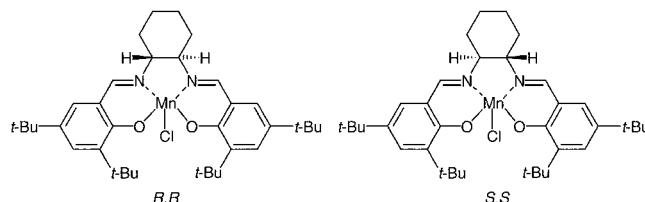


SYNLETT

Spotlight 53

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Jacobson's Catalyst



Compiled by Massimo Corsi



Massimo Corsi was born on 27th July 1970 in Florence (Italy). He achieved his first degree in Chemistry at the Organic Chemistry Department 'Ugo Schiff' (Florence University) guided by Prof. A. Goti. After experience as an NMR analyst, he moved to The University of Reading, where he is currently in the 2nd year of his Ph.D. studies, working towards the total synthesis of phorbol, under the supervision of Prof. L. M. Harwood.

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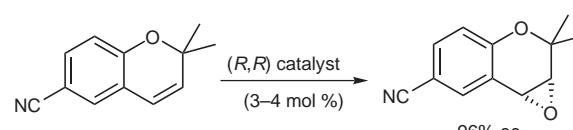
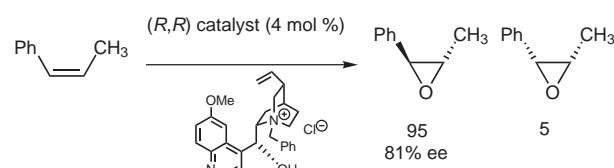
Enantioselective epoxidation of olefins is a challenging and useful synthetic transformation.¹ Since its introduction in the early nineties, Jacobsen's catalyst has proved reliable for highly enantioselective epoxidation of prochiral olefins.² Belonging to the salen-ligand class,³ the catalyst has a manganese core in a square planar geometry, stabilised with a chlorine atom in the axial position.² Several stoichiometric oxidants have been used successfully,⁴ with NaOCl the most frequently in-

volved.^{1a,1b,5} Easy to prepare, the catalyst has become commercially available in both enantiomeric forms.⁶ Applied also for the enantioselective oxidation of sulfides to sulfoxides,^{4c} and for the oxidation of hydrocarbons at the benzylic position,^{4c} the catalyst has even been synthesised in a dimeric form for the epoxidation of olefins under heterogeneous conditions.⁷ Recently, it has provided the first example of didehydrogenation of secondary hydroxylamines to the corresponding nitrones.⁸

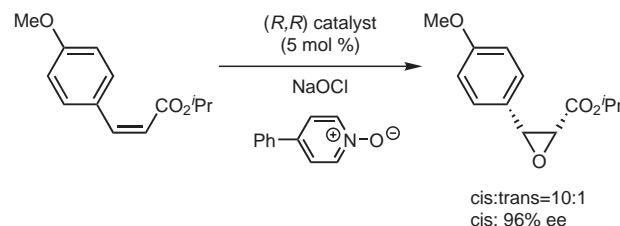
Abstracts

Different cyclic and acyclic doubly substituted *cis*-olefins were chosen to demonstrate the enantioselective efficiency of the catalyst.^{1b} *Trans*-disubstituted olefins were found to be epoxidised with low enantioselectivity. However, inclusion of chiral quaternary ammonium salts of chincona alkaloids proved useful to provide *trans*-epoxides from *cis*-olefins.^{5g}

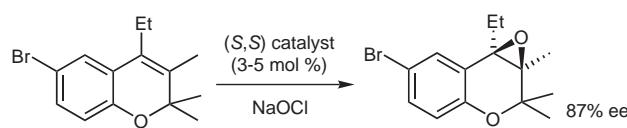
Enantioselective epoxidation of several 2,2-dimethylchromenes has been performed in high yields,^{4d,5} providing a straightforward route to biologically active building blocks.⁹



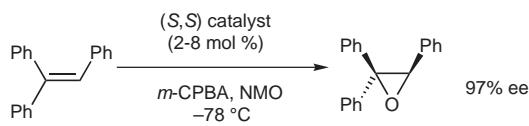
Since the first results of *cis*-olefin epoxidation,^{1b} an investigation into cinnamate epoxidation was carried out,^{5f} as it represented an opportunity for constructing important chiral building blocks.^{10,11} Steric properties of the ester group have a large influence on enantioselectivity, whereas electronic properties of the aromatic ring show no relationship to the observed ee. Addition of pyridine *N*-oxide derivatives was found to increase the reaction turnover, keeping the same level of stereoselectivity.^{5f}



