6-Amino-2-(*N*-phenylamino)deca-2,5-dien-4-one (**11hf**): 83%; oil; IR ($CCl_4$) 3496, 3239 ($NH_2$) 1572 (CO) $cm^{-1}$; $^1$H-NMR (200 MHz) $\delta$ 0.87 (t, $J$ = 7.3, 3 H, $Me(CH_2)_3$, 1.2–1.7 (m, 4 H, $Me(CH_2)_2CH_2$), 2.31 (s, 3 H, Me), 2.55 (t, $J$ = 7.6, 2 H, $Me(CH_2)_2CH_2$), 6.14 (s, 1 H, CH=), 6.15 (s, 1 H, CH=), 6.6–6.8 and 7.0–7.2 (m, 7 H, ArH + $NH_2$), 12.17 (br s, 1 H, NH); $^{13}$C-NMR (200 MHz) $\delta$ 13.87 (q), 19.16 (q), 22.35 (t), 31.24 (t), 33.02 (t), 114.07 (d), 115.04 (d), 115.53 (d), 118.74 (d), 129.46 (s), 129.69 (d), 149.69 (s), 154.04 (s), 180.72 (s); MS $m/z$ 258 ($M^+$, 48), 201 (19), 166 (100), 160 (86), 126 (61). Anal. Calcd for $C_{16}H_{22}N_2O$: C, 74.4; H, 8.6; N, 10.8. Found: C, 74.5; H, 8.7; N, 10.7.

**B. Synthesis of 4-Pyridinones. Method A.** Products **11ga, ha, hb** (2 mmol) were dissolved in 10 mL of 10% hydrochloric acid in methanol. The solution was stirred at room temperature for 45 min, evaporated, neutralized with aqueous $NaHCO_3$, extracted with ether, washed with water, dried, and evaporated under reduced pressure, and the residue submitted to a chromatographic separation with silica gel (hexane:ether:methanol = 2:2:1 as eluant).

**Method B.** A THF solution of the appropriate nitrile 4 (8 mmol) was added to a cooled (−50 °C) solution of the $\alpha'$-dianion (5 mmol), and the mixture was allowed to stir for 15 min under a nitrogen atmosphere. The solution was poured into 10% aqueous HCl and then treated as described above.

Yields of compounds **12** are reported in Table IV. Physical data for isolated compounds **12** follow.

2-Methyl-6-phenyl-4(1*H*)-pyridinone (**12ha**) and 2-phenyl-6-(2-phenylethyl)-4(1*H*)-pyridinone (**12ga**) were recognized by comparison with data of literature.[3]

2-Methyl-6-(2-chlorophenyl)-4(1*H*)-pyridinone (**12hb**): mp 83–86 °C; IR ($CCl_4$) 3420 (NH) 1623 (C=O) $cm^{-1}$; $^1$H-NMR (200 MHz) $\delta$ 2.33 (s, 3 H, Me), 5.98 (d, $J$ = 1.9, 1 H, H3 or H5), 6.05 (d, $J$ = 1.9, 1 H, H5 or H3), 7.20–7.42 (m, 5 H, ArH + NH); MS $m/z$ 221 (16), 219 ($M^+$, 47), 184 (100). Anal. Calcd for $C_{12}H_{10}NOCl$: C, 65.6; H, 4.6; N, 6.4. Found: C, 65.5; H, 4.7; N, 6.4.

**X-ray Data Collection and Structure Refinement.** Diffraction data were collected on a Siemens R3m/V automatic four-circle diffractometer, using a graphite-monochromated MoKa radiation. A 0.12 × 0.36 × 0.51 mm crystal was used for intensity data collection. Lattice parameters were obtained from least-squares refinement of the setting angles of 25 reflections in the $15 \leq 2\theta \leq 30°$ range. Lorentz-polarization corrections were applied to the intensity data.

The structures were solved by standard direct methods and subsequently completed by Fourier recycling. The full-matrix least-squares refinement was based on $|F_o|$. The non-hydrogen atoms, except C atoms of the phenyl groups, were refined anisotropically. All hydrogen atoms were set in calculated positions and refined as riding atoms, with a common thermal parameter. The final $R$ values were 0.069, $R'$ = 0.079. The weighting scheme used in the last refinement cycles was $w = 1.0000/s^2(F_o) + 0.006000(F_o)^2$.

Solutions and refinements were performed with the SHELXL-PLUS system (1989).[18] The final geometrical calculations were performed with the PARST[19] program. Additional material is available from the Cambridge Crystallographic Data Centre.

**Acknowledgment.** The financial support of Ministero dell'Università e Ricerca Scientifica e Tecnologica (MURST) is acknowledged.

**Supplementary Material Available:** Conditions of crystallographic data collection and structure refinement, tables of atom coordinates, thermal parameters, relevant least-squares planes, possible H-bonds, and bond lengths and angles, and an ORTEP drawing and view of the cell (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(18) SHELXL-PLUS, version 3.4, Siemens Analytical X-ray Instruments Inc., Madison, WI, 1989.
(19) Nardelli, M. *J. Comput. Chem.* **1983**, *7*, 95.

# Epoxidation of 5-(Tosylamido)-3-hexen-2-ol Derivatives. Stereochemical Assignment of Product Configuration by NMR and Molecular Mechanics Studies

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*Received March 31, 1992*

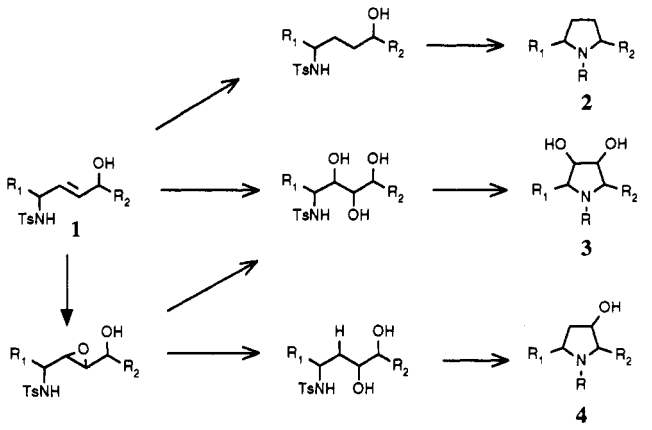
Epoxidation of *syn*- and *anti*-5-(tosylamido)-3-hexen-2-ol derivatives was studied using three different epoxidation reagents: (i) *m*-CPBA, (ii) *t*-BuOOH/VO(acac)$_2$, and (iii) *t*-BuOOH/Ti(O-*i*-Pr)$_4$. A method for the stereochemical assignment of the 3,4-epoxy-5-(tosylamido)-3-hexen-2-ol derivatives obtained was developed by the use of NMR spectroscopy.

Palladium-catalyzed 1,4-oxidations of conjugated dienes offer unique opportunities to obtain 1,4-stereocontrol in both cyclic and acyclic systems.[1-3] In particular, 1,4-chloroacetates and 1,4-diacetates obtained from such oxidations have proved useful in this respect, and recently their use for obtaining a *dual* 1,4-stereocontrol in acyclic systems was demonstrated.[4,5] In one application *syn*- and *anti*-amido alcohols **1** were transformed into cis 2,5- and trans 2,5-disubstituted pyrrolidines **2**, respectively, via hydrogenation and ring closure (Scheme I). The synthetic utility of this methodology would be further enhanced by stereoselective mono or dihydroxylation of the double bond prior to cyclization.[6] In this way stereodefined pyrrolidine

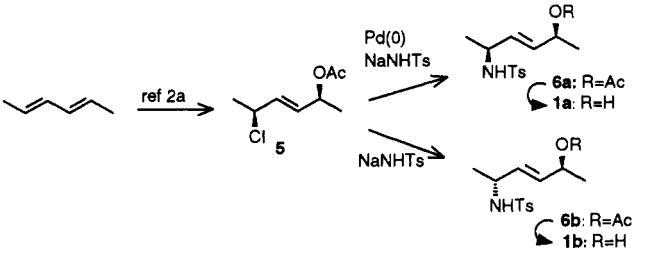
(1) Bäckvall, J. E. *Pure Appl. Chem.*, **1992**, *64*, 429.
(2) (a) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676. (b) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619.
(3) (a) Bäckvall, J. E.; Andersson, P. G. *J. Am. Chem. Soc.* **1990**, *112*, 3683. (b) Bäckvall, J. E.; Andersson, P. G. *J. Org. Chem.* **1991**, *56*, 2274.
(4) (a) Bäckvall, J. E.; Byström, S. E.; Nyström, J. E. *Tetrahedron* **1985**, *41*, 5761. (b) Schink, H. E.; Bäckvall, J. E. *J. Org. Chem.* **1992**, *57*, 1588.
(5) Bäckvall, J. E.; Schink, H. E.; Renko, Z. D. *J. Org. Chem.* **1990**, *55*, 826.

