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ASYMMETRIC OXIDATION OF OLEFINS TO VICINAL DIOLS WITH OSMIUM TETROXIDE

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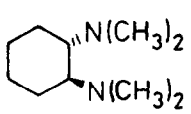
Summary: High levels of asymmetry can be achieved in the osmium tetroxide cis-hydroxylation of olefins by employing (-)-(R,R)-N,N,N',N'-tetramethylcyclohexane-1,2-*trans*-diamine as a chiral ligand for the osmium.

Osmium tetroxide oxidation of olefins is an excellent method for forming vicinal diols under mild conditions with a minimum of side reactions.[1] The oxidation can be carried out under both catalytic and stoichiometric conditions, with a nitrogenous base, usually pyridine, added to accelerate the reaction.[2] Facial selectivity in the approach of the osmium to the olefinic π-system can be directed by steric factors,[3] or by interactions between a heteroatom and the π-system of the double bond. Thus, oxidation occurs on the face opposite an allylic, non-acylated oxygen,[4] but can be facially guided in a *syn*-approach by prior coordination between the osmium and a remote nitrogen[5] or sulfur.[6]

Sharpless and coworkers have demonstrated that a high degree of enantioselectivity can be achieved if a chiral alkaloid is used as the nitrogenous ligand.[7] Enantiomeric excesses of 89.7% were reported using dihydroquinidine acetate. The use of a chiral alcohol as an auxiliary in the oxidation of tiglate esters has also enabled high levels of asymmetry to be achieved.[8] With the recent appearance in the literature of a report concerning the use of chiral diamines derived from tartaric acid as asymmetry inducing ligands in this oxidation,[9] we are now presenting our preliminary studies which complement these results.



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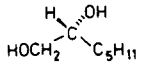
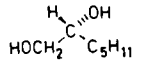
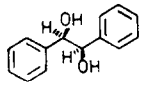
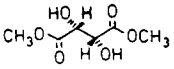
While any chiral amine which functions as an osmium ligand can theoretically lead to asymmetric induction, we anticipated that ligands capable of chelation would yield the highest degree of asymmetric induction. We now report a high enantiomeric excess using the readily available (-)-(R,R)-N,N,N',N',-tetramethylcyclohexane-1,2-diamine, 1.[10]

The oxidation of 1-heptene with OsO_4 (1.1 equiv.) in the presence of 1 yielded (R)-1,2-heptanediol (86% enantiomeric excess) in 75% isolated yield (room temperature, 2 hrs). Cooling to -35°C had led to a slight decrease in the e.e., Table 1. In sharp contrast, the oxidation of *trans*-stilbene was noticeably slower, and proceeded with lower optical yield (34% e.e.), while chalcone did not undergo any oxidation in 3 days under comparable conditions.

Table 1. Asymmetric Osmium Tetroxide Oxidation of Olefins[a]

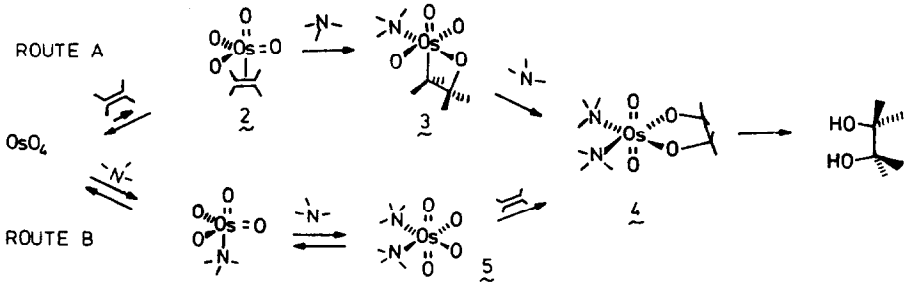
Olefin	Time	Product	Yield(%)[b]	e.e.(%)[c]
1-heptene	2 hrs		75	86 (+)-(2R)
1-heptene[d]	6 hrs		59	79 (+)-(2R)
trans-stilbene	24 hrs		69[e]	34 (+)-(1R,2R)
dimethylfumarate	2 hrs		59[f]	48 (+)-(2R,3R)
1-methylcyclohexene	5 hrs		71	66 (+)-(1S,2R)
chalcone	3 days	no reaction, 100% recovered chalcone[g]	0	--

a) All reactions were run in CH_2Cl_2, using 1.1 equiv. of OsO_4, room temperature unless otherwise noted. All reported values of yield and e.e are the average of two experiments.
b) Isolated yields of diols.
c) Dominant enantiomer is given in parentheses. Enantiomeric excesses (e.e.) were calculated from the observed optical rotations based on reported values of $[\alpha]_D$ in the literature.[11]
d) Reaction run at -35°C.
e) Recovered starting material: 29%.
f) Recovered starting material: 34%.
g) Using a 10-fold excess of chalcone, < 10% diol product could be isolated after 3 days at room temperature with 88% recovered starting material.