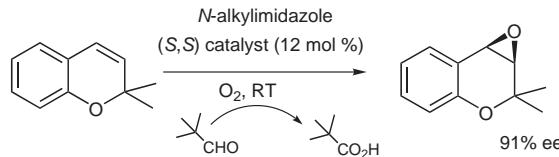
Jacobsen's catalyst proves less effective when applied to the epoxidation of a variety of tetrasubstituted olefins. For highly hindered double bonds, tuning of the ligand was required to afford both high levels of ee and yields.^{5h}



Following an earlier study on styrene,^{4a} the combination *m*-CPBA/NMO proved successful for the preparation of epoxides at low temperature from a wide range of mono-, di- and tri-substituted olefins.^{4b}



The combination of molecular oxygen and pivaldehyde has been used as an alternative oxidation system to activate the manganese core of the catalyst. Differently substituted olefins were successfully epoxidised enantioselectively, with alkyl imidazoles as superior axial ligands for the catalyst.¹²



References

- (1) (a) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801; and references cited therein. (b) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063. (c) Irie, R.; Noda, K.; Ito, Y.; Katsuki, T. *Tetrahedron Lett.* **1991**, *32*, 1055.
- (2) Zhang, W.; Jacobsen, E. N. *J. Org. Chem.* **1991**, *56*, 2296.
- (3) (a) Srinivasan, K.; Michaud, P.; Kochi, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 2309. (b) Srinivasan, K.; Perrier, S.; Kochi, J. K. *J. Mol. Catal.* **1986**, *36*, 297. (c) Irie, R.; Noda, K.; Ito, Y.; Katsuki, T. *Tetrahedron Lett.* **1991**, *32*, 1055. (d) For recent reviews, see: Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, **1993**, 4.2.
- (e) See also: Katsuki, T. *Coord. Chem. Rev.* **1995**, *140*, 189.
- (4) (a) Palucki, M.; Pospisil, P. J.; Zhang, W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 9333. (b) Palucki, M.; McCormick, J.; Jacobsen, E. N. *Tetrahedron Lett.* **1995**, *36*, 5457. (c) Lee, N. H.; Lee, C. S.; Jung, D. S. *Tetrahedron Lett.* **1998**, *39*, 1385. (d) Adam, W.; Jek, J.; Lévai, A.; Nemes, C.; Patonay, T.; Sebők, P. *Tetrahedron Lett.* **1995**, *36*, 3669. (e) Palucki, M.; Hanson, P.; Jacobsen, E. N. *Tetrahedron Lett.* **1992**, *33*, 7111. (f) To compare the results of other salen catalysts, see: Noda, K.; Hosoya, N.; Yanai, K.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **1994**, *35*, 1887. (g) Kokubo, C.; Katsuki, T. *Tetrahedron* **1996**, *52*, 13895.
- (5) (a) Lee, N. H.; Muci, A. R.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 5055. (b) Lee, N. H.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 6533. (c) Chang, S.; Lee, N. H.; Jacobsen, E. N. *J. Org. Chem.* **1993**, *58*, 6939. (d) Chang, S.; Heid, R. M.; Jacobsen, E. N. *Tetrahedron Lett.* **1994**, *35*, 669. (e) Brandes, B. D.; Jacobsen, E. N. *J. Org. Chem.* **1994**, *59*, 4378. (f) Jacobsen, E. N.; Deng, L.; Furukawa, Y.; Martinez, L. E. *Tetrahedron* **1994**, *50*, 4323. (g) Chang, S.; Galvin, J. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 6937. (h) Brandes, B. D.; Jacobsen, E. N. *Tetrahedron Lett.* **1995**, *36*, 5123.
- (6) *Chem. Eng. News* **1993**, July 19, 50.
- (7) Janssen, K. B. M.; Laquiere, I.; Dehaen, W.; Parton, R. F.; Vankelekom, I. F. J.; Jacobs, P. A. *Tetrahedron Asymmetry* **1997**, *8*, 3481.
- (8) Cicchi, S.; Cardona, F.; Brandi, A.; Corsi, M.; Goti, A. *Tetrahedron Lett.* **1999**, *40*, 1989.
- (9) Lockhart, I. M. *Chromenes Chromanones, and Chromones*, In *The Chemistry of Heterocyclic Compounds*; Ellis, G. P., Ed.; 31, Wiley: New York, **1977**, 2.
- (10) Deng, L.; Jacobsen, E. N. *J. Org. Chem.* **1992**, *57*, 4320.
- (11) (a) Parker, R. E.; Isaacs, N. C. *Chem. Rev.* **1959**, *59*, 737. (b) Behrens, C. H.; Sharpless, K. B. *Aldrichimica Acta* **1983**, *16*, 67.
- (12) (a) Yamada, T.; Imagawa, K.; Nagata, T.; Mukayama, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 248. (b) Imagawa, K.; Nagata, T.; Yamada, T.; Mukayama, T. *Chem. Lett.* **1994**, 527.