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KATSUKI-SHARPLESS ASYMMETRIC EPOXIDATION OF ALLYLIC-HOMOALLYLIC ALCOHOLS SHARING THE CENTRAL OLEFINIC BOND

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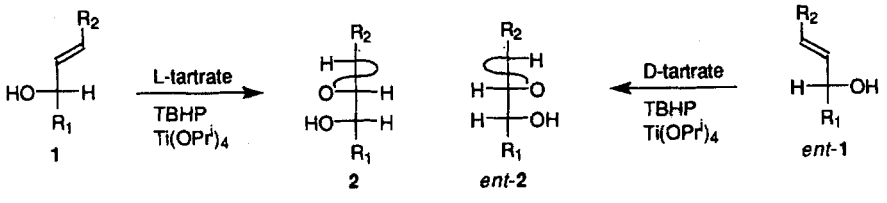
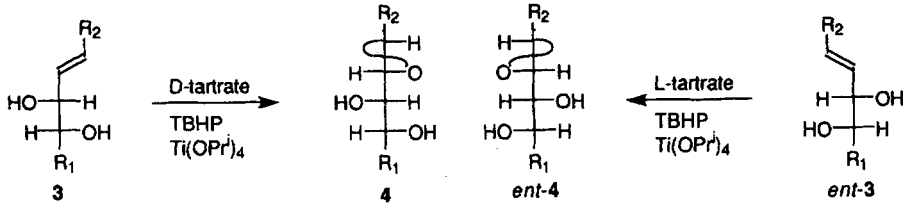
Summary: Katsuki-Sharpless asymmetric epoxidation of four isomeric chiral allylic-homoallylic diols sharing the central olefinic bond has been examined. Among these, three heptenediols having (3*E*,2*R*,6*R*), (3*E*,2*R*,6*S*), and (3*Z*,2*R*,6*R*) configurations underwent diastereospecific epoxidation to give the corresponding epoxides each as a single epimer in the presence of L-DIPT, but the diol having (3*Z*,2*R*,6*S*) configuration did not show high diastereoselection in the presence of either L- or D-DIPT. Interestingly, (3*Z*,2*R*,6*R*)-diol afforded the same epoxide irrespective of the chirality of DIPT used.

Stereochemistry of the Katsuki-Sharpless epoxidation of allylic alcohols is empirically well-established to furnish always *erythro*-epoxides† in preference to *threo*-counterparts[1] (**Scheme 1**). We have recently discovered that this stereochemical relationship was totally inverted when the substrates having allylic and homoallylic hydroxy groups on the same side of olefinic bond were subjected to the same oxidation conditions. Thus, the reaction proceeded only in the presence of the tartrate having mismatching stereochemistry for the simple allylic alcohols to give rise to the *threo*-epoxides exclusively[2] (**Scheme 2**). Intrigued with this finding, we examined the same reaction using four isomeric heptenediols having the olefinic bond between allylic and homoallylic hydroxy groups, and, here, disclose our new findings in this letter.

