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Asymmetric Epoxidation of Homoallylic Alcohols Using Zirconium Tetrapropoxide, Dicyclohexyltartramide, and t-Butyl Hydroperoxide System#

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In the asymmetric epoxidation of homoallylic alcohols, a combination of zirconium tetrapropoxide, dicyclohexyltartramide, and t-butyl hydroperoxide was found to give good enantiomeric selectivities (up to 77% ee) especially for (Z)-homoallylic substrates.

2,3-Epoxy alcohols are versatile building blocks for the synthesis of natural products[1)] especially since the discovery of asymmetric epoxidation (A.E.) using a system of titanium tetraisopropoxide, diethyl tartrate (DET), and t-butyl hydroperoxide (TBHP).[2)] On the other hand, 3,4-epoxy alcohols are in a limited use because of their poor availability in optically active forms, though they are considered to be as useful as 2,3-epoxy alcohols. In this communication, we describe an A.E. reaction of homoallylic alcohols using zirconium tetrapropoxide and dialkyltartramide system.

Recently, Sharpless et al. applied the $Ti(OPr^i)_4$-DET system to the epoxidation of homoallylic alcohols and observed therein a modest asymmetric induction in a range of 23 to 55% ee though the enantioface selection was opposite to that observed in allylic alcohols.[3)] A CPK model examination (Fig. 1),[4)] however, suggests that there is an appreciable repulsion between a hydrogen atom at C-1 and the substituent R in the transition state which leads to the major enantiomer. It is therefore expected that if the repulsion in the folded conformation of the carbon chain can be reduced, the asymmetric induction will be enhanced. Thus, we examined the metal catalysts (Zr, Hf, and Ta) which have longer metal-oxygen bonds than titanium, hoping that they bring about the stretching of the folded chain, mitigating the above repulsion, especially in the case of (Z)-homoallylic alcohols. The results are shown in Table 1. Combinations of these metal alkoxides and L-(+)-dialkyltartramide or L-(+)-dialkyl tartrate ligands were first examined by using (Z)-3-hexen-1-ol (entries 1, 2, 3, and 4). Zirconium catalysts were the most effective though reaction was slow. It was also found that asymmetric induction was dependent on the steric bulkiness of alkyl groups on amide nitrogens and that the amide bearing large alkyl groups gave the enhanced enantiomeric excess. Thus, the best result (72% ee) was realized by using a combination of $Zr(OPr)_4$ and (+)-DCTA. However, the tantalum or the hafnium catalyst showed

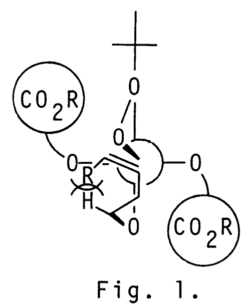

Fig. 1.

#Dedicated to Professor Teruaki Mukaiyama on the occasion of his sixtieth birthday.

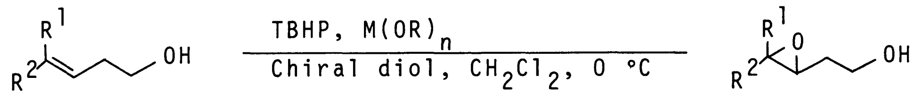

Table 1. Asymmetric Epoxidation of Homoallylic Alcohols[a)]

Entry	R^1	R^2	$M(OR)_n$	Chiral diols	Reaction time/d	Yield %	%ee[b)]	Abs.[c)] conf.
1	Et	H	$Zr(OPr)_4$	(+)-DBuTA[d)]	8	16	39	3R,4S
2	Et	H	$Zr(OPr)_4$	(+)-DBTA[e)]	7	22	62	3R,4S
3	Et	H	$Zr(OPr)_4$	(+)-DCTA[f)]	8	23	72	3R,4S
4	Et	H	$Zr(OPr)_4$	(+)-DIPT[g)]	3	7	31	3R,4S
5	Et	H	$Ta(OEt)_5$	(+)-DCTA	15	22	<5	
6	Et	H	$Hf(OEt)_4$	(+)-DIPT	8	4	<5	
7	Me	H	$Zr(OPr)_4$	(+)-DCTA	9	25	77	
8	Pr	H	$Zr(OPr)_4$	(+)-DCTA	8	28	74	
9	n-C_5H_{11}	H	$Zr(OPr)_4$	(+)-DCTA	16	21 (76)[h)]	53	
10	H	Et	$Zr(OPr)_4$	(+)-DCTA	14	38 (56)[h)]	43	3R,4R
11	H	H	$Zr(OPr)_4$	(+)-DCTA	12	4	40	3R
12	Me	Me	$Zr(OPr)_4$	(+)-DCTA	35	25	10	3R

a) A mixture of $M(OR)_n$ (1 mmol), chiral diol (1.3 mmol), TBHP (2 mmol), and homoallylic alcohol (1 mmol) in CH_2Cl_2 (10 ml) was stirred for a mentioned reaction time. The mixture was quenched with a saturated KF solution and, after usual work-up, the product was isolated by silica gel chromatography. b) Enantiomeric excess was determined by ^{1}H NMR (400 MHz) on the corresponding acetate in the presence of $Eu(hfc)_3$. c) Absolute configuration was determined by comparison of optical rotation (reference 3). d) DBuTA= dibutyltartramide. e) DBTA= dibenzyltartramide. f) DCTA= dicyclohexyltartramide. g) DIPT= diisopropyl tartrate. h) The recovered yield of the starting material.

poor asymmetric induction (entries 5 and 6). Further examples of (Z)-homoallylic alcohols also gave good asymmetric induction (53-77% ee) (entries 7, 8, and 9), while other types of homoallylic alcohols gave results comparable with those obtained by Ti-DET system[3)] (entries 10, 11, and 12). Although the yield was not satisfactory, this zirconium-mediated reaction gave the epoxy alcohol as a sole product and almost all unreacted starting material could be recovered (entries 9 and 10). Both the present zirconium- and the reported titanium-mediated epoxidations showed the same sense of asymmetric induction.[5)]

References

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