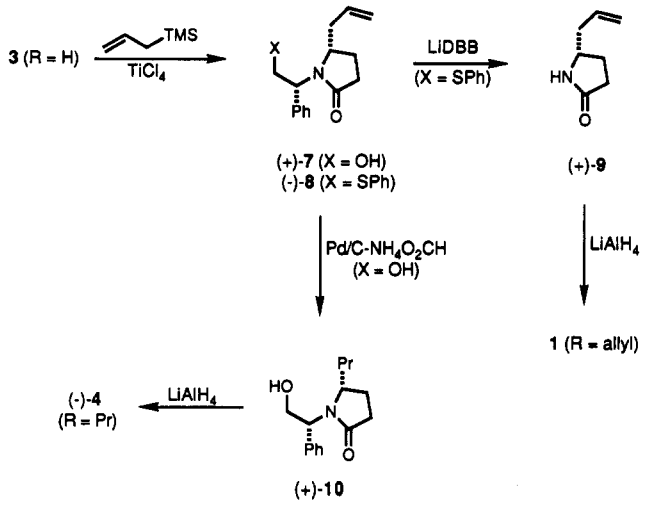
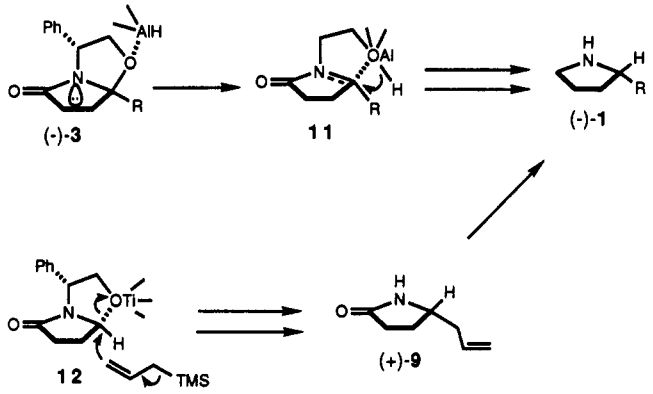


hydride delivery as depicted by 11 thus furnishing the pyrrolidine 1. However, it is unknown at this time whether the carbonyl is reduced prior to or after the hydride is delivered at the angular position. The configuration of the resulting pyrrolidines agrees well with all the earlier assignments in this series.[1] In the case of the allylsilane addition the analogy is seen to work on acetals[11] where Lewis acid initiated ring opening proceeds in an S_N2-like fashion.[12] Thus, we consider 12 as the key step in the allylation reaction and this leads to 9 and ultimately to 1.

Once again, it is noteworthy to mention that the hydride cleavage proceeds with retention while the allylsilane proceeds with inversion resulting in both processes furnishing the same absolute stereochemical alignment in the pyrrolidines.

Further studies are in progress to reach more elaborate systems as well as 2,5-dialkylpyrrolidines.



Acknowledgment. Financial support by the National Institutes of Health is gratefully acknowledged.

Supplementary Material Available: Experimental details and physical properties of all compounds and an HPLC plot of enantiomeric 2-benzylpyrrolidine (14 pages). Ordering information is given on any current masthead page.

Asymmetric Olefin Epoxidation with Sodium Hypochlorite Catalyzed by Easily Prepared Chiral Mn(III) Salen Complexes

Wei Zhang and Eric N. Jacobsen*

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801

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Summary: A practical method is described for the asymmetric epoxidation of *cis*-β-methylstyrene by commercial bleach with up to 86% ee.

We recently reported a new method for the asymmetric epoxidation of simple olefins involving catalysis by chiral salen (*N,N'*-bis(salicylideneamino)ethane) Mn(III) complexes.[1] These constitute the most enantioselective nonenzymatic olefin epoxidation catalysts reported thus far in which asymmetric induction results solely from nonbonded interactions.[2] The utility of the initially reported method was restricted, however, by a technically difficult catalyst synthesis and by the prescribed use of iodosylarenes as stoichiometric oxidants. We describe herein key improvements to this technology, including a simplified synthesis of the chiral salen-based Mn(III) epoxidation catalysts and a highly practical epoxidation procedure that employs commercial bleach as the stoichiometric oxidant.

The chiral catalysts **1a–c** used in this study were prepared from the readily available chiral auxiliary (*R,R*)- or (*S,S*)-1,2-diamino-1,2-diphenylethane (**2**; Scheme I).[3,4] The requisite hindered salicylaldehydes **4a–c** were con-

(1) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801.

(2) For other studies directed toward the asymmetric catalytic epoxidation of unfunctionalized olefins, see refs 1 and 4 in ref 1. For more recent work, see: (a) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628. (b) Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T. *Tetrahedron Lett.* **1990**, *31*, 7345.