0022-3263/92/1957-6025$03.00/0 

**Scheme I**



**Scheme II**



derivatives **3** and **4** would be accessible (Scheme I). The latter are structural elements found in a number of natural products.[7,8]

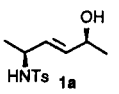
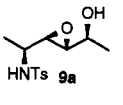
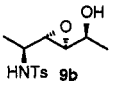
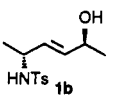
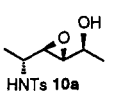
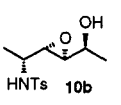
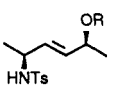
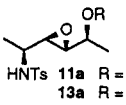
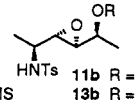
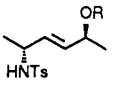
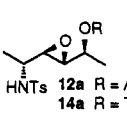
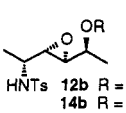
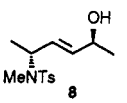
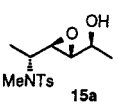
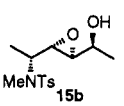
We previously studied epoxidation of cyclic 4-(tosylamido)-2-alken-1-ols related to **1**.[9] In this paper we present a study of the stereochemistry of the epoxidation of the 5-(tosylamido)-3-hexen-2-ol derivatives **1** and **6–8** and an NMR spectroscopic method for direct stereochemical assignment of the epoxides.

## Results and Discussion

Three different epoxidation reagents have been tested in the present investigation: (i) *m*-chloroperbenzoic acid (*m*-CPBA)[10] (method A), (ii) *tert*-butyl hydroperoxide/$VO(acac)_2$[11] (method B), and (iii) *tert*-butyl hydroperoxide/$Ti(O\text{-}i\text{-}Pr)_4$[10b,12] using racemic diethyl tartrate (method C). All these reagents have been investigated thoroughly concerning mechanism and selectivity. In epoxidations with *m*-CPBA it is well established that an allylic hydroxyl group[13] or allylic amide[14,15] has a syn-directive effect in cyclic systems. The effects are cooperative in 1-amido-4-hydroxy-2-cyclohexene derivatives when the stereochemistry between N and O is cis,[16] but for seven-membered rings the situation is more complicated, leading to nonstereoselective epoxidation of the corresponding bis-allylic *cis*- and *trans*-amido alcohol derivatives.[9] In the latter trans system a face selectivity opposite to the oxygen was obtained by transformation to a bulky silyl ether,[17] which was recently applied by us in the total synthesis of pseudoscopine.[9]

An alternative selective epoxidation reagent is $VO(acac)_2$ in combination with *t*-BuOOH.[11,18] The mechanism is quite different from that of peroxybenzoic acid epoxidation since the vanadium complex forms an ester with the allylic alcohol. Nitrogen groups do not bind to the vanadium complex[19] and therefore can direct the epoxidation only

**Table I. Epoxidation of 5-(Tosylamido)-3-hexen-2-ol Derivatives**

| starting material | method[a] | products[b] | | | % yield[c] |
|---|---|---|---|---|---|
|  | |  | |  | |
| | A | 1 | : | 1 | 83 |
| | B | 2 | : | 3 | 83 |
| | C | 2 | : | 1 | 50 |
|  | |  | |  | |
| | A | 2 | : | 1 | 86 |
| | B | 1 | : | 1 | 87 |
| | C | 1 | : | 5 | 30 |
|  | |  | |  | |
| **6a** R = Ac | A | 1 | : | 1 | 90 |
| **7a** R = TBDMS | A | 1 | : | 1 | 85 |
|  | |  | |  | |
| **6b** R = Ac | A | 1 | : | 4 | 70 |
| **7b** R = TBDMS | A | 2 | : | 3 | 76 |
|  | |  | |  | |
| | A | 1 | : | 3 | 91 |
| | B | 3 | : | 1 | 80 |

[a] See Experimental Section. A = *m*-CPBA, $CH_2Cl_2$; B = $VO(acac)_2$, *t*-BuOOH, benzene; C = $Ti(O\text{-}i\text{-}Pr)_4$, *t*-BuOOH, diethyl tartrate, 4-Å molecular sieves. [b] Relative ratio of isomers determined on the crude product. [c] Isolated combined yield of isomer mixture.

(6) Direct cis dihydroxylation will lead to the *trans*-3,4-dihydroxypyrrolidine **3**, whereas trans dihydroxylation via the epoxide and hydrolytic ring opening will give the *cis*-3,4-dihydroxypyrrolidine **3**.

(7) (a) Iida, H.; Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1985**, *26*, 3255. (b) Iida, H.; Yamazaki, N.; Kibayashi, C. *J. Org. Chem.* **1987**, *52*, 1956.

(8) Pak, C. S.; Lee, G. H. *J. Org. Chem.* **1991**, *56*, 1128. Takahata, H.; Banba, Y.; Tajima, M.; Momose, T. *J. Org. Chem.* **1991**, *56*, 240.

(9) Schink, H. E.; Pettersson, H.; Bäckvall, J. E. *J. Org. Chem.* **1991**, *56*, 2769.

(10) (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63. (b) Pfenninger, A. *Synthesis* **1986**, 89.

(11) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *50*, 6136. (b) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733. (c) Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979**, *101*, 159.

(12) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(13) Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.* **1957**, 1958.

(14) (a) Roush, W. R.; Straub, J. A.; Brown, R. J. *J. Org. Chem.* **1987**, *52*, 5127. (b) Kočovský, P. *Tetrahedron Lett.* **1988**, 2475.

(15) This has been established in cyclic *N*-tosylamido-substituted olefins. Bäckvall, J. E.; Oshima, K.; Palermo, R. E.; Sharpless, K. B. *J. Org. Chem.* **1979**, *44*, 1953.

(16) (a) Pettersson, H. Unpublished results. (b) For an acyclic case see: Kogen, H.; Nishi, T. *J. Chem. Soc., Chem. Commun.* **1987**, 311. Here benzyloxycarbonyl ($NCO_2Ar$) is protected instead of toluenesulfonamido ($NSO_2Ar$), but the same effect is observed.

(17) (a) Chavdarian, C. G.; Heathcock, C. H. *Synth. Commun.* **1976**, *6*, 277.

(18) Sheng, M. N.; Zajacek, J. G. *J. Org. Chem.* **1970**, *35*, 1839.

(19) Hiyama, T.; Obayashi, M. *Tetrahedron Lett.* **1983**, *24*, 395.

**Table II. Selected NOE Data for the Epoxides Discussed in the Text[a]**

| compd[b] | irradiated signal: % NOE on: | $H_C$ | | $H_{Ox}$ | | $H_a$ | | $H_b$ | | assnt[c] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | $H_a$ | $H_b$ | $H_a$ | $H_b$ | $H_C$ | $H_{Ox}$ | $H_C$ | $H_{Ox}$ | |
| **16** | | 6 | 5 | 7 | 0 | 1 | 4 | 2 | 0 | |
| **17**[d] | | 3 | 3 | 4 | 0 | 1 | 3 | 2 | 0 | |
| **18a** | | 6 | 10 | | | 4 | | 7 | | syn |
| **18b** | | | | 9 | 4 | | 6 | | 3 | anti |
| **9a** | | | | | | 4 | | nd[e] | | syn |
| **9b** | | | | | | | 8 | | 7 | anti |
| **10a** | | | | | | 6 | | 5 | | syn |
| **10b** | | | | | | | 8 | | 3 | anti |

[a] At 23 °C, $CDCl_3$ solution, degassed. [b] For **9** and **10**, only the CH(OH) part of the molecule is considered. [c] Stereochemistry between OH and epoxide. [d] At −40 °C. [e] Not measured because of signal overlap.

in cases of steric hindrance. In the Sharpless epoxidation, $Ti(O\text{-}i\text{-}Pr)_4$ forms a similar complex with the substrate as vanadium.[18,20] For steric reasons the titanium complex is more rigid, and as a consequence a higher selectivity may be expected.

The *anti*- and *syn*-amido acetates **6** were obtained from chloroacetate **5**[2a] via previously described procedures (Scheme II).[5,21] (Tosylamido)hexenols **1a** and **1b** were transformed into epoxides according to methods A, B, and C as described in the Experimental Section. All methods gave mixtures of isomeric products (Table I). The use of *m*-CPBA (A) or $VO(acac)_2/t$-BuOOH (B) gave a poor selectivity for these substrates. Sharpless epoxidation of **1b** using racemic tartrate (C) was slow but led to a higher selectivity, and **10a** and **10b** were formed in a 1:5 ratio.

