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BIOTECHNOLOGY

Edited by C. F. PHELPS and P. H. CLARKE

The fourteen contributions forming this volume were presented at a London meeting of the Biochemical Society including the Society's Forty-Eighth Symposium 'Biotechnology', in December 1982. With today's increasing pressures to develop latest laboratory findings into practical industrial processes as quickly as possible the chosen theme of this Symposium was a timely one. The papers represent up-to-date reports from international biochemists whose work is of direct relevance to the wide areas of interests concerned with biotechnology, together with glimpses of the early development of its techniques and a look at its exciting future.

List of contents and authors:

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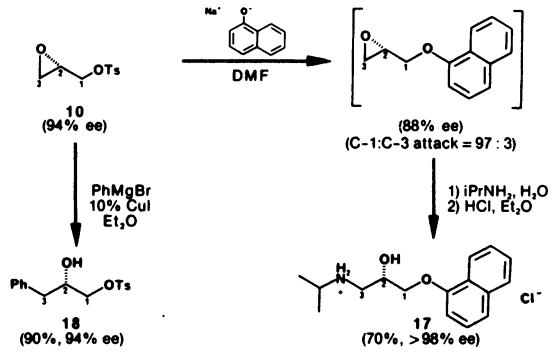
Chiral Building Blocks

The Sharpless group at MIT recently discovered that the presence of 3Å or 4Å molecular sieves renders the ***Sharpless Asymmetric Epoxidation*** truly catalytic.[1]

Hundreds of applications,[2] most of them using full equivalents of the titanium-tartrate catalyst, have been reported since the Sharpless Epoxidation's discovery in 1980.[3] The latest Sharpless breakthrough enables most allylic alcohols to be quickly epoxidized using 5% catalyst.[1] Moreover, product isolation is simplified, yields are improved and large-scale applications are much easier to perform. Both enantiomers are available, and at the same price, since a unique characteristic of the Sharpless Epoxidation is the ability to make one enantiomer as easily as the other.

Glycidyl tosylate (**10**), with its simple structure and double activation, is likely to prove the most versatile epoxy alcohol derivative. The tosylate is the foundation of one of the most efficacious routes to homochiral β-blockers, a one-pot, two-step sequence devised at MIT[4] and already used to make the eutomers[5] (active enantiomers) of penbutolol and propranolol (**17**). Unlike Grignard reagents under copper catalysis which attack **A** with high selectivity at C-3 (*i.e.*, **10**→**18**),[4] these β-blocker syntheses hang on the high regioselectivity for aryloxide substitution at C-1 of **10**.



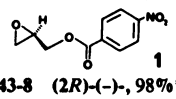
The three 4-nitrobenzoate derivatives are proving[4] operationally equivalent (as expected) to the parent epoxy alcohols for Payne rearrangement-opening applications, such as those described in references 2a and 2d. Note that, by its very nature, this rearrangement does not racemize glycidol or 2-methylglycidol (soon to be offered as the 4-nitrobenzoate).

References:

1) Hanson, R.M.; Ko, S.Y.; Chong, J.M.; Sharpless, K.B., unpublished results.
2) a) Sharpless, K.B.; Behrens, C.H.; Katsuki, T.; Lee, A.W.M.; Martin, V.S.; Takatani, M.; Viti, S.M.; Walker, F.J.; Woodward, S.S. *Pure Appl. Chem.* **1983**, *55*, 589; b) Rossiter, B.E. In "Asymmetric Synthesis"; Morrison, J.D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 7; c) Finn, M.G.; Sharpless, K.B. *ibid.* Vol. 5, Chapter 8; d) Behrens, C.H.; Sharpless, K.B. *Aldrichim. Acta* **1983**, *16*(4), 67; e) Caron, M.; Sharpless, K.B. *J. Org. Chem.* **1985**, *50*, 1557; f) Chong, J.M.; Sharpless, K.B. *ibid.* **1985**, *50*, 1560; g) Chong, J.M.; Sharpless, K.B. *Tetrahedron Lett.* **1985**, *26*, 4683.
3) Katsuki, T.; Sharpless, K.B. *J. Am. Chem. Soc.* **1980**, *102*, 5974; US Patent 4,471,130.
4) Klunder, J.M.; Sharpless, K.B., unpublished results.
5) Ariens, E.J. *Eur. J. Clin. Pharmacol.* **1984**, *26*, 663.
6) Ko, S.Y.; Masamune, H.; Sharpless, K.B., unpublished results.

*Only chemical purities are indicated here. The enantiomeric purities for **1**, **2**, **9** and **10** are 90-94% ee, while the rest are 98+ % ee. These products are licensed under U.S. Patent 4,471,130.

Glycidyl 4-Nitrobenzoates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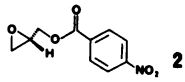
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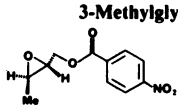
30,043-8	(2*R*)-(-)-, 98%* (1)	1g $14.00
30,044-6	(2*S*)-(+)-, 98% (2)	1g $14.00

3-Methylglycidyl 4-Nitrobenzoates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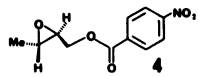
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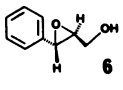
30,045-4	(2*R*,3*R*)-(+)-, 98% (3)	1g $14.00
30,046-2	(2*S*,3*S*)-(-)-, 98% (4)	1g $14.00

3-Phenylglycidols


5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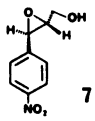
30,047-0	(2*R*,3*R*)-(+)-, 99% (5)	1g $19.00
30,048-9	(2*S*,3*S*)-(-)-, 99% (6)	1g $19.00

3-(4-Nitrophenyl)glycidols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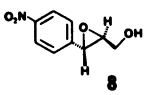
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30,049-7	(2*R*,3*R*)-, 98% (7)	1g $19.00
30,050-0	(2*S*,3*S*)-, 98% (8)	1g $19.00

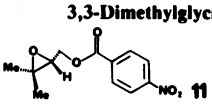
Glycidyl Tosylates


9


10

30,051-9	(2*R*)-, 99% (9)	1g $14.00
30,052-7	(2*S*)-, 99% (10)	1g $14.00

3,3-Dimethylglycidyl 4-Nitrobenzoates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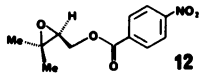
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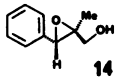
30,053-5	(2*R*)-(+)-, 98% (11)	1g $14.00
30,054-3	(2*S*)-(-)-, 98% (12)	1g $14.00

2-Methyl-3-phenylglycidols


13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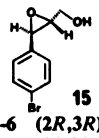
30,055-1	(2*R*,3*R*)-, 97% (13)	1g $14.00
30,057-8	(2*S*,3*S*)-, 97% (14)	1g $14.00

3-(4-Bromophenyl)glycidols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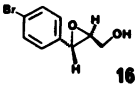
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30,058-6	(2*R*,3*R*)-(+), 97% (15)	1g $19.00
30,059-4	(2*S*,3*S*)-(-), 97% (16)	1g $19.00

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