The observed enantioselectivity can be rationalized by either the [3+2]-cycloaddition mechanism,[12] or the mechanism recently proposed by Sharpless and Hentges,[7] Figure 1, Routes A and B, respectively. According to the Sharpless mechanism, reversible, nucleophilic coordinations of the olefin and the amine compete for the coordinatively unsaturated, electrophilic osmium tetroxide. The osmium-olefin complex 2 undergoes nucleophilic addition of the amine to form the organometallic intermediate, 3, which rapidly adds the second nucleophilic amino group to form the well known osmate ester, 4.[13]

Asymmetric induction results from steric differentiation of the enantiomeric olefin-osmium complexes, 2a and 2b, by the approach of the chiral amine, Figure 2. The greater

Figure 1.



steric interactions in the approach of 1 to the complex 2b results in the greater production of (R)-1,2-heptanediol. The successful induction of asymmetry using the diamine 1, which is sterically quite small compared to dihydroquinidine acetate, could be a consequence of a significant degree of chelation in the transition state of the nucleophilic addition of 1 to the complex 2. This chelation would increase the degree of steric interaction by increasing the effective size of the approaching nucleophilic moiety.

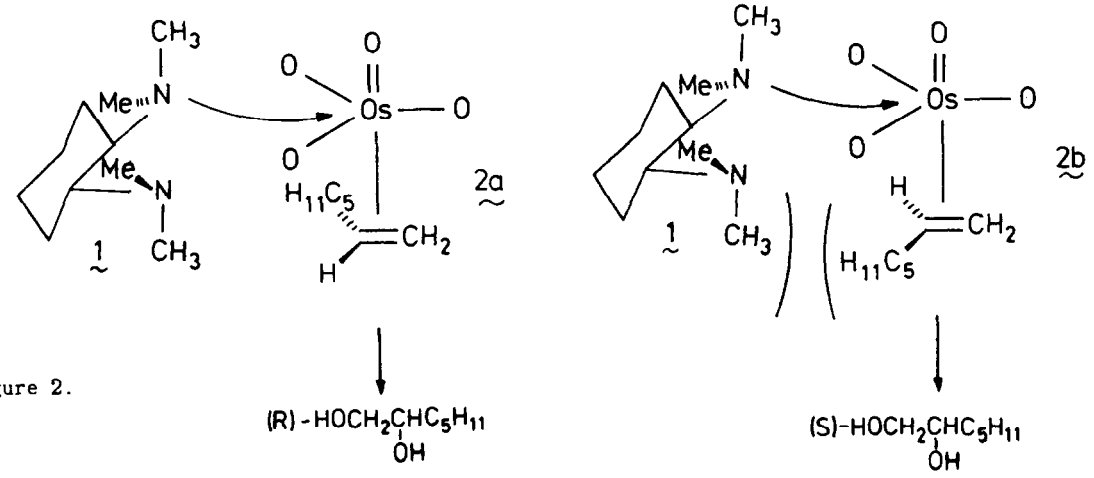


Figure 2.

According to the [3+2]-cycloaddition[12] pathway, facial selectivity in the addition of the osmium tetroxide to the olefin would be established by steric interactions between the methyl groups on the nitrogen and the double bond substituents which occur across the osmium plane, analogous to the use of diamine derivatives as chiral ligands in asymmetric reductions.[14] The N-methyl groups adopt axial or equatorial type orientations dependent upon specific rotamer stability viewing down the C-N bond. Steric interactions between the axial type methyl group on the ligand and the double bond substituent, 5b, would hinder the approach of the coordinated osmium complex relative to the approach in 5a, Figure 3. A stereochemical outcome identical to that predicted by the Sharpless mechanism would be anticipated, and is in agreement with the observed dominant chirality of the products. Consequently, neither one of the two proposed pathways for the osmium tetroxide hydroxylation of olefins can be ruled out by our results.

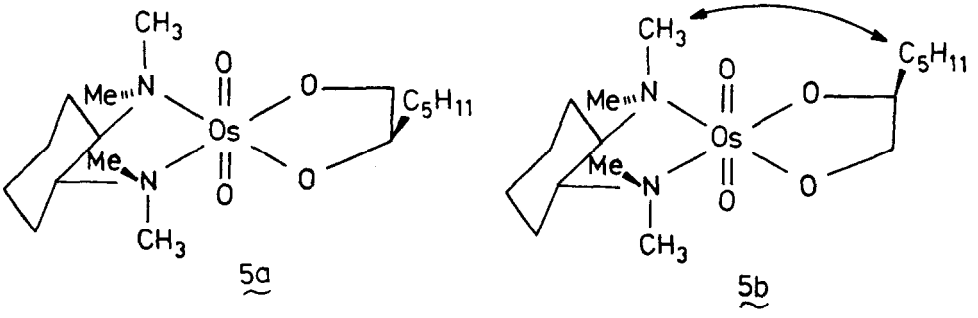


Figure 3.

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