Oxygen-protected derivatives of **1** were also studied. *m*-CPBA epoxidation of the acetate and silyl derivatives **6a** and **7a**, respectively, was completely nonselective, and in each case a 1:1 mixture of the possible epoxides was obtained. Epoxidation of the corresponding anti amidoacetate **6b** with *m*-CPBA was more selective and afforded a 1:4 mixture of **12a** and **12b**, while the corresponding silyl derivative **7b** reacted less selectively. Finally, in the epoxidation of *N*-methylamido alcohol **8** the selectivity between epoxides **15a** and **15b** was reversed from 1:3 with *m*-CPBA to 3:1 with $VO(acac)_2/t$-BuOOH.

The yields are generally good except for method C, which gave only moderate yields. The results show, as might be expected, that it is much more difficult to obtain high selectivity in epoxidation of acyclic derivatives compared to cyclic ones. Derivatization of the hydroxyl group to a silyl ether[17a,22] or an acetate did not improve the selectivity, except in one case (**6b**).

**Strategy for Stereochemical Assignment.** The assignment of the relative stereochemistry of functional groups in acyclic compounds is an important but difficult problem. Apart from X-ray crystallography, which is limited to crystalline compounds, no general and straightforward methods exist today. Conversion into cyclic derivatives, which then are amenable to conformational analysis via homonuclear coupling constants,[23] or conversion into compounds of known stereochemistry are the most commonly applied methods. Direct investigations have been attempted for vicinal polyacetates[24] and polyols[25] via homonuclear coupling constants in conjunction

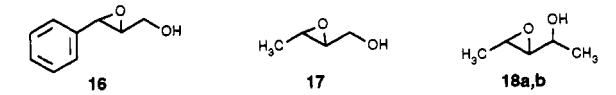



**Figure 1.** Model compounds for the investigated epoxides. The epoxides were synthesized by *m*-CPBA epoxidation of the corresponding allylic alcohol.

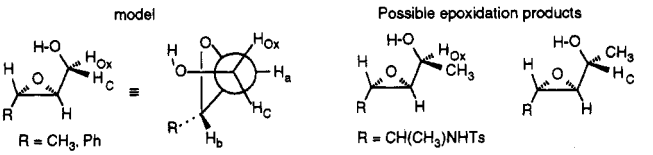
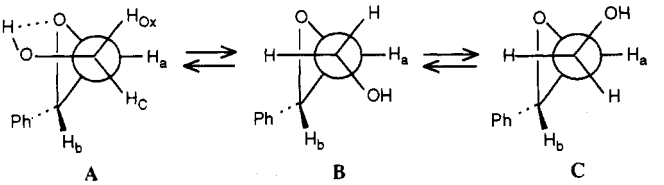



**Figure 2.** Relation between the diastereotopic methylene protons of model compounds and H-2 of the target molecules. Protons in the same position relative to the oxygen ring are expected to exhibit similar NMR spectral data.

**Scheme III**




with molecular modeling studies. The relative and absolute stereochemistry of vicinal aminopolyols has been determined by circular dichroism (CD) after introduction of a chromophore.[26] An empirical method based on steric effects of γ-substituents on $^{13}C$ NMR chemical shifts has been suggested by Whitesell et al.,[27] and empirical relationships between stereochemistry and NMR parameters have been found for various groups of compounds.

Our objective was to develop a method for direct assignment of the stereochemistry of the components of a diastereomeric mixture without further chemical transformations. We began our approach with simple model epoxides, which resemble the epoxy alcohol part of the diastereomers **9** and **10** (Figure 1). The NMR spectra of the model compounds reveal more readily the stereochemically important spectral characteristics, which then are also found for our products. In the present substrates the relative stereochemistry between positions 2 and 5 is known,[5,21] but the orientation of the substituents at pos-

(20) (a) Woodard, S. S.; Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 106. (b) Jörgensen, K. A.; Wheeler, R. A.; Hoffmann, R. *J. Am. Chem. Soc.* **1987**, *109*, 3240.

(21) Bystrōm, S. E.; Aslanian, R.; Bäckvall, J. E. *Tetrahedron Lett.* **1985**, *26*, 1749.

(22) Sabol, J. S.; Cregge, R. J. *Tetrahedron Lett.* **1989**, *30*, 3377.

(23) (a) Cirillo, P. F.; Panek, J. S. *J. Org. Chem.* **1990**, *55*, 6071. (b) Hawkes, G. E.; Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1984**, 2073.

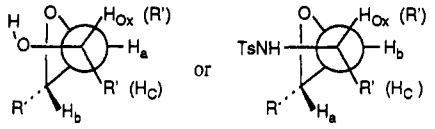
(24) (a) Moore, R. E.; Barchi, J. J.; Bartolini, G. *J. Org. Chem.* **1985**, *50*, 374. (b) Masamune, S.; Ma, P.; Moore, R. E.; Fujiyoshi, T.; Jaime, C.; Osawa, E. *J. Chem. Soc., Chem. Commun.* **1986**, 261.

(25) (a) Kingsbury, C. A. *J. Org. Chem.* **1970**, *35*, 1319. (b) Gallwey, F. B.; Hawkes, J. E.; Haycock, P.; Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1979. (c) Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1986**, 467. (d) Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1349. (e) Gillies, D. G.; Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1155. (f) Hawkes, G. E.; Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1984**, 2073.

(26) (a) Zhou, P.; Berova, N.; Nakanishi, K.; Rohmer, M. *J. Chem. Soc., Chem. Commun.* **1991**, 256. (b) Wiesler, W. T.; Nakanishi, K. *J. Am. Chem. Soc.* **1989**, *111*, 9205.

(27) Whitesell, J. K.; LaCour, T.; Lovell, R. L.; Pojman, J.; Ryan, P.; Yamada-Nosaka, A. *J. Am. Chem. Soc.* **1988**, *110*, 991.

**Table III. Comparison of NMR Spectral Data for the Epoxides Studied**




| compd or substructure[a] | R | R' | δ (ppm) $H_C$ | δ (ppm) $H_{Ox}$ | $^3J_{HH}$[b] $H_C$ | $^3J_{HH}$[b] $H_{Ox}$ | $^3J_{CH}$[c] $H_C$ | $^3J_{CH}$[c] $H_{Ox}$ | $J_{CH-XH}$[d] | assnt |
|---|---|---|---|---|---|---|---|---|---|---|
| epoxy alcohol (part) | | | | | | | | | | |
| **16** | Ph | H | 3.78 | 4.03 | 4.0 | 2.4 | 2.3 | 3.75 | | |
| **17** | $CH_3$ | H | 3.60 | 3.90 | 4.5 | 2.6 | 2.8 | 3.0 | | |
| **18a** | $CH_3$ | $CH_3$ | 3.63 | | 5.2 | | 2.5 | | 5.6 | syn |
| **18b** | $CH_3$ | $CH_3$ | | 3.93 | | 3.3 | | 4.1 | 2.4 | anti |
| **9a** | $CH(CH_3)NHTs$ | $CH_3$ | 3.64 | | 4.7 | | 2.6 | | | syn |
| **9b** | $CH(CH_3)NHTs$ | $CH_3$ | | 3.81 | | 4.0 | | 5.3 | | anti |
| **10a** | $CH(CH_3)NHTs$ | $CH_3$ | 3.62 | | 4.5 | | nd | | | syn |
| **10b** | $CH(CH_3)NHTs$ | $CH_3$ | | 3.94 | | 3.0 | | nd | | anti |
| epoxy tosylamide (part) | | | | | | | | | | |
| **9a** | $CH(OH)CH_3$ | $CH_3$ | 3.56 | | 3.0 | | 2.5 | | 8.5 | syn |
| **9b** | $CH(OH)CH_3$ | $CH_3$ | | 3.10 | | 6.3 | | 3.5 | 6.5 | anti |
| **10a** | $CH(OH)CH_3$ | $CH_3$ | | 3.21 | | 6.0 | | nd | 6.9 | anti |
| **10b** | $CH(OH)CH_3$ | $CH_3$ | 3.58 | | 3.2 | | nd | | 8.3 | syn |

[a] All compounds racemic. [b] Vicinal coupling constant to $H_a$ or $H_b$. [c] Vicinal coupling constant to $C_b$ or $C_a$. [d] Vicinal coupling to OH or NH.

itions 3 and 4 (i.e. oxirane ring syn or anti to the hydroxy group) relative to the 2 and 5 substituents is unknown. Part of the assignment might be provided by $^3J_{HH}$ and $^3J_{CH}$ coupling constants between C*H*OH or C*H*NH and the vicinal epoxy proton and corresponding epoxy carbon, respectively.[28] Further information is accessible by NOE measurements.[29] The very likely occurrence of a mixture of rotamers has to be taken into consideration.[30]