(3) Williams, O. F.; Bailar, J. C. *J. Am. Chem. Soc.* **1959**, *81*, 4464. Resolution: Saigo, K.; Kubota, N.; Takebayashi, S.; Hasegawa, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 931. An extremely convenient route to **2** was recently reported: Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493.

(4) General procedure for the preparation of **1**. Salicylaldehyde derivative **4** (2.0 equiv) is added as a solid to a 0.2 M solution of (*R,R*)- or (*S,S*)-**2** (1.0 equiv) in absolute ethanol. The mixture is heated to reflux for 1 h and then H_2O is added dropwise to the cooled bright yellow solution (occasionally product begins to crystallize prior to addition of water). The resulting yellow crystalline solid is collected by filtration and washed with a small portion of 95% ethanol. The yields of analytically pure **5** obtained in this manner are in the range of 91–97%. The ligand **5** is redissolved in hot absolute ethanol to give a 0.1 M solution. Solid $Mn(OAc)_2 \cdot H_2O$ (2.0 equiv) is added in one portion and the solution is refluxed for 1 h. Approximately 3 equiv of solid LiCl are then added and, the mixture is heated to reflux for an additional 0.5 h. Cooling the mixture to 0 °C affords the Mn(III) complex **1** as dark brown crystals that are washed thoroughly with H_2O and isolated by filtration in ~75% yield. An additional crop of material can be obtained by dropwise addition of H_2O to the mother liquor. Combined yields of catalyst **1** are 89–96% for this step and 81–93% overall from the optically pure diamine **2**. Acceptable C, H, N, Cl, and Mn analyses of **1** have been obtained (±0.4%), but these vary according to the extent of water and ethanol incorporation in the powdery product. Enantioselectivities in the epoxidation reactions are invariant with different batches of a given catalyst, indicating that the solvent content of **1** does not influence its effectiveness.

0022-3263/91/1956-2296$02.50/0

Scheme I

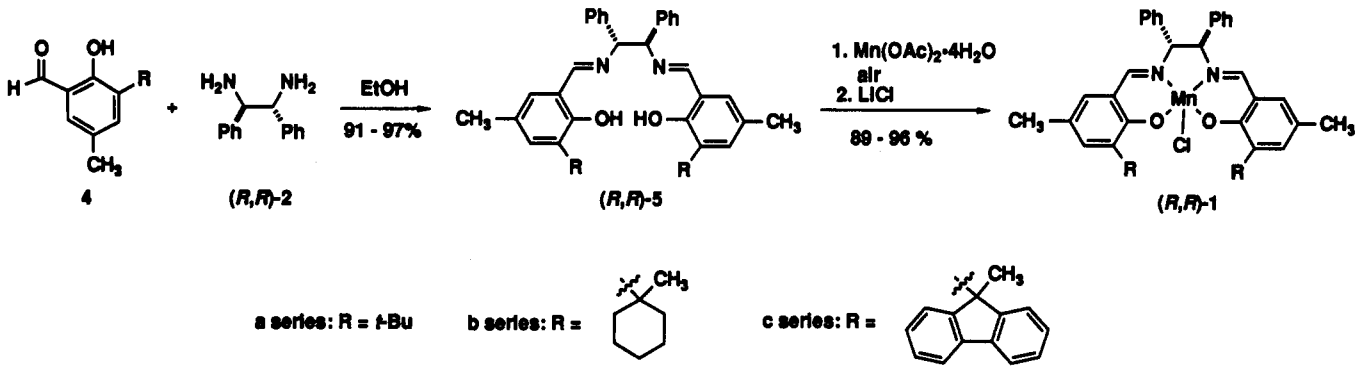
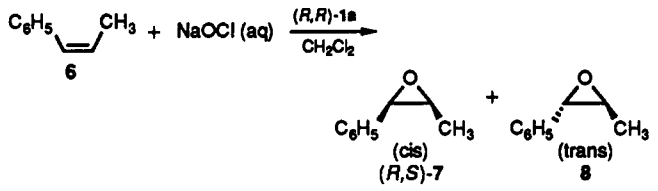


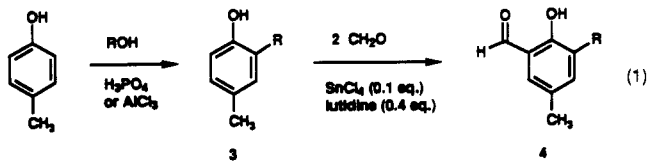
Table I. Effects of pH on the Asymmetric Epoxidation of 6 Catalyzed by 1a[a]



pH[b]	yield of 7[c]	% ee of 7	yield 7/ yield 8	total catalyst turnovers	initial rate[d] (turnovers/ min)
9.5	56	80	7.4	37	7.3
10	74	79	11.5	35	5.8
10.5	81	81	15	37	3.0
11	86	81	15	37	2.9
11.5	87	82	14	35	2.2

