

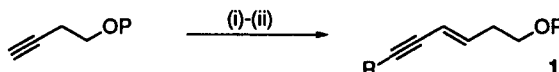
Asymmetric Dihydroxylation of Homoallylic Enynols

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Abstract: The presence of the *p*-methoxyphenyl protecting group enables the asymmetric dihydroxylation of homoallylic enynols to be carried out in good yield and with high levels of enantioselectivity. © 1997 Elsevier Science Ltd.

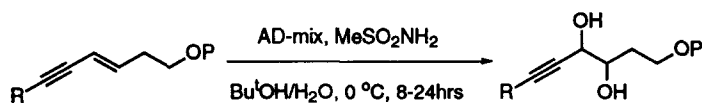
The asymmetric dihydroxylation (AD) of alkenes is an extremely well-established transformation which generally proceeds in good to excellent yields with predictable and high levels of asymmetric induction. Numerous classes of alkenes have been shown to participate in this type of transformation and the procedures developed by the Sharpless group using the commercially available AD-mixes are now generally accepted as the method of choice for this type of transformation.¹ As part of an ongoing programme of research directed toward the synthesis of natural and unnatural enediynes² we identified the asymmetric dihydroxylation of homoallylic enynols as an appropriate tactic for our synthetic requirements. We were surprised to find that AD of this important class of compound had not previously been reported and the feasibility of such a process was in doubt, as AD of enynes had been reported in moderate to good yields but with variable levels of enantioselectivity.³ We herein present the results of a preliminary study of the asymmetric dihydroxylation of homoallylic enynols **1**. These can be most readily prepared using the sequence described in scheme 1. The use of the Schwartz reagent is essential for obtaining products in high yields and with good levels of stereoselectivity;⁴ a related stannane approach (Bu₃SnH, AIBN, then I₂) can be used but leads to reduced yields (c.a. 50%) and tedious separation problems.



Scheme 1: (i) Cp₂ZrCl₂ LiBH(Et)₃, THF, r.t. then I₂, (70%); (ii) Pd(0), RCCH, PrNH₂, CuI, r.t. (78%)

The results of a range of dihydroxylation experiments are shown in table 1; these results highlight the importance of the protecting group on the efficiency of the transformation. The isolated yields of the oxidation reactions using a range of standard protecting groups were poor to moderate, even with extended reaction times (several days) and with addition of further catalyst and/or methanesulfonamide. In an attempt to improve the yields we elected to use the *p*-methoxyphenyl group (PMP) which dramatically improves the enantioselectivities obtained with AD reactions of certain alcohol derivatives.⁵ We found that these reactions were generally more efficient and proceeded with much improved isolated yields (entries 10-12). HPLC analysis of the PMP derivatives indicate an optical purity of 88-97% ee (Chiracel OD-H, 30% IPA in Hexanes).

Table 1: Reaction of Homoallylic Alcohol Derivatives with AD-mixes



Entry	R	P	Yield AD-mix α	Yield AD-mix β
1	TMS	H	0	-
2	TMS	Ac	31	28
3	TMS	TIPS	38	32
4	TMS	TBS	47	44
5	TMS	TBDPS	30	24
6	H	H	0	-
7	H	Ac	11	12
8	H	TIPS	36	42
9	H	TBDPS	43	35
10 ^a	TMS	PMP	>85	86
11 ^a	H	PMP	84	91
12 ^b	Ph	PMP	87	95

*HPLC analysis indicates a minimum enantiomeric excess of ^a95%; ^b88%

We have shown that asymmetric dihydroxylation of homoallylic enynols is sensitive to the hydroxyl-protecting group used. The majority of commonly employed groups result in slow reactions which lead to poor yields of products even over extended reaction times. The use of the PMP group for substrates incorporating terminal and substituted enynes improves the yields and leads to products with a high degree of optical purity.⁶ The derived products have some obvious potential for organic synthesis.

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References and Notes

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- 6 The PMP group can be removed in good yield (CAN, MeOH/H₂O, 0 °C, c.a. 70%). All compounds exhibited satisfactory spectroscopic data.

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