**Stereochemical Assignment of Epoxidation Products.** In the model epoxy alcohols with a terminal OH group the protons $H_{Ox}$ (gauche to epoxy oxygen) and $H_C$ (gauche to epoxy carbon) resemble the protons on C-2 for the syn- and anti-configuration of the target compounds (Figure 2). The assignment of these diastereotopic hydrogens was performed by a combination of H–H and C–H coupling constants and NOE data (Table II) and is described here for cinnamyl alcohol epoxide (**16**). The two diastereotopic methylene protons ($CH_2OH$) have different chemical shifts and different vicinal coupling constants with $H_a$ as well as with $C_b$ (Table III). The considerably different NOEs with the epoxy protons are used to assign the signals (Table II). These findings suggest that the three rotamers (Scheme III) have different populations. Molecular modeling[31] and semiempirical quantum mechanical calculations[32] add further support to this view. According to these, the rotamer A is the one with the lowest energy and most abundant,[33a] thus giving the major contribution to the NMR spectral data.[33b] This is certainly

**Table IV. Correlation between the $^1$H NMR Shift of CHO and the Stereochemistry**

| compd | $\delta_{CHO}$ | rel stereochem between O and epoxide | $\delta_{syn} - \delta_{anti}$ |
|---|---|---|---|
| **9a** | 3.64 | syn | −0.17 |
| **9b** | 3.81 | anti | |
| **10a** | 3.62 | syn | −0.32 |
| **10b** | 3.94 | anti | |
| **11a** | 4.74 | syn | −0.04 |
| **11b** | 4.78 | anti | |
| **12a** | 4.67 | syn | −0.12 |
| **12b** | 4.79 | anti | |
| **13a** | 3.55 | syn | −0.20 |
| **13b** | 3.75 | anti | |
| **14a** | 3.50 | syn | −0.22 |
| **14b** | 3.72 | anti | |
| **15a** | 3.62 | syn | −0.35 |
| **15b** | 3.97 | anti | |

an effect of the intramolecular hydrogen bond between the hydroxy group and the epoxy oxygen,[34] which previously has been observed in the IR spectra of epoxy alcohols.[35] For **16**, both diastereotopic protons exhibit an NOE to $H_a$, but only one of them gives an NOE to $H_b$ (Table II), as is expected for the hydrogen bonded conformer A. Also, the C–H long-range coupling ($^3J_{CH}$) between each of these protons and $C_b$ agrees best with the predominance of this conformer. The vicinal coupling constants of these diastereotopic protons with the epoxide proton $H_a$ would seem to give less information since the HC–CH dihedral angles for both protons are quite similar, and the coupling constants are expected to be further modulated by electronegative substituent effects, which might reverse their order. This is less likely for the more different C–C–C–H dihedral angles, making these a more reliable indicator of

(28) (a) Murrell, J. N. *Progr. Nucl. Magn. Reson. Spectrosc.*; Emsley, J. W., Feeney, J., Sutcliffe, L. H., Eds.; Pergamon: Oxford, 1971; Vol. 6, p 1. (b) Kessler, H.; Griesinger, C.; Wagner, K. *J. Am. Chem. Soc.* **1987**, *109*, 6927.

(29) Neuhaus, D.; Williamson, M. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*; VCH: Weinheim, 1989; Chapter 11.

(30) (a) Pachler, K. G. R. *Spectrochim. Acta* **1964**, *20*, 581. (b) Whitesides, G. M.; Sevenair, J. P.; Goetz, R. W. *J. Am. Chem. Soc.* **1967**, *89*, 1135.

(31) The MMX force field as present in PC-MODEL, version 3.2, from Serena Software, Bloomington, IN, was applied.

(32) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. AM1 version 1.0, QCPE no. 506, Indiana University, was used.

(33) (a) Relative energies of rotamers about the $C_{epoxy}$–C(OH) bond are available as Table A2, supplementary material. (b) Upon cooling to −60 °C, no significant changes of the $^1$H NMR coupling patterns were observed, indicating that the solutions contain almost exclusively one single conformer.

(34) The OH signals appear either as doublets with different coupling constants or as broad signals of different widths for two corresponding syn–anti isomers. Solvents which interfere with hydrogen bonds change the coupling constants, e.g., $J_{CH-OH}$ for **18a** and **18b** from 5.6 and 2.4 Hz, respectively, in $CDCl_3$ to 5.0 and 4.5 Hz in DMSO-$d_6$. The $CH_{ox}$–$CH_b$ and $CH_C$–$CH_b$ couplings (Table III) become more similar in solvents which interfere with hydrogen bonds, e.g., for **16**: $J(CH_{ox}–CH_b)$ = 2.4 Hz ($CDCl_3$), 2.5 Hz ($CCl_4$), 3.3 Hz (DMSO-$d_6$), 4.9 Hz (pyridine-$d_5$); $J(CH_C–CH_b)$ = 4.0 Hz ($CDCl_3$), 3.9 Hz ($CCl_4$), 4.9 Hz (DMSO-$d_6$), 4.6 Hz (pyridine-$d_5$).

(35) (a) Oki, M.; Murayama, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 259. (b) For comparison, the IR spectrum of **9a** shows a broad signal at 3589 $cm^{-1}$, which is absent in the spectra of **11a** and **13a**.

**Table V. Correlation between the $^1H$ NMR Shift of CHN and the Stereochemistry**

| compd | $\delta_{CHN}$ | rel stereochem between N and epoxide | $\delta_{syn} - \delta_{anti}$ |
|---|---|---|---|
| **9a** | 3.56 | syn | 0.46 |
| **9b** | 3.10 | anti | |
| **10a** | 3.21 | anti | 0.37 |
| **10b** | 3.58 | syn | |
| **11a** | 3.64 | syn | 0.47 |
| **11b** | 3.17 | anti | |
| **12a** | 3.18 | anti | 0.43 |
| **12b** | 3.61 | syn | |
| **13a** | 3.56 | syn | 0.24 |
| **13b** | 3.32 | anti | |
| **14a** | 3.17 | anti | 0.33 |
| **14b** | 3.50 | syn | |
| **15a** | 4.08 | anti | 0.05 |
| **15b** | 4.13 | syn | |

the conformation. Modified Karplus equations which take into consideration an epoxy substituent are currently not available. In all, the NOE and C–H couplings, together with the molecular modeling studies, allow an unambiguous assignment of the diastereotopic methylene protons. Comparable results have been obtained for the other model compounds.

With these assignments in hand, a common pattern for the chemical shifts and coupling constants is observed (Table III). By relating the C*H*OH protons of the amido alcohol epoxides to the diastereotopic protons in the model compounds, the relative stereochemistry of the isomers could be assigned. The shift of the C*H*OH proton is 0.2–0.3 ppm lower for the syn compounds **18a**, **9a**, and **10a** (OH syn to epoxy oxygen) compared to the corresponding anti compounds (**18b**, **9b**, and **10b**). Since the relative stereochemistry of the OH and NHTs substituents in the 2- and 5-positions is already known from the starting materials, the complete stereochemical assignment is obtained. In addition, a general trend concerning the chemical shifts of C*H*N and the vicinal coupling constants is observed for the tosylamido epoxy subunit.

The corresponding correlation between stereochemistry and shift of the C*H*O and C*H*N proton, respectively, was also observed for derivatives **11–15**. The C*H*O and C*H*N shifts for all products shown in Table I together with the assignments are given in Tables IV and V, respectively. The C*H*O chemical shift is indicative of the stereochemistry between the C-2 oxygen and epoxy oxygen, the $(\delta_{CHO})_{syn}$ (syn between C-2 oxygen and epoxy oxygen) being lower than $(\delta_{CHO})_{anti}$ and (Table IV). In all cases studied the C*H*N shift was significantly higher (less pronounced for the methylated analogue **15**) for the compounds in which the nitrogen is syn to the epoxide compared to the compounds with the corresponding anti stereochemistry (Table V).[36] The stereochemistry of compounds **11–15** was confirmed by transformation of **9a** → **11a**, **10a** → **12a**, **9a** → **13a**, **10a** → **14a**, and **10a** → **15a**. An X-ray structure of the *p*-nitrobenzoyl ester of **9a** (**19**) confirmed the structures assigned for **9a** and **9b**.[37]

The $^3J_{CH}$ coupling constants were measured by a semiselective 2D *J* spectrum with an initial DEPT $^1H \rightarrow {}^{13}C$ polarization transfer step.[38] The low sensitivity and fast relaxation at higher concentrations precluded the measurement of this parameter for the *trans*-amido alcohol epoxides. A more sensitive method has recently been devised by Keeler et al.,[39] but was unavailable to us.

**Relative Rotamer Populations.** It has been shown that the semiempirical quantum mechanical model AM1 is well suited to describe conformational energies in the presence of hydrogen bonds.[32] To confirm the predominance of the hydrogen-bonded conformers around the C-epoxy/CXH bond in the investigated compounds, we calculated the heat of formation for the three gauche rotamers and from these energies estimated the rotamer populations via a Boltzmann distribution. For all molecules the predominating conformer (i.e., ≥50%)[33] was the one which had an intramolecular hydrogen bond between the epoxy oxygen and the OH or NH group. The NMR data are obtained as a weighted average for all the populations, since the barriers to rotation are low, and do not allow for a similar quantification, since coupling constants for the individual rotamers are unknown.