[a] Runs were carried out in duplicate with each enantiomer of 1a at 25 °C, [alkene]$_0$ = 1.0 M, [1a]$_0$ = 0.01 M, 2.5 equiv of NaOCl. All tabulated numbers were reproducible to within 2 units in the last significant figure. [b] Buffered bleach solutions were prepared with 50 mL of Clorox bleach and 20 mL of 0.05 M $Na_2B_4O_7 \cdot 10H_2O$ or Na_2HPO_4, with the pH's adjusted by addition of 1 N HCl or 1 N NaOH. Runs at pH 10.5 yielded results identical with either buffer system. [c] Determined by capillary GC integration against an internal quantitative standard (dodecane) and corrected for the extent of olefin conversion. [d] Determined by measuring the extent of conversion of 6 within the first 60 s of the reaction.

veniently synthesized by direct formylation of 3a–c according to the method reported by Casiraghi (eq 1).[5] The



(1)

use of *p*-cresol derivatives ensures the desired regiochemical outcome of Friedel–Crafts alkylation reactions to generate 3b–c (3a is commercially available and inexpensive). The corresponding salicylaldehydes 4a–c are solids at room temperature that are easy to isolate in pure form by recrystallization.[6]

Preparation of the (salen)MnCl complexes 1a–c was effected in excellent isolated yields by reaction of 5 with excess $Mn^{II}(OAc)_2 \cdot 4H_2O$ in air and treatment of the resultant brown solution with LiCl.[7,8] This procedure circumvents the manipulation of highly sensitive Mn(II) intermediates and the use of special one-electron oxidants to carry out the Mn(II) to Mn(III) conversion.[1,9] The Mn(III) salen complexes are thermally stable, and they can be stored indefinitely in the solid state without any precautions to exclude light, air, or moisture.

Table II. Enantioselectivities in the Epoxidation of 6 (% ee)[a]

temp (°C)	1a	1b	1c
25	81	83	76
0	84	86	80

[a] All reactions were carried out to complete conversion of alkene, with 4 mol % catalysts and NaOCl solutions buffered to pH 11.3. Yields of 7 determined by GC integration were 77–85% in all cases, and 7/8 ratios were 9:1 to 15:1.

Solutions of buffered commercial bleach[10] have proven to be useful oxygen atom sources for epoxidation reactions catalyzed by 1, as illustrated by the reactions of the model substrate *cis*-β-methylstyrene (6; Table I).[11] Both the yield and the cis/trans selectivity of the epoxidation improve at higher pH, and chlorinated byproducts are not observed above pH 10.5. Although the initial rate of epoxidation is attenuated with increasing pH, presumably as a result of the lower concentration of HOCl in the organic phase,[12]

(5) Casiraghi, G.; Casnati, G.; Puglia, G.; Sartori, G.; Terenghi, G. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1862.

(6) Catalysts derived from 3-*tert*-butylsalicylaldehyde[1] display essentially the same selectivities in alkene epoxidation as those derived from 4a. The latter systems are preferred, however, because 3-*tert*-butylsalicylaldehyde is a liquid that is difficult to isolate from the direct formylation of 2-*tert*-butylphenol.

(7) This is a modification of a procedure reported for the preparation of achiral salen complexes: Boucher, L. J. *J. Inorg. Nucl. Chem.* **1974**, *36*, 531.

(8) Complex 1 can also be prepared in one pot from 2 and 4 without isolation of the salen ligand.

(9) Srinivasan, K.; Michaud, P.; Kochi, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 2309.

(10) The use of NaOCl in epoxidations catalyzed by salen complexes has been reported: Yoon, H.; Burrows, C. J. *J. Am. Chem. Soc.* **1988**, *110*, 4087. For examples of alkene epoxidations by NaOCl catalyzed by Mn(III) porphyrin complexes, see: (a) Collman, J. P.; Kodadek, T.; Raybuck, S. A.; Meunier, B. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 7039. (b) Lee, R. W.; Nakagaki, P. C.; Balasubramanian, P. N.; Bruice, T. C. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 641. (c) Suslick, K. S.; Cook, B. R. *J. Chem. Soc., Chem. Commun.* **1987**, 200.