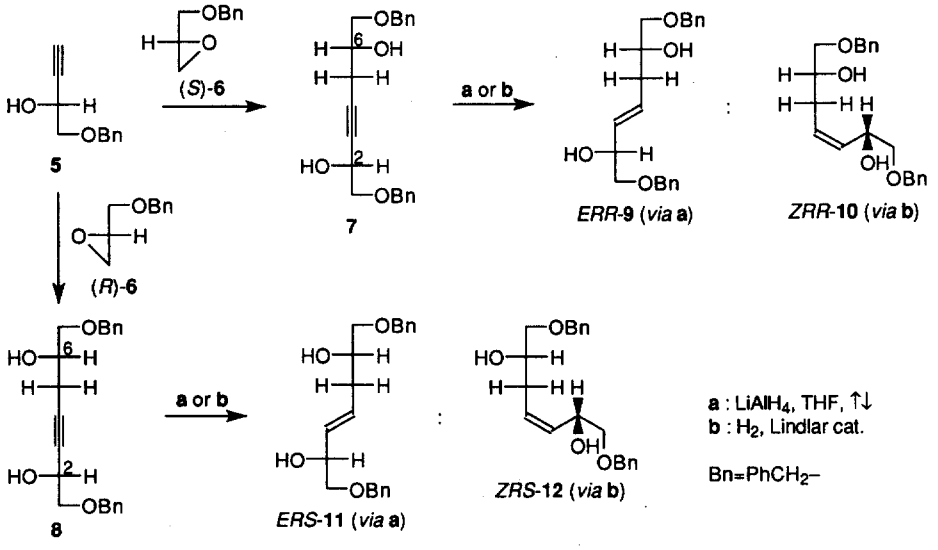


Scheme 1



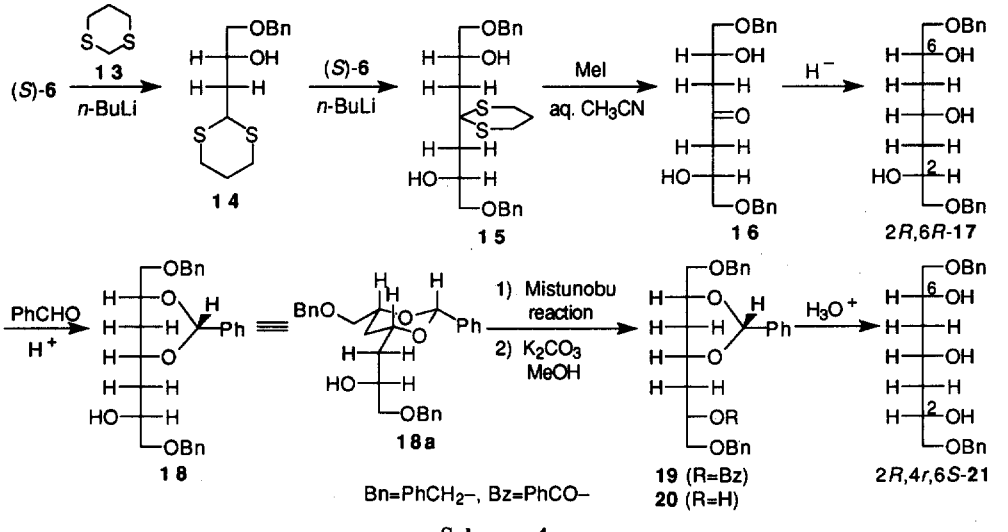
Scheme 2

Condensation of the terminal acetylene[3] (**5**) with (*S*)-*O*-benzylglycidol[4] [(*S*)-**6**] gave the ynediol (**7**) which was transformed into (*E*,2*R*,6*R*)-diol (*ERR*-**9**) on reduction with lithium aluminum hydride[5] and (*Z*,2*R*,6*R*)-diol (*ZRR*-**10**) on hydrogenation with Lindlar catalyst, both in excellent yields. Similarly, the diastereomeric (*E*,2*R*,6*S*)-diol (*ERS*-**11**) and (*Z*,2*R*,6*S*)-diol (*ZRS*-**12**) were prepared in excellent overall yields from **5** and (*R*)-*O*-benzylglycidol[4] [(*R*)-**6**] *via* the ynediol (**8**) (**Scheme 3**).