## Experimental Section

**General.** $^1H$ and $^{13}C$ NMR spectra were recorded for $CDCl_3$ solutions, unless stated otherwise, at 300 and 400 MHz ($^1H$) and at 75.4 and 100.6 MHz ($^{13}C$), respectively. The isomeric ratios were determined by integration of the N*H*Ts signals. $^{13}C$ NMR signals were assigned from HMQC spectra.[40] Elemental analyses were performed by Analytische Laboratorien, Engelskirchen, Germany, and Mikrokemi AB, Uppsala, Sweden. Mass spectra were obtained by direct inlet at 70 eV. Flash chromatography was run using silica gel (230–400 mesh) and diethyl ether/*n*-pentane. Commercially available chemicals were used as delivered. The *m*-CPBA was of 80–90% technical grade. Solvents were dried according to standard procedures. Palladium tetrakis(triphenylphosphine) and *p*-toluenesulfoneamide monosodium salt (NaNHTs) were prepared according to known procedures. All salt solutions were saturated, unless stated otherwise.

**(2*S**,5*S**)-2-Acetoxy-5-chloro-3-hexene (5).**[2a] (*E*,*E*)-2,4-Hexadiene was chloroacetoxylated according to the procedure described in ref 2a.

**(2*S**,5*S**)-2-Acetoxy-5-(tosylamido)-3-hexene (6a).**[5,21] The chloroacetate **5** was allowed to react with NaNHTs in the presence of $Pd(PPh_3)_4$.[5,21]

**(2*S**,5*R**)-2-Acetoxy-5-(tosylamido)-3-hexene (6b).**[5] The chloroacetate **5** was subsituted with NaNHTs according to ref 5.

**Hydrolysis of Amidoacetates 6a and 6b.** The acetate[6] (1 mmol) was dissolved in MeOH (3 mL), and 2 M NaOH (1 mL) was added. The mixture was refluxed at 50 °C for 5 h. The MeOH was evaporated, the pH was adjusted to 5, and the aqueous phase was extracted twice with EtOAc. The organic layer was washed with brine and dried ($MgSO_4$). Evaporation afforded the crude product which was purified by flash chromatography to give the 5-(tosylamido)-3-hexen-2-ol (**1a** or **1b**). Spectral data are in agreement with those reported previously.[5]

**2-[(*tert*-Butyldimethylsilyl)oxy]-5-(tosylamido)-3-hexene (7a, 7b).** To tosylamido alcohol **1a** or **1b** (353 mg) and imidazole (160 mg) in dimethyl formamide (DMF, 4 mL) at 0 °C was added *tert*-butyldimethylsilyl chloride (TBDMSCl, 360 mg).[9] The mixture was allowed to reach ambient temperature and stirred for 4 h. Brine was added, and the mixture was extracted with ether. The organic phase was collected, dried ($MgSO_4$), and concentrated in vacuo and the crude product obtained was purified by flash chromatography. The silyl ether was obtained in quantitative yield.

(36) Additional NMR data also indicate the stereochemistry between nitrogen and epoxy oxygen. For example the $(\delta_{NH})_{syn}-(\delta_{NH})_{anti}$ (syn or anti between N and epoxy oxygen) is between −0.10 and −0.28 for compounds **9–14**. In addition, the $J_{CH-NH}$ is in the range of 8.0–8.7 Hz for the syn compounds and between 6.4–6.9 Hz for the corresponding anti compounds (cf. Table III for **9** and **10**).

(37) Details of the crystal structure of **19** will be published elsewhere: Gogoll, A.; Pettersson, H.; Tellgren, R. To be submitted to *Acta Crystallogr. C.*

(38) (a) Bax, A.; Freeman, R. *J. Am. Chem. Soc.* **1982**, *104*, 1099. (b) Uhrin, D.; Liptaj, T.; Hricovini, M.; Capek, P. *J. Magn. Reson.* **1989**, *85*, 137.

(39) Titman, J. J.; Neuhaus, D.; Keeler, J. *J. Magn. Reson.* **1989**, *85*, 111.

(40) Summers, M. E.; Marzilli, I. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285.

**(2S*,5S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-5-(tosylamido)-3-hexene (7a)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 5.43 (dd, *J* = 4.5, 15.0 Hz, H, olefin), 5.35 (dd, *J* = 5.0, 15.0 Hz, 1 H, olefin), 4.20 (d, *J* = 8.0 Hz, 1 H, N*H*), 4.08 (dq, *J* = 4.5, 6.5 Hz, 1 H, C*H*OSi), 3.84 (ddq, *J* = 5.0, 6.5, 8.0 Hz, 1 H, C*H*NH), 2.45 (s, 3 H, C$H_3$Ts), 1.18 (d, *J* = 6.5 Hz, 3 H, C$H_3$ N-side), 1.05 (d, *J* = 6.5 Hz, 3 H, C$H_3$ O-side), 0.80 (s, 9 H, *t*-BuSi), 0.0 (s, 6 H, MeSi).

**(2S*,5R*)-2-[(*tert*-Butyldimethylsilyl)oxy]-5-(tosylamido)-3-hexene (7b)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 5.43 (dd, *J* = 4.8, 15.4 Hz, 1 H, =C*H*CHOSi), 5.36 (dd, *J* = 5.7, 15.4 Hz, 1 H, =C*H*CHN), 4.38 (d, *J* = 8.0 Hz, 1 H, N*H*), 4.12 (dq, *J* = 6.3, 4.8 Hz, 1 H, C*H*OSi), 3.90 (ddq, *J* = 8.0, 6.5, 5.7 Hz, 1 H, C*H*NH), 2.45 (s, 3 H, C$H_3$Ts), 1.10 (d, *J* = 6.5 Hz, 3 H, $CH_3$ N-side), 1.0 (d, *J* = 6.3 Hz, 3 H, C$H_3$ O-side), 0.80 (s, 9 H, *t*-BuSi), 0.0 (s, 6 H, MeSi); $^{13}$C NMR: δ 143.2 (*p*-Ts), 138.2 (*ipso*-Ts), 135.7 (=*C*HCHOSi), 129.7 (*m*-Ts), 129.0 (=*C*-HCHN), 127.1 (*o*-Ts), 68.3 (CHOSi), 50.8 (CHN), 25.8 ((C$H_3$)$_3$C), 24.1 ($CH_3$ O-side), 22.1 ($CH_3$ N-side), 21.5 ($CH_3$Ts), 18.2 ((C$H_3$)$_3$*C*), −4.7 ($CH_3$Si), −4.8 ($CH_3$Si).

**(2S*,5R*)-5-(*N*-Methyltosylamido)-3-hexen-2-ol (8).** A mixture of **6b** (220 mg, 0.71 mmol), MeI (110 μL), and $K_2CO_3$ (0.65 g) in acetone (9 mL) was refluxed for 22 h. The solvent was removed under vacuo, and 10 mL of methanol and 4 mL of 2 M NaOH were added. The mixture was refluxed for 4 h, concentrated (≈5 mL), and neutralized, and the residue was extracted with ethyl acetate (2 × 10 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography of the crude product on a short column afforded 200 mg (99%) of **8**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 5.56 (ddd, *J* = 1.3, 5.8, 15.5 Hz, 1 H, =C*H*CHOH), 5.44 (ddd, *J* = 1.0, 5.0, 15.5 Hz, 1 H, =C*H*CHN), 4.63 (m, C*H*N) 4.22 (m, 1 H, C*H*OH), 2.68 (s, 3 H, C$H_3$N), 2.45 (s, 3 H, C$H_3$Ts), 1.18 (d, *J* = 6.4 Hz, 3 H, C$H_3$ O-side), 1.09 (d, *J* = 6.9 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 143.1 (*p*-Ts), 136.9 (*ipso*-Ts), 136.3 (=*C*HCHOH), 126.9 (*m*-Ts), 128.6 (=*C*HCHN), 127.2 (*o*-Ts), 68.1 (*C*HOH), 53.1 (*C*HNCH$_3$), 28.4 (*C*H$_3$N), 23.3 (*C*H$_3$ O-side), 21.5 (*C*H$_3$Ts), 16.7 (*C*H$_3$ N-side).

**Epoxidation with *m*-CPBA (Method A).** To a solution of the substrate in $CH_2Cl_2$ at 0 °C was added *m*-CPBA (1.5 equiv) in portions. After being stirred for 1 h at 0 °C, the mixture was kept in the refrigerator overnight. The filtered solution was washed successively with $Na_2SO_3$, $NaHCO_3$, $H_2O$, and brine. The combined aqueous phases were extracted with $CH_2Cl_2$. The combined organic layers were dried ($MgSO_4$) and concentrated and the crude product purified by flash chromatography.

