



## Diastereoselectivity in the dihydroxylation of isopropenyl substituted three-membered rings

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## Abstract

The diastereoselectivity of the dihydroxylation of isopropenylcyclopropanes, oxiranes and aziridines has been investigated. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: cyclopropanes; oxiranes; aziridines; dihydroxylation.

The stereoselective preparation of organic compounds containing cyclopropanes, oxiranes or aziridines is of great interest due to the versatile reactivity of these strained three-membered rings. The control of the relative configuration between these three-membered rings and their adjacent stereocenters usually involves one of two strategies consisting of either a substrate directed cyclopropanation, epoxidation or aziridination, or the chemical transformation of a prochiral group directly attached to the ring, as illustrated by nucleophilic additions onto cyclopropyl, oxiranyl and aziridinylcarbonyl derivatives. However, the diastereoselectivity of electrophilic reactions of the corresponding alkenyl derivatives has received much less attention.

Recently, we have reported that the hydroboration of *cis*-substituted isopropenylcyclopropanes proceeded with a high degree of stereocontrol. In continuation of our studies on developing diastereoselective synthetic transformations of alkenyl substituted three-membered rings, the dihydroxylation reaction was investigated (Scheme 1).

Scheme 1. Dihydroxylation of alkenyl substituted three-membered rings

Alkenylcyclopropanes,<sup>4</sup> oxiranes<sup>5</sup> and aziridines<sup>6</sup> were synthesized and subjected to an osmium tetroxide catalyzed dihydroxylation (Table 1).<sup>7</sup>

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Table 1
Dihydroxylation of alkenyl substituted three-membered rings

Substrate	Product(s)		d.r.*	Yield
H. A.H	HO Me			
1 X= CH <sub>2</sub> R= CH <sub>2</sub> OTBDPS	10a	10b	≥ 96/4	72%
2 X= CH <sub>2</sub> R= Th	11a	11b	93/7	85%
OAc 3 X= O R= (CH <sub>2</sub> ) <sub>2</sub> Ph	12a	12b	96/4	95%
4 X= NTs R= <i>i</i> -Pr	13a	13b	82/18	86%
TBSO H., A.H OTBDPS	TBSO HO H.	≥ 96/4	90%	
TBSO 5 H. A H OTBDPS	HO MA	<b>∆</b> .H <sub>OTBDPS</sub>	≥ 96/4	93%
OTBDPS	HO Me	OTBDPS H 16	50/50	91%
H.A.H R	ŏн	HOOH R		
8 X= CH <sub>2</sub> R= CH <sub>2</sub> OTBDPS	17a	17b	55/45	90%
9 X= O R= $(CH_2)_2$ Ph	18a	18b	50/50	85%

<sup>\*</sup> Diastereoisomeric ratio estimated from the <sup>1</sup>H NMR spectrum of the crude product

Under these conditions, high levels of diastereoselectivity were observed for cisisopropenylcyclopropane 1 (d.r. $\geq$ 96/4). Cyclopropane 2, bearing an adjacent stereocenter, was also dihydroxylated with a synthetically useful level of diastereoselectivity. The dihydroxylation of the isopropenyloxirane 3 also proceeded with a high degree of stereocontrol, whereas the diastereomeric ratio was lower in the case of the cis-isopropenylaziridine 4. Whatever the olefinic configuration, the trisubstituted alkenylcyclopropanes 5 and 6 underwent a highly diastereoselective reaction. In contrast, little or no diastereoselectivity was observed in the dihydroxylation of either trans-isopropenylcyclopropane 7 or cis-vinylcyclopropane 8 and oxirane 9.

The relative configuration of 10a and 12a was established by a chemical correlation starting, respectively, from 17a,b and 18a,b. The primary alcohol function of the latter compounds was first protected as a silyl ether and the secondary hydroxyl was subsequently oxidized with PCC to give, respectively, the corresponding ketones. Condensation with MeMgBr proceeded in a highly diastereoselective fashion (d.r.≥96/4) to give the corresponding tertiary alcohols 19 and 20, whose relative configuration was attributed on the basis of the known sense of nucleophilic additions onto oxiranyl and cyclopropylketones.<sup>3</sup> The establishment of the relative configuration of 10a and 12a was thus straightforward, since protection of their primary alcohol function as a silyl ether also gave the tertiary alcohols 19 and 20, respectively (Scheme 2). The relative configuration of the other compounds was assumed to be similar by analogy with this result.

Scheme 2. Correlation of configuration for 10a and 12a

The results obtained during the course of this study clearly demonstrate that hydroboration and dihydroxylation of cis-isopropenyl substituted three-membered rings occur on the same face of the prochiral alkene moiety. Although the ground state and the reactive conformer are not necessarily the same, the ground state conformation of various olefinic molecules bearing the propene moiety plays an important role in the stereochemical outcome of  $\pi$ -facial selectivity. We initially suggested that electrophilic additions onto alkenylcyclopropanes could occur on the more reactive bissected conformer, in which overlap between the cyclopropane  $\pi$ -system and the alkene is supposed to be maximal. However, in light of these new results indicating a closely related behaviour of all the cis-isopropenyl substituted three-membered rings, another plausible explanation of the uniform diastereoselectivity of these processes would be to consider that the electrophilic additions are occurring on the less-crowded face of the olefin in the *gauche* conformation (Scheme 3), which has been shown, in the case of isopropenyloxiranes and HNMR spectroscopic analyses. It is thus clear that the lack of steric interactions in the case of cis-vinyl or trans-isopropenyl substituted three-membered rings results in stereorandom reactions.

Ritrans
Rcis

Rois

Rois

Rois

Ritrans

Ritrans

Ritrans

Ritrans

Ritrans

Ritrans

Rcis

major side of electrophilic attack

$$(E^+=OsO_4)$$
 $(E^+=R_2BH)$ 

Scheme 3. Gauche conformation of isopropenyl substituted three-membered rings

We have thus shown that dihydroxylation of *cis*-isopropenyl substituted cyclopropanes, oxiranes and aziridines proceeds with good to excellent levels of diastereoselectivity. Since these compounds can undergo a variety of ring-opening reactions, the present methodology should find useful applications in the stereocontrolled synthesis of acyclic chiral building blocks.

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