Scheme 3

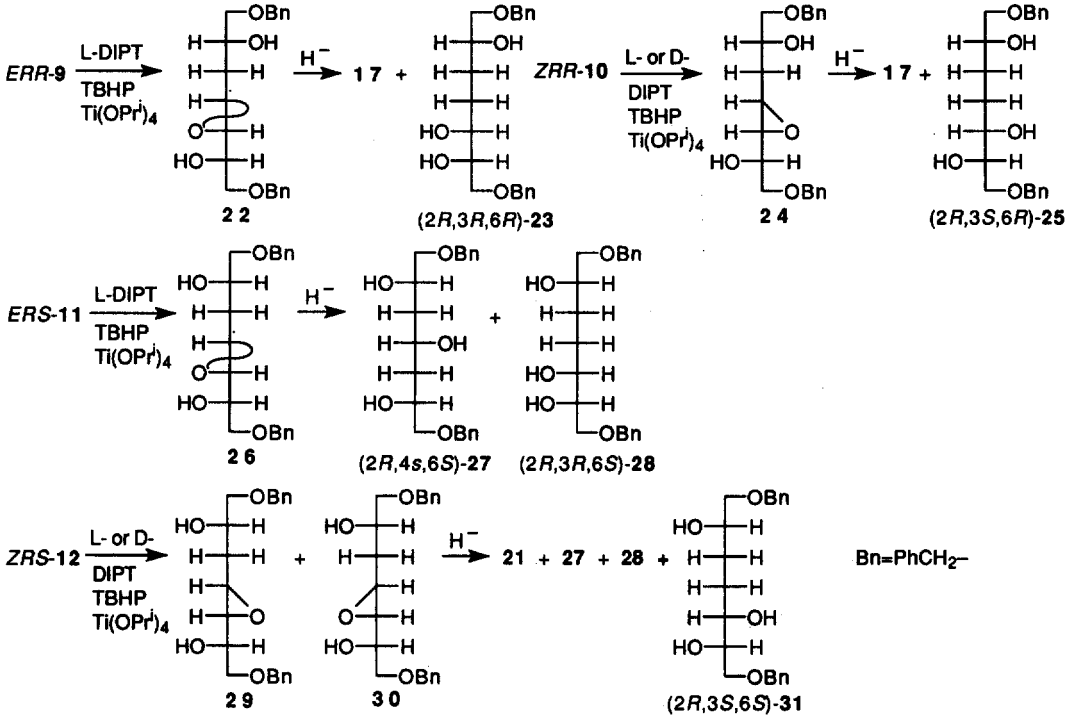
On the other hand, two reference compounds, (2*R*,6*R*)-2,4,6-triol (**17**) and *meso*-(2*R*,4*r*,6*S*)-2,4,6-triol (**21**), were prepared from (*S*)-*O*-benzylglycidol [(*S*)-**6**]. Thus, double condensation of two molar equivalents of (*S*)-**6** with 1,3-dithiane[6] afforded the C_2-symmetric diol (**15**) which on hydrolysis[7] followed by hydride reduction afforded (2*R*,6*R*)-2,4,6-triol (**17**). Upon acid-catalyzed reaction with benzaldehyde, **17** generated the 1,3-dioxane (**18**) having all equatrial substituents (**18a**), selectively, whose secondary hydroxy group was then inverted by Mitsunobu reaction[8] to give the epimeric alcohol (**20**) *via* the benzoate (**19**). Finally acid hydrolysis of **20** yielded the *meso*-(2*R*,4*r*,6*S*)-2,4,6-triol (**21**) (**Scheme 4**).



Scheme 4

Having obtained the reference compounds, four substrates were oxidized respectively with 1.5 equivalent of *tert*-butyl hydroperoxide (TBHP) in the presence of 1.2 equivalent of L- or D-diisopropyl tartrate (DIPT), 1.1 equivalent of titanium tetraisopropoxide, and powdered 4 Å molecular sieves and the epoxides obtained were reduced with bis(2-methoxyethoxy)aluminum hydride[9] to give the corresponding triols. As shown three of four diols underwent diastereoselective epoxidation in the presence of L-DIPT to give rise to the corresponding epoxides each as a single epimer. High diastereoselection, however, was not observed in *ZRS*-diol (**12**) with both DIPT. Interestingly, *ZRR*-**10** afforded the same epoxide (**24**) selectively as a single product even in the presence of enantiomeric D-DIPT.

Although the hydride reduction of the epoxides did not proceed in a regioselective fashion,[9] comparison of the products with the reference compounds allowed unambiguous stereochemical assignment.[10] Thus, the epoxide (**22**) obtained from *ERR*-**9** gave (*R*,*R*)-2,4,6-triol (**17**) accompanied by (*R*,*R*,*R*)-2,3,6-triol (**23**), the former of which was identical with the reference material (**17**) indicating that the precursor epoxide (**22**) should have *erythro*-configuration. On the same reduction, since the epoxide (**26**) obtained from *ERS*-**11** did not generate the *meso*-(*R*,*r*,*S*)-2,4,6-triol (**21**), the product was assigned as the isomeric *meso*-(*R*,*s*,*S*)-2,4,6-triol (**27**) and, therefore, the stereochemistry of the precursor epoxide (**26**) was deduced to have *erythro*-configuration. The epoxide (**24**) obtained from *ZRR*-**10** afforded (*R*,*R*)-2,4,6-triol (**17**) and (*R*,*S*,*R*)-2,3,6-triol (**25**) indicating that the precursor epoxide (**24**) should have *threo*-configuration. *ZRS*-Diol (**12**) gave an inseparable mixture of two epoxides **29** and **30** with both L- and D-DIPT. However, the mixture gave four separable products, *meso*-(*R*,*r*,*S*)- and *meso*-(*R*,*s*,*S*)-triols, (**21**) and (**27**), and (*R*,*R*,*S*)- and (*R*,*S*,*S*)-2,3,6-triols, (**28**) and (**31**), indicating unambiguously that the starting mixture consisted of *threo*-(**29**) and *erythro*-(**30**) epoxides (**Scheme 5** and Table 1).



