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Kinetic Resolution of 1-Methyl-1-phenylpropyl Hydroperoxide via Sharpless Epoxidation

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Abstract: The kinetic resolution of 1-methyl-1-phenylpropyl hydroperoxide via catalytic Sharpless epoxidation with various allylic alcohols has been investigated. An enantiomeric excess of nearly 20 % of the resolved hydroperoxide has been observed.

Optically active hydroperoxides which may be used as potential stereoselective oxidizing reagents are of great interest. Early attempts to obtain homochiral hydroperoxides by the oxidation of optically active alcohols or their derivatives with highly concentrated hydrogen peroxide showed that this oxidation proceeds with inversion accompanied by a high degree of racemisation [1]. Some chiral hydroperoxides were obtained by photooxidation of thiazolidines [2], oxidation of 2,3-unsaturated glycosides with hydrogen peroxide [3], or enzymatic oxidation of linoleic acid by dioxygen [4]. Recently, the resolution of 1-phenylethyl hydroperoxide and unsaturated hydroperoxide enantiomers by liquid chromatography of the diastereomeric derivatives [5] and the formation of optically active diene hydroperoxides by olefination of a peroxyaldehyde have been reported [6].

It is well known that the Sharpless epoxidation is not only a versatile method for the preparation of epoxy alcohols with high enantioselectivity [7], but it also represents a possibility for the kinetic resolution of secondary allylic alcohols [8]. Analogously, in the ideal case, the application of racemic hydroperoxides in the Sharpless epoxidation should lead to the slower reacting hydroperoxide enantiomer and the corresponding alcohol with the opposite rotation in addition the homochiral epoxy alcohol should be formed [9].

We present the first results for the kinetic resolution of 1-methyl-1-phenylpropyl hydroperoxide[10] by the catalytic variant of Sharpless epoxidation with various allylic alcohols. Using a molar ratio of allylic alcohol and hydroperoxide of 1 : 2, the reaction was quenched after half the amount of hydroperoxide had been consumed:

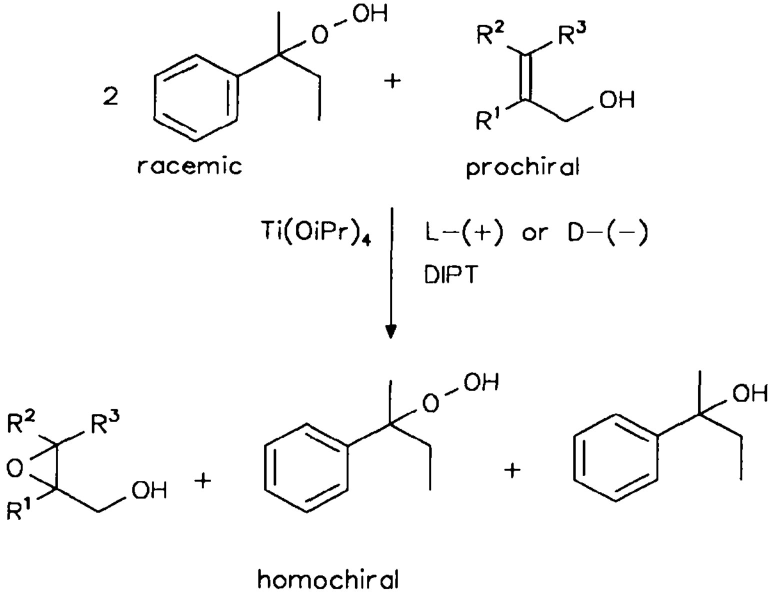

Table 1 clearly shows that, in principle, the expected stereodifferentiation occurs. As could be determined by a recently elaborated HPLC method[11], after workup the solution contains one hydroperoxide enantiomer in excess as well as the corresponding alcohol with the opposite rotation depending on the enantiomer of diispropyl tartrate (DIPT) used.

The enantiomeric excess (e.e.) obtained is low in the case of allyl alcohol and its methyl-substituted derivatives. Using cinnamyl alcohol and its phenyl-substituted derivatives, an e.e. up to 16 % was reached. By application of the stoichiometric Sharpless method the enantiomeric excess increases to 20-22 %. In every case, the e.e. of the alcohol determined is lower than that of the hydroperoxide. This observation can be explained by partial decomposition of the hydroperoxide which may be an additional source of optically inactive alcohol.

Surprisingly, the allylic alcohol used can be arranged in two groups according to the rotation of the resulting enriched hydroperoxide enantiomer. Thus, applying e.g. 2-phenylallyl alcohol in the presence of L-(+)-DIPT, an excess of the (+)-hydroperoxide was found in the solution, whereas the use of α-phenylcinnamyl alcohol in the presence of the same DIPT affords the enriched (-)-hydroperoxide enantiomer. This effect has been confirmed by the opposite optical rotation using the other DIPT enantiomer as optical auxiliary. So far, we have no plausible interpretation for this effect.