**Epoxidation with VO(acac)$_2$/*t*-BuOOH (Method B).** To a refluxing solution of VO(acac)$_2$ (0.03 equiv) and the substrate in benzene was added *t*-BuOOH (1.6 equiv) during a period of 25 min. The mixture was refluxed for 4 h and then allowed to cool to rt. The solution was washed with 1 M HCl, $NaHSO_3$, $NaHCO_3$, and brine. Drying ($MgSO_4$), concentration of the organic layer, and flash chromatography afforded the product.

**Epoxidation with Ti(O-*i*-Pr)$_4$/*t*-BuOOH (Method C).** The usual procedure by Sharpless[12] was used, but the reaction was performed at 20 °C for 40 h.

**3,4-Epoxy-5-(tosylamido)hexan-2-ol (9 and 10).** The appropriate amido alcohol (**1a** or **1b**) was epoxidized according to methods A, B, and C.

**(2S*,3R*,4S*,5S*)-3,4-Epoxy-5-(tosylamido)hexan-2-ol (9a)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 4.92 (d, *J* = 8.5 Hz, 1 H, N*H*), 3.64 (dq, *J* = 4.7, 6.5 Hz, 1 H, C*H*OH), 3.56 (ddq, *J* = 3.0, 7.0, 8.5 Hz, 1 H, C*H*NH), 2.94 (dd, *J* = 2.3, 3.0 Hz, 1 H, epoxide N-side), 2.89 (dd, *J* = 2.3, 4.7 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts), 1.19 (d, *J* = 6.5 Hz, 3 H, C$H_3$ O-side), 1.12 (d, *J* = 7.0 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 143.6, 137.9, 129.7, 126.9, 66.5 (*C*HOH), 59.8 (epoxide O-side), 58.7 (epoxide N-side), 48.4 (*C*HNH), 21.5 (*C*H$_3$Ts), 20.0 (*C*H$_3$ O-side), 19.1 (*C*H$_3$ N-side); MS *m*/*z* (relative intensity) 285 (M$^+$, 0.4), 267 (2), 241 (2), 198 (47), 155 (50), 91 (100), 65 (33). Anal. Calcd for $C_{13}H_{19}NSO_4$: C, 54.72; H, 6.71. Found: C, 54.51; H, 6.59.

**(2S*,3S*,4R*,5S*)-3,4-Epoxy-5-(tosylamido)hexan-2-ol (9b)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 5.02 (d, *J* = 6.5 Hz, 1 H, N*H*), 3.81 (dq, *J* = 4.0, 6.3 Hz, 1 H, C*H*OH), 3.10 (ddq, *J* = 6.3, 6.5, 6.6 Hz, 1 H, C*H*NH), 2.96 (dd, *J* = 2.3, 6.3 Hz, 1 H, epoxide N-side), 2.84 (dd, *J* = 2.3, 4.0 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts), 1.21 (d, *J* = 6.3 Hz, 3 H, C$H_3$ O-side), 1.13 (d, *J* = 6.6 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 143.8, 137.0, 129.8, 127.1, 65.2 (*C*HOH), 61.0 (epoxide O-side), 57.7 (epoxide N-side), 50.0 (*C*HNH), 21.5 (*C*H$_3$Ts), 18.8 (*C*H$_3$ O-side), 17.8 (*C*H$_3$ N-side).

**(2S*,3R*,4S*,5R*)-3,4-Epoxy-5-(tosylamido)hexan-2-ol (10a)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 5.02 (d, *J* = 6.9 Hz, 1 H, N*H*), 3.62 (dq, *J* = 4.5, 6.5 Hz, 1 H, C*H*OH), 3.21 (ddq, *J* = 6.0, 6.7, 6.9 Hz, 1 H, C*H*NH), 2.92 (dd, *J* = 2.2, 6.0 Hz, 1 H, epoxide N-side), 2.83 (dd, *J* = 2.2, 4.5 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts), 1.23 (d, *J* = 6.5 Hz, 3 H, C$H_3$ O-side), 1.11 (d, *J* = 6.7 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 143.5, 137.5, 129.8, 126.9, 66.5 (*C*HOH), 61.8 (epoxide O-side), 58.5 (epoxide N-side), 49.9 (*C*HNH), 21.4 (*C*H$_3$Ts), 19.5 (*C*H$_3$ O-side), 17.4 (*C*H$_3$ N-side). Anal. Calcd for $C_{13}H_{19}NSO_4$ (isomeric mixture of **10a** and **10b**): C, 54.72; H, 6.71; N, 4.91. Found: C, 55.0; H, 7.1; N, 4.7.

**(2S*,3S*,4R*,5R*)-3,4-Epoxy-5-(tosylamido)hexan-2-ol (10b)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 4.87 (d, *J* = 8.3 Hz, 1 H, N*H*), 3.94 (dq, *J* = 3.0, 6.5 Hz, 1 H, C*H*OH), 3.58 (ddq, *J* = 3.2, 7.0, 8.3 Hz, 1 H, C*H*NH), 3.02 (dd, *J* = 2.3, 3.2 Hz, 1 H, epoxide N-side), 2.92 (dd, *J* = 2.3, 3.0 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts), 1.15 (d, *J* = 6.5 Hz, 3 H, C$H_3$ O-side), 1.12 (d, *J* = 7.0 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 143.3, 137.8, 129.8, 126.9, 64.5 (*C*HOH), 59.1 (epoxide O-side), 57.3 (epoxide N-side), 48.8 (*C*HNH), 21.4 (*C*H$_3$Ts), 19.5 (*C*H$_3$ O-side), 18.4 (*C*H$_3$ N-side); MS *m*/*z* (relative intensity) 285 (M$^+$, 1), 267 (5), 241 (3), 198 (82), 155 (73), 91 (100), 65 (33). Anal. Calcd for $C_{13}H_{19}NSO_4$ (isomeric mixture of **10a** and **10b**): C, 54.72; H, 6.71; N, 4.91. Found: C, 55.0; H, 7.1; N, 4.7.

**Epoxidation of 6a (Method A). (2S*,3R*,4S*,5S*)-2-Acetoxy-3,4-epoxy-5-(tosylamido)hexane (11a)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 4.87 (dq, *J* = 6.2, 4.0 Hz, 1 H, C*H*OAc), 4.52 (d, *J* = 8.6 Hz, 1 H, N*H*), 3.63 (ddq, *J* = 2.5, 6.0, 8.6 Hz, 1 H, C*H*NH), 2.87 (dd, *J* = 2.0, 4.0 Hz, 1 H, epoxide O-side), 2.83 (dd, *J* = 2.0, 2.5 Hz, 1 H, epoxide N-side), 2.45 (s, 3 H, C$H_3$Ts), 2.1 (s, 3 H, C$H_3$C=O), 1.21 (d, *J* = 6.2 Hz, 3 H, C$H_3$ O-side), 1.10 (d, *J* = 6.0 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 170.2, 143.6, 137.9, 129.8, 126.9, 69.6, 58.3, 57.1, 48.1, 21.5, 21.1, 19.0, 16.5; MS *m*/*z* (relative intensity) 327 (M$^+$, 4), 312 (1), 198 (70), 155 (62), 129 (15), 91 (100), 65 (32).

**(2S*,3S*,4R*,5S*)-2-Acetoxy-3,4-epoxy-5-(tosylamido)hexane (11b)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 4.74 (dq, *J* = 6.0, 6.8 Hz, 1 H, C*H*OAc), 4.68 (d, *J* = 6.8 Hz, 1 H, N*H*), 3.15 (ddq, *J* = 6.0, 6.0, 6.8 Hz, 1 H, C*H*NH), 3.02 (dd, *J* = 2.0, 6.0 Hz, 1 H, epoxide O-side), 2.88 (dd, *J* = 2.0, 6.0 Hz, 1 H, epoxide N-side) 2.45 (s, 3 H, C$H_3$Ts), 2.1 (s, 3 H, C$H_3$C=O), 1.22 (d, *J* = 6.8 Hz, 3 H, C$H_3$ O-side), 1.10 (d, *J* = 6.0 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 170.3, 143.7, 137.4, 129.8, 127.1, 68.5, 58.9, 58.2, 49.9, 21.5, 21.1, 17.7, 16.0.

**Reference Sample of 11a.** Amido alcohol epoxide **9a** (20 mg), dicyclohexylcarbodiimide (20 mg), and 4-pyrrolidinopyridine (1 mg) were dissolved in dry THF (1 mL). Acetic acid (5 μL) was added and the solution stirred at room temperature for 8 h. After filtration, addition of water, extraction with diethyl ether, and flash chromatography (ether), a compound identical to **11a** was obtained as a colorless oil.