Scheme 5

Table 1: Katsuki-Sharpless oxidation of the substrates and reductive cleavage of the products

substrate	DIPT	product	ratio	(%)	triol 2,4,6-	triol 2,3,6-	ratio	(%)
9	L	**22**	exclusive	82	**17**	**23**	4 : 1	80[a]
	D	**22** + *threo*	1 : 1.3	54[a]				
10	L	**24**	exclusive	70	**17**	**25**	1 : 17	90[a]
	D	**24**	exclusive	70				
11	L	**26**	exclusive	89	**27**	**28**	2.8 : 1	72[a]
	D	**26** + *threo*	1.3 : 1	54[a]				
12	L	**29** + **30**	1 : 1.6	29[a]				
	D	**29** + **30**	3.1 : 1	28[a]	**21**[b]/**27**[c]	**28**[b]/**31**[c]	1 : 7.8	83[a]

a: total yield of the products. b: minor component. c: major component.

Inversion of diastereofacial selection and high stereoselectivity regardless of the chirality of DIPT in the *ZRR*-**10** may be due to the formation of the doubly coordinated transition state such as **32** disposing both benzyloxymethyl groups outward in which epoxidation can take place only from one direction. The *ZRS*- **12**, however, cannot take such rigid doubly coordinated transition state (**33**) owing to steric repulsion of the inward benzyloxymethyl group (**Figure 1**).

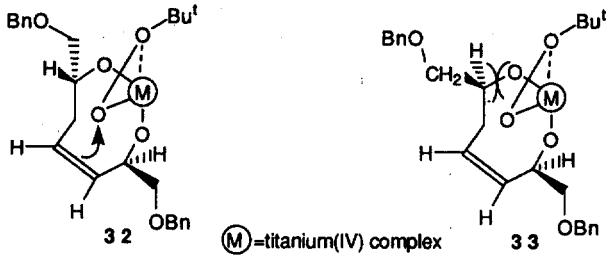


Figure 1

In conclusion, stereochemistry of the Katsuki-Sharpless epoxidation of the present chiral allylic-homoallylic alcohols sharing the central olefinic bond was directed by the chirality of the allylic carbon following the empirical rule,[1] when the substrates have *E* configuration. It was, however, not applicable to the substrates having *Z* configuration in which relative stereochemical relationship between the allylic and the homoallylic carbon centers directed the stereochemistry of the reaction irrespective of the chirality of DIPT.

References and Notes

† For brevity, structures are depicted by Fischer projection. *Threo-/Erythro-* indicates the stereochemical relationship between allylic hydroxy group and vicinal epoxide oxygen bond.

1. Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974; Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*, Trost, B. M. Ed.; Pergamon, Oxford, 1991; Vol. 7, Chapter 3.2.
2. Takano, S.; Iwabuchi, Y.; Ogasawara, K. *J. Am. Chem. Soc.* **1991**, *113*, 2686; *idem. J. Chem. Soc., Chem. Commun.* **1991**, 820; *idem. Synlett* **1991**, 547.
3. Takano, S.; Samizu, K.; Sugihara, T.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1989**, 1344; Takano, S.; Akiyama, M.; Sugihara, T.; Ogasawara, K. *Heterocycles* **1992**, **33**, in press.
4. cf. Takano, S.; Sugihara, T.; Kamikubo, T.; Ogasawara, K. *Heterocycles* **1991**, *32*, 1587.
5. Bates, E. B.; Jones, E. R.; Whiting, M. C. *J. Chem. Soc. C* **1954**, 1854.
6. cf. Mori, Y. *J. Syn. Org. Chem. Jpn.* **1990**, *48*, 1092.
7. cf. Takano, S.; Hatakeyama, S.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1977**, 68; *idem. J. Chem. Soc., Perkin Trans 1* **1980**, 457
8. cf. Mitsunobu, O. *Synthesis* **1981**, 1.
9. Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719; Viti, S. M. *ibid.* **1982**, *23*, 4541.
10. All new compounds described in this paper have satisfactory analytical and spectral data. Distinguish between the 1,2- and 1,3-glycols described was made by cleavage reaction using sodium periodate.

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