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Table 1. Kinetic Resolution of 1-Methyl-1-phenylpropyl hydroperoxide [a]

allylic alcohol	DIPT [b]	hydroperoxide [c]			alcohol [c]		
		(+)%	(-)%	e.e.	(+)%	(-)%	e.e.
allyl alcohol	L-(+)	51.5	48.5	3.0	48.8	51.2	2.4
	D-(-)	48.4	51.5	3.2	51.6	48.3	3.3
3-methyl-2-butenol	L-(+)	52.1	47.9	4.2	48.6	51.4	2.8
	D-(-)	48.2	51.8	3.6	51.0	49.0	2.0
geraniol	L-(+)	53.0	47.0	6.0	47.2	52.8	5.6
	D-(-)	47.3	52.7	5.4	51.8	48.2	3.6
2-phenylallyl alcohol	L(+)	54.8	45.2	9.6	46.3	53.7	7.4
	D(-)	45.8	54.2	8.4	54.1	45.9	8.2
crotyl alcohol	L(+)	46.6	53.4	6.8	51.8	48.2	3.6
	D(-)	53.6	46.4	7.2	47.2	52.8	5.6
(E)-2-hexen-1-ol	L(+)	46.9	53.1	6.2	52.4	47.6	4.8
	D(-)	53.2	46.8	6.4	47.3	52.7	5.4
cinnamyl alcohol	L-(+)	44.3	55.7	11.4	52.5	47.5	5.0
	D-(-)	56.9	43.1	13.8	46.6	53.4	6.7
α-phenylcinnamyl alcohol	L(+)	41.8	58.2	16.4	55.0	45.0	10.0
	D-(-)	57.4	42.6	14.8	44.4	55.6	11.2

[a] All reactions were carried out using hydroperoxide and allylic alcohol in the molar ratio of 2 : 1 with 10 mol % $Ti(O\text{-}i\text{-}Pr)_4$ and 15 mol % DIPT in the presence of powdered 3A molecular sieves in dichloromethane at -20° C. After consumption of nearly half the starting hydroperoxide amount, the reaction mixture was worked up with aqueous Na_2SO_4 solution, dried over Na_2SO_4, and analysed.

[b] DIPT = diisopropyl tartrate

[c] The determination of the enantiomeric excess of the hydroperoxide and the corresponding alcohol was accomplished by HPLC analysis on a CHIRALCEL OD column [11].

References and Notes

1. A.G. Davies, Organic Peroxides, Butterworths, London, 1961
   A.G. Davies, R. Feld, J. Chem. Soc. **1956**, 665
2. T. Takata, W. Ando, Bull. Chem. Soc. Jpn. **1986**, *59*, 1275
3. M. Chmielewski, J. Jurczak, S. Maciejewski, Carbohydrate Res. **1987**, *165*, 111
4. G. Iacazio, G. Legrand, J. Baratti, G. Buono, Ch. Triantaphylidès, J. Org. Chem. **1990**, *55*, 1690
5. P. Dussault, N.A. Porter, J. Am. Chem. Soc. **1988**, *110*, 6276
6. P. Dussault, I.Q. Lee, S. Kreifels, J. Org. Chem. **1991**, *56*, 4087
7. T. Katsuki, K.B. Sharpless, J. Am. Chem. Soc. **1980**, *102*, 5974
   B. E. Rossiter in Asymmetric Synthesis, (ed.: J. D. Morrison), vol. 5, Academic Press, New York, **1985**, p. 193
   A. Pfenninger, Synthesis **1986**, 89
   E. Höft, H.-J. Hamann, Mitteilungsbl.-Chem. Ges. D.D.R. **1987**, *34*, 10
8. V.S. Martin, S.C. Woodard, T. Katsuki, Y. Yamada, M. Ikeda, K.B. Sharpless, J. Am. Chem. Soc. **1981**, *103*, 6237
   P.R. Carlier, W.S. Mungall, G. Schröder, K.B. Sharpless, J. Am. Chem. Soc. **1988**, *110*, 2978
9. As we were informed by Dr. Shum (Arco Chem. Corp.) first results concerning the kinetic resolution of phenylethyl hydroperoxide by Sharpless epoxidation were reported in the thesis of M.G. Finn (MIT, 1985)
10. 1-Methyl-1-phenylpropyl hydroperoxide (CAUTION!) was obtained in 72 % yield by reaction of 2-phenyl-2-butanol with hydrogen peroxide (44 %), catalysed by sulfuric acid.
11. A. Kunath, E. Höft, H.-J. Hamann, J. Wagner, J. Chromatogr. **1991**, *588*, 351