**Epoxidation of 6b (Method A). (2S*,3R*,4S*,5R*)-2-Acetoxy-3,4-epoxy-5-(tosylamido)hexane (12a)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 4.67 (dq, *J* = 6.7, 6.4 Hz, 1 H, C*H*OAc), 4.60 (d, *J* = 6.8 Hz, 1 H, N*H*), 3.18 (ddq, *J* = 6.8, 6.7, 6.0 Hz, 1 H, C*H*NH), 2.96 (dd, *J* = 2.0, 6.4 Hz, 1 H, epoxide O-side), 2.82 (dd, *J* = 2.0, 6.0 Hz, 1 H, epoxide N-side), 2.45 (s, 3 H, C$H_3$Ts), 2.05 (s, 3 H, C$H_3$C=O), 1.25 (d, *J* = 6.7 Hz, 3 H, C$H_3$ O-side), 1.11 (d, *J* = 6.7 Hz, 3 H, C$H_3$ N-side).

**(2S*,3S*,4R*,5R*)-2-Acetoxy-3,4-epoxy-5-(tosylamido)hexane (12b)**: $^1$H NMR δ 7.75 (AA′XX′, 2 H, Ts), 7.30 (AA′XX′, 2 H, Ts), 4.79 (dq, *J* = 6.7, 4.8 Hz, 1 H, C*H*OAc), 4.45 (d, *J* = 8.3 Hz, 1 H, N*H*), 3.61 (ddq, *J* = 8.3, 6.7, 5.0 Hz, 1 H, C*H*NH), 2.91 (dd, *J* = 2.3, 5.0 Hz, 1 H, epoxide N-side), 2.87 (dd, *J* = 2.3, 4.8 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts); 2.05 (s, 3 H, C$H_3$C=O), 1.20 (d, *J* = 6.7 Hz, 3 H, C$H_3$ O-side), 1.10 (d, *J* = 6.7 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR δ 170.2 (C=O), 143.5 (*p*-Ts), 137.9 (*ipso*-Ts), 129.7 (*m*-Ts), 127.0 (*o*-Ts), 68.5 (*C*HOAc), 58.9 (epoxide N-side), 56.4 (epoxide O-side), 48.3 (*C*HNH), 21.5

($CH_3$Ts), 21.0 (OAc), 19.0 ($CH_3$ N-side), 16.3 ($CH_3$ O-side).

**Epoxidation of 7a. (2*S**,3*R**,4*S**,5*S**)-2-[(*tert*-Butyldimethylsilyl)oxy]-3,4-epoxy-5-(tosylamido)hexane (13a):** $^1$H NMR $\delta$ 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 4.42 (d, $J$ = 8.3 Hz, 1 H, N*H*), 3.56 (m, 1 H, C*H*NH), and 3.55 (m, 1 H, C*H*OSi), 2.78 m, 1 H, epoxide O-side), 2.77 m, 1 H, epoxide N-side), 2.42 (s, 3 H, C$H_3$Ts), 1.13 (d, $J$ = 6.9 Hz, 3 H, C$H_3$ N-side), 1.10 (d, $J$ = 6.4 Hz, 3 H, C$H_3$ O-side), 0.87 (s, 9 H, *t*-BuSi), 0.05 and 0.03 (2s, 6 H, MeSi); $^{13}$C NMR $\delta$ 143.7, 138.0, 129.7, 126.9, 68.6, 60.2, 58.2, 48.8, 25.8, 21.5, 20.2, 19.1, 18.1, -4.7, -4.9. Anal. Calcd for $C_{19}H_{33}NSSiO_4$ (isomeric mixture of **13a** and **13b**): C, 57.14; H, 8.33; N, 3.51. Found: C, 57.1; H, 8.5; N, 3.7.

**(2*S**,3*S**,4*R**,5*S**)-2-[(*tert*-Butyldimethylsilyl)oxy]-3,4-epoxy-5-(tosylamido)hexane (13b):** $^1$H NMR $\delta$ 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 4.57 (d, $J$ = 6.8 Hz, 1 H, N*H*), 3.75 (dq, $J$ = 3.6, 6.4 Hz, 1 H, C*H*OSi), 3.32 (m, 1 H, C*H*NH), 2.86 (dd, $J$ = 2.3, 5.0 Hz, 1 H, epoxide O-side), 2.75 (dd, $J$ = 2.3, 3.7 Hz, 1 H, epoxide N-side), 2.42 (s, 3 H, C$H_3$Ts), 1.14 (d, $J$ = 6.4 Hz, 3 H, C$H_3$ O-side), 1.10 (d, $J$ = 6.7 Hz, 3 H, C$H_3$ N-side), 0.85 (s, 9 H, *t*-BuSi), 0.02 and 0.00 (2s, 6 H, MeSi); $^{13}$C NMR $\delta$ 143.5, 137.5, 129.8, 127.1, 69.3, 60.2, 57.4, 49.3, 25.7, 21.5, 20.5, 19.1, 17.5, -4.8, -4.9. Anal. Calcd for $C_{19}H_{33}NSSiO_4$ (isomeric mixture of **13a** and **13b**): C, 57.14; H, 8.33; N, 3.51. Found: C, 57.1; H, 8.5; N, 3.7.

**Reference Sample of 13a.** To amido alcohol epoxide **9a** (18.7 mg) and imidazole (8 mg) in dimethylformamide (0.2 mL) was added TBDMSCl (18 mg). The solution was stirred at ambient temperature for 6 h. Diethyl ether and brine (0.5 mL of each) were added, the aqueous phase was extracted once with ether, and the combined organic phases were washed (water) and dried ($Na_2SO_4$). After evaporation of the solvent, the remaining oil was purified by flash chromatography (ether). The product was identical to **13a**.

**Epoxidation of 7b. (2*S**,3*S**,4*R**,5*S**)-2-[(*tert*-Butyldimethylsilyl)oxy]-3,4-epoxy-5-(tosylamido)hexane (14a):** $^1$H NMR $\delta$ 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 5.11 (d, $J$ = 6.4 Hz, 1 H, N*H*), 3.50 (dq, $J$ = 6.7, 4.9 Hz, 1 H, C*H*OSi), 3.17 (ddq, $J$ = 5.0, 6.7, 6.4 Hz, 1 H, C*H*NH), 2.78 (dd, $J$ = 2.2, 5.0 Hz, 1 H, epoxide N-side), 2.66 (dd, $J$ = 2.2, 4.9 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts), 1.18 (d, $J$ = 6.7 Hz, 3 H, C$H_3$ O-side), 1.10 (d, $J$ = 6.7 Hz, 3 H, C$H_3$ N-side), 0.80 (s, 9 H, *t*-BuSi), 0.0 (s, 6 H, MeSi).

**(2*S**,3*R**,4*S**,5*S**)-2-[(*tert*-Butyldimethylsilyl)oxy]-3,4-epoxy-5-(tosylamido)hexane (14b):** $^1$H NMR $\delta$ 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 4.83 (d, $J$ = 8.0 Hz, 1 H, N*H*), 3.72 (dq, $J$ = 6.7, 4.9 Hz, 1 H, C*H*OSi), 3.50 (ddq, $J$ = 5.0, 6.7, 8.0 Hz, 1 H, C*H*NH), 2.78 (dd, $J$ = 2.2, 5.0 Hz, 1 H, epoxide N-side), 2.76 (dd, $J$ = 2.2, 4.9 Hz, 1 H, epoxide O-side), 2.45 (s, 3 H, C$H_3$Ts), 1.18 (d, $J$ = 6.7 Hz, 3 H, C$H_3$ N-side), 1.10 (d, $J$ = 6.7 Hz, 3 H, C$H_3$ O-side), 0.80 (s, 9 H, *t*-BuSi), 0.0 (s, 6 H, MeSi); $^{13}$C NMR $\delta$ 143.3 (*p*-Ts), 138.0 (*ipso*-Ts), 129.7 (*m*-Ts), 126.9 (*o*-Ts), 66.2 (*C*HOSi), 59.2 (epoxide O-side), 57.6 (epoxide N-side), 48.9 (*C*HNH), 25.7 ((C$H_3$)$_3$CSi), 21.5 (C$H_3$Ts), 20.6 (C$H_3$ O-side), 19.4 (C$H_3$ N-side), 18.1 ((CH$_3$)$_3$*C*Si), -4.8 (C$H_3$Si), -4.9 (C$H_3$Si).

