*, **1975**, 4057; H. Wynberg and K. Hermann, unpublished results.
[5] V. Prelog and H. Wilhelm, *Helv. Chim. Acta*, **1954**, **37**, 1634.
[6] The relation between the dielectric constant and the entropy of activation has been studied in achiral reactions; see for example J. F. Bunnett in 'Investigations of Rates and Mechanisms of Reactions,' ed. E. S. Lewis, in 'Techniques of Chemistry,' Vol. VI, 3rd edn., ed. A. Weissberger, Wiley, New York, 1974, p. 423.