

CONVENIENT SYNTHESIS OF CHIRAL EPOXYISOPRENOIDS BY YEAST REDUCTION

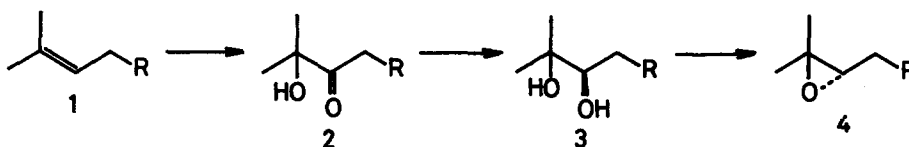
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Abstract The terminal double bond of acyclic isoprenoids was converted into chiral epoxide in high optical yield by using asymmetric reduction of α -ketol with baker's yeast.

Acyclic isoprenoids with epoxide ring at the terminal position have been used widely as a synthetic intermediate of terpenoids. The representative example is the synthesis of various polycyclic terpenoids based on the biomimetic cyclization¹⁾ and of macrocyclic terpenoids by the intramolecular cyclization of epoxysulfides.²⁾ In these syntheses, however, racemic epoxides have been used usually and synthetic studies of terpenoids starting from chiral epoxyisoprenoids were quite limited.³⁾ While the chiral epoxidation of allylic alcohols has been established,⁴⁾ generally applicable method for the conversion of double bond to chiral epoxide without any assistance of neighboring hetero-atoms has not yet been explored.⁵⁾

In this communication we wish to report a simple method for the transformation of terminal double bond of acyclic isoprenoids to chiral epoxide. The key step in the present method is the asymmetric reduction of prochiral α -ketols of type 2 with baker's yeast as shown in the following general scheme.



The substrates, α -ketols, were readily available by the following sequence. Thus, the terminal double bond of acyclic isoprenoids 1 was first epoxidized (mCPBA or NBS then K_2CO_3) and the epoxides were hydrolyzed with acid to the racemic diols which were oxidized to the α -ketols 2 by Swern's method. The ketols 2 thus obtained were treated with baker's yeast in water-ethanol (10:1) containing glucose at room temperature for 2-3 days. The chiral diols can be obtained by simple chromatography after filtration through celite and extraction (EtOAc). In all cases examined, the newly formed chiral center was found to have (*R*)-configuration. The chiral diols thus obtained was converted to (*S*)-epoxides through mesylates. The results were summarized in the Table. The α -ketols corresponding to mono- and sesquiterpenoids were reduced in high chemical and optical yields irrespective of the other terminal functionalities. However, the

Table

Substrates 2 R =	Diols 3			Epoxides 4	
	Yields	$[\alpha]_D$ (lit.)	Conf. ^a	Yields	% ee ^b
	96.5%	+26.8° (+25.1°) ^{5c)}	<u>R</u>	66.2%	>95
	78.1%	+19.2°	<u>R</u>	75.0%	>95
	75.2%	+30.1°	<u>R</u>	62.8%	>95
	89.1%	+34.8°	<u>R</u>	52.9% ^c	>95
	68.6%	+21.3°	<u>R</u>	89.7%	>95
	77.9 %	+20.2° + 3.3° (+1.3°) ^{5b)}	<u>R</u>	61.5%	>95
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^aDetermined by the CD spectra in the presence of $\text{Eu}(\text{fod})_3$. ^bDetermined by the ^1H NMR spectra (400 MHz) in the presence of $\text{Eu}(\text{hfc})_3$. No signals due to the corresponding enantiomer have been detected in each case.

^cThe low yield is due to the instability of the product.

long chain bis-ketol derived from squalene did not undergo any reduction under the conditions. These results revealed that the present method can be applied to the acyclic olefins having various type of functional groups and the synthesis of optically active terpenoids using the enantio-selective reduction is under proceeding.

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References

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