**Epoxidation of 8. (2*S**,3*R**,4*S**,5*R**)-3,4-Epoxy-5-(*N*-methyltosylamido)hexan-2-ol (15a):** $^1$H NMR $\delta$ 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 4.08 (dq, $J$ = 4.7, 6.7 Hz, 1 H, C*H*NCH$_3$), 3.63 (ddq, $J$ = 4.7, 5.5, 6.5 Hz, 1 H, C*H*OH), 2.96 (dd, $J$ = 2.3, 4.7 Hz, 1 H, epoxide N-side), 2.72 (dd, $J$ = 2.3, 4.7 Hz, 1 H, epoxide O-side), 2.82 (s, 3 H, C$H_3$N), 2.42 (s, 3 H, C$H_3$Ts), 1.70 (d, $J$ = 5.5 Hz, 1 H, O*H*), 1.25 (d, $J$ = 6.5 Hz, 3 H, C$H_3$ O-side), 0.91 (d, $J$ = 6.7 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR: $\delta$ 143.4, 136.3, 129.8, 127.1, 66.8 (*C*HOH), 59.7 (epoxide O-side), 57.9 (epoxide N-side), 52.8 (*C*HN), 29.6 (C$H_3$N), 21.5 (C$H_3$Ts), 20.0 (C$H_3$ O-side), 12.0 (C$H_3$ N-side). Anal. Calcd for $C_{14}H_{21}NSO_4$ (isomeric mixture of **15a** and **15b**): C, 56.17; H, 7.07; N, 4.68. Found: C, 56.6; H, 7.3; N, 4.5.

**(2*S**,3*S**,4*R**,5*R**)-3,4-Epoxy-5-(*N*-methyltosylamido)-hexan-2-ol (15b):** $^1$H NMR $\delta$ 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 4.13 (dq, $J$ = 4.8, 7.0, 1 H, C*H*NCH$_3$), 3.98 (ddq, $J$ = 2.5, 3.1, 6.4 Hz, 1 H, C*H*OH), 3.02 (dd, $J$ = 2.1, 4.8 Hz, 1 H, epoxide N-side), 2.99 (dd, $J$ = 2.1, 2.5 Hz, 1 H, epoxide O-side), 2.78 (s, 3 H, C$H_3$N), 2.42 (s, 3 H, C$H_3$Ts), 1.79 (d, $J$ = 3.1 Hz, 1 H, O*H*), 1.24 (d, $J$ = 6.4 Hz, 3 H, C$H_3$ O-side), 1.04 (d, $J$ = 7.0 Hz, 3 H, C$H_3$ N-side); $^{13}$C NMR $\delta$ 143.3, 136.6, 129.6, 127.2, 64.4 (*C*HOH), 59.6 (epoxide O-side), 55.7 (epoxide N-side), 52.6 (*C*HN), 29.5 (C$H_3$N), 21.5 (C$H_3$Ts), 18.7 (C$H_3$ O-side), 13.8 (C$H_3$ N-side); MS $m/z$ (relative intensity) 299 ($M^+$, 3), 281 (1), 212 (100), 155 (21), 91 (23). Anal. Calcd for $C_{14}H_{21}NSO_4$ (isomeric mixture of **15a** and **15b**): C, 56.17; H, 7.07; N, 4.68. Found: C, 56.6; H, 7.3; N, 4.5.

**Reference Sample of 15a.** To a solution of amido alcohol epoxide **10a** (18 mg) in acetone (1.5 mL) were added $K_2CO_3$ (81 mg) and MeI (0.20 mL). The mixture was refluxed at 40 °C for 20 h. The acetone was removed in vacuo, and then water (2 mL) and ether were added. The water phase was extracted twice with ether, and the combined organic layers were washed with brine. After drying ($MgSO_4$) and concentration in vacuo, a colorless oil was obtained. This compound was identical to the product from the epoxidation of **8** assigned as **15a**.

**Cinnamyl Alcohol Epoxide (16).**[12b] The epoxide was synthesized from the corresponding alcohol according to method A: $^1$H NMR $\delta$ 7.30 (m, 5 H, Ph), 4.03 (dd, $J$ = 12.8, 2.4 Hz, 1 H, *H*-1), 3.92 (d, $J$ = 2.1 Hz, 1 H, *H*-3), 3.78 (dd, $J$ = 12.8, 3.9 Hz, 1 H, *H*-1), 3.15 (ddd, $J$ = 3.9, 2.4, 2.1 Hz, 1 H, *H*-2); $^{13}$C NMR $\delta$ 136.6, 128.4, 128.2, 125.6, 62.5 (C-2), 61.2 (C-1), 55.6 (C-3).

**2,3-Epoxy-1-butanol (17).** The epoxide was synthesized according to ref 35: $^1$H NMR $\delta$ 3.79 (dd, $J$ = 12.5, 2.6 Hz, 1 H, $CH_2$), 3.49 (dd, $J$ = 12.5, 4.5 Hz, 1 H, $CH_2$), 2.92 (dt, $J$ = 5.3, 2.5 Hz, 1 H, $CH_3CH_{epoxy}$), 2.78 (ddd, $J$ = 4.5, 2.6, 2.5 Hz, $CH_2CH_{epoxy}$), 1.34 (d, $J$ = 5.3, 3 H, $CH_3$); $^{13}$C NMR $\delta$ 61.6 (C-1), 59.6 (C-2), 52.0 (C-3), 17.1 (C-4).

**3,4-Epoxy-2-pentanol (18).** The epoxide was synthesized according to ref 41.

**Syn Isomer 18a.** Spectral data are in accord with those reported in ref 41: $^1$H NMR $\delta$ 3.62 (m, 1 H, CHOH), 2.98 (dq, $J$ = 2.3, 5.3 Hz, 1 H, $CH_3CH_{epoxy}$), 2.68 (dd, $J$ = 2.3, 5.2 Hz, 1 H, CH(OH)CH), 2.10 (bd, $J$ = 5.6 Hz, 1 H, OH), 1.32 (d, $J$ = 5.3 Hz, 3 H, $CH_3$), 1.27 (d, $J$ = 6.5 Hz, 3 H, $CH_3$CH(OH)); $^{13}$C NMR $\delta$ 67.4 (C-2), 52.8 (C-4), 63.5 (C-3), 19.6 (C-1), 17.0 (C-5).

**Anti Isomer 18b.** Spectral data are in accord with those reported in ref 41: $^1$H NMR $\delta$ 3.91 (m, 1 H, CHOH), 3.06 (dq, $J$ = 5.3, 2.3 Hz, 1 H, $CH_3CH_{epoxy}$), 2.73 (dd, $J$ = 3.3, 2.3 Hz, 1 H, CH(OH)CH), 2.01 (d, $J$ = 2.4 Hz, OH), 1.33 (d, $J$ = 5.3 Hz, 3 H, $CH_3$CH), 1.24 (d, $J$ = 6.4 Hz, 3 H, $CH_3$CH(OH)); $^{13}$C NMR $\delta$ 64.9 (C-2), 51.0 (C-4), 62.5 (C-3), 18.5 (C-1), 17.0 (C-5).

***p*-Nitrobenzoyl Ester of Epoxy Alcohol 9a (19).** The epoxy alcohol **9a** was dissolved in $CH_2Cl_2$ and cooled to 0 °C. Triethylamine (1.2 equiv) and *p*-nitrobenzoyl chloride (1 equiv) were added, and the mixture was stirred at 0 °C for 24 h. The organic layer was washed with aqueous $NaHCO_3$ and brine and dried ($Na_2SO_4$). After concentration the crude product was purified by recrystallization (diethyl ether): $^1$H NMR $\delta$ 8.30 (AA'XX', 2 H, $PhNO_2$), 8.21 (AA'XX', 2 H, *Ph*-$NO_2$), 7.75 (AA'XX', 2 H, Ts), 7.30 (AA'XX', 2 H, Ts), 5.02 (dq, $J$ = 6.2, 6.6 Hz, 1 H, C*H*O), 4.34 (d, $J$ = 8.7 Hz, 1 H, N*H*), 3.70 (ddq, $J$ = 2.2, 7.0, 8.7 Hz, 1 H, C*H*NH), 3.25 (dd, $J$ = 2.0, 6.2 Hz, 1 H, epoxide O-side), 2.93 (dd, $J$ = 2.0, 2.2 Hz, epoxide N-side), 2.43 (s, 1 H, C$H_3$Ts), 1.42 (d, $J$ = 6.6 Hz, C$H_3$ O-side), 1.12 (d, $J$ = 7.0 Hz, C$H_3$ N-side); $^{13}$C NMR $\delta$ 163.8, 157.4, 143.7, 137.8, 135.3, 130.8, 129.8, 126.9, 123.6, 71.8, 58.6, 57.0, 47.9, 21.5, 18.9, 16.7.

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**Supplementary Material Available:** Interatomic distances in cinnamyl alcohol epoxide **16**, rotamer energies and populations of epoxy alcohols, and $^1$H NMR spectra for compounds **8**, **12b**, **14b**, and **19** (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(41) Whalen, D. L.; Brown, S.; Ross, A. M.; Russell, H. M. *J. Org. Chem.* **1978**, *43*, 428.