(11) The following procedure for the epoxidation of *cis*-β-methylstyrene by 1a is general. A solution of 0.05 M Na_2HPO_4 (10.0 mL) was added to a 25 mL solution of undiluted commercial household bleach (Clorox). The pH of the resulting buffered solution (~0.55 M in NaOCl) was adjusted to pH 11.3 by addition of a few drops of 1 M NaOH solution. This solution was cooled to 0 °C and then added at once to a 0 °C solution of 1a (260 mg, 0.4 mmol) and *cis*-β-methylstyrene (1.18 g, 10 mmol) in 10 mL of CH_2Cl_2. The two-phase mixture was stirred at room temperature, and the reaction progress was monitored by TLC. After 3 h, 100 mL of hexane was added to the mixture and the brown organic phase was separated, washed twice with 100 mL of H_2O and once with 100 mL of saturated NaCl solution, and then dried (Na_2SO_4). After solvent removal, the residue was purified by flash chromatography on silica gel to afford 0.912 g of pure 6 (68% isolated yield). The ee of the epoxide was determined to be 84% by ^1H NMR analysis in the presence of Eu(hfc)$_3$ and by capillary GC using a commercial chiral column (J & W Scientific, Folsom, CA 95630, Cyclodex-B column, 30 m × 0.25 mm i.d., 0.25-μm, oven temperature 110 °C isothermal).

(12) Banfi, S.; Montanari, F.; Quici, S. *J. Org. Chem.* **1989**, *54*, 1850.

the total number of catalyst turnovers and the enantioselectivities are remarkably invariant over the pH range studied. After 35–40 turnovers of **1a**, the epoxidation of **6** ceases and the catalyst is inactive.[13] The constant ee values for **7** measured during the course of the reactions indicate that the as-yet unidentified decomposition products of **1a** are inert as epoxidation catalysts.[14] Enantioselectivities also do not differ significantly according to whether the stoichiometric oxidant is an iodosylarene derivative or sodium hypochlorite, providing evidence for a common oxo intermediate as the active oxidant.[15] In contrast, recently reported Ni(salen)- and Co(salen)-catalyzed epoxidations by sodium hypochlorite appear to involve free ClO• as the oxidizing agent.[16,17]

The presence of bulky R groups in **1** is crucial to the selectivity and stability of these catalysts. The analogue of **1** derived from salicylaldehyde (R = H) catalyzes the epoxidation of **6** with only 0–3% ee and ca. five catalyst turnovers, and in general, substituents smaller than *tert*-butyl lead to poor results.[18] Increasing the size of the R group as in **1b** leads to minor improvements in selectivity, but more hindered systems such as **1c** tend to be less selective (Table II). At this stage, **1a** is the catalyst of choice for most epoxidation reactions on the basis of its synthetic accessibility.

The procedure for olefin epoxidation embodies several appealing features. Good isolated yields of epoxide are achievable with inexpensive reagents under mild conditions. No phase-transfer catalyst is required, purification of solvents is unnecessary, the reactions are run in air, and the workup protocol is simple. The substrate scope and the levels to which enantioselectivities may be raised by catalyst modification are under investigation and will be reported shortly.

Acknowledgment. We are grateful to Alexander Muci and to Peter Hanson for valuable experimental assistance. This work was supported in part by a National Science Foundation PYI Award (CHE-9057740) to E.N.J. and by a generous contribution from the Monsanto Corp.

Supplementary Material Available: Spectroscopic data for compounds **3b,c** and **4a–c**, experimental data for the preparation of **4a**, spectroscopic and analytical data for **5a–c**, and analytical data for **1a–c** (3 pages). Ordering information is given on any current masthead page.

(13) Interestingly, solutions of **1** are indefinitely stable to aqueous NaOCl in the absence of olefin, so substrate, epoxide, or some minor byproduct of epoxidation must play a key role in the catalyst decomposition.

(14) The ee values determined for byproduct **8** are generally the same (±5%) as those for **7**, but they tend to decrease slightly during the reaction.

(15) With appropriate substitution on the salen ligand, we have been able to isolate (salen)Mn(V) oxo intermediates from NaOCl reactions. Zhang, W.; Jacobsen, E. N. Work in progress.

(16) Yoon, Heungsik; Wagler, T. R.; O'Connor, K. J.; Burrows, C. J. *J. Am. Chem. Soc.* **1990**, *112*, 4568.

(17) Nishinaga, A.; Kakutani, M.; Umeda, T.; Maruyama, K. *Abstracts of Papers*, Seventh International Symposium on Homogeneous Catalysis, Lyon-Villeurbanne, Société Française de Chimie: Lyon, France, 1990; Abstract P-89.

(18) Katsuki very recently reported epoxidation catalysts closely related to **1** in which R bears a secondary stereogenic center.[2b] Enantioselectivities were substantially lower (44% ee for **6**) than those observed with **1a–c**, suggesting that a tertiary center is essential.