Microbial Resolution and Asymmetric Oxidation Related to Optically Active 1,2-Bis(methoxyphenyl)ethane-1,2-diol

Koji Yamamoto,* Hiroyuki Ando, Takashi Shuetake, and Hiroaki Chikamatsu

Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan

An efficient microbial resolution of 1,2-bis-(methoxyphenyl)ethane-1,2-diol (**2**) has been achieved by exposing the corresponding diacetate to *Trichoderma viride* (*T. konigii*); stereoselective epoxidation of allylic alcohols and oxidation of sulphides are achieved with Bu^tOOH using $Ti(OPr^i)_4$–optically active diols (**2**) as chiral catalysts.

Our recent work involved microbial resolution and asymmetric reduction related to optically active 1,3-diphenylpropane-1,3-diol.[1] As an extension to this work, we report the efficient microbial stereo-differentiating hydrolysis of the diesters (**1**) to provide the optically active 1,2-diols (**2**), and an asymmetric epoxidation of allylic alcohols and oxidation of sulphides with a titanium(IV) catalyst in the presence of the optically active diol (**2**) as the chiral inducing source. Incubation of the (±)-diester (**1a**)† (0.5 g) with resting cells of *Trichoderma viride* (IFO 9065) (*T. konigii*)[3] at 25 °C for 39 h gave a 54 : 46 mixture of the recovered diester (**1a**) and 1,2-bis(2-methoxyphenyl)ethane-1,2-diol (**2a**), which was chromatographed to yield (+)-(1*R*,3*R*)-(**1a**)‡ (240 mg), $[\alpha]_D^{25}$ +1.3° (MeOH) [75% enantiomeric excess (e.e.)] and (−)-(1*S*,3*S*)-(**2a**) (210 mg), m.p. 71—72 °C, $[\alpha]_D^{25}$ −8.2° (MeOH) (88% e.e.).§

The optically active 1,2-bis(4-methoxyphenyl)ethane-1,2-

† The racemic substrate (**1a**), m.p. 171—172 °C, was readily prepared from the corresponding (±)-diol (**2a**), m.p. 88—89 °C, which was obtained by $NaBH_4$ reduction of 2,2′-dimethoxybenzoin[2] followed by recrystallization from MeOH for separation of the *meso* and (±)-diol.

‡ C.d. spectral comparison with (+)-(*R*,*R*)-1,2-bis(4-methoxyphenyl)ethane-1,2-diol (**2b**)[4] indicated the (*R*,*R*)-configuration for (+)-(**2a**).

§ The optical purity of (+)-(**2a**) was determined by h.p.l.c. analysis with a column packed with cellulose tris(3,5-dimethylphenylcarbamate)[5] [elution with hexane–propan-2-ol (49 : 1)].

Table 1. Catalytic asymmetric epoxidations.[a]

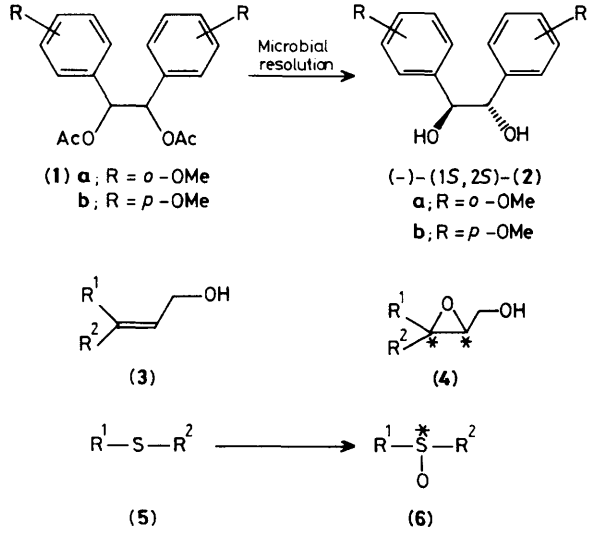
Allylic alcohol (3)	Chiral source (2)	Epoxy alcohol (4) Yield (%)	% E.e.[b]	Configuration
$R^1 = H, R^2 = Ph$	(−)-(*S*,*S*)-(**2a**)	66	96	(+)-(2*R*,3*R*)[c]
	(−)-(*S*,*S*)-(**2b**)	64	61	(−)-(2*S*,3*S*)
$R^1 = Me$, $R^2 = Me_2C{=}CH(CH_2)_2$	(−)-(*S*,*S*)-(**2a**)	78	95	(+)-(2*R*,3*R*)[c]
	(−)-(*S*,*S*)-(**2b**)	75	64	(−)-(2*S*,3*S*)

[a] $Ti(OPr^i)_4$/(**2**)/allylic alcohol/Bu^tOOH, 1:1.2:1:2, in CH_2Cl_2, −20 °C, 18 h. [b] E.e. was determined by h.p.l.c. analysis of the benzoate of (**4**) with a column packed with cellulose tris(3,5-dimethylphenylcarbamate)[5] on silica gel [elution with hexane–propan-2-ol (19:1)]. [c] Optical rotation values of (**4**) were: $[\alpha]_D^{24}$ +48° (*c* 1.8, $CHCl_3$) for R^1 = H, R^2 = Ph; $[\alpha]_D^{24}$ +5.6° (*c* 2.0, $CHCl_3$) for R^1 = Me, $R^2 = Me_2C{=}CH(CH_2)_2$.

Table 2. Asymmetric oxidation of sulphides.[a]

Sulphide (5)	Chiral source (2)	Sulphoxide (6) Yield (%)	% E.e.[b]	Configuration
$R^1 = Me$, $R^2 = Ph$	(−)-(*S*,*S*)-(**2a**)	81	84	(−)-(*S*)[c]
	(−)-(*S*,*S*)-(**2b**)	75	49	(+)-(*R*)
$R^1 = Me$, $R^2 = CH_2Ph$	(−)-(*S*,*S*)-(**2a**)	61	66	(−)-(*S*)[c]
	(−)-(*S*,*S*)-(**2b**)	55	43	(+)-(*R*)

[a] $Ti(OPr^i)_4$/(**2**)/H_2O/sulphide/Bu^tOOH, 1:2:1:1:1.1 in CH_2Cl_2, −20 °C, 18 h. [b] E.e. was determined by h.p.l.c. analysis with a column packed with cellulose tris(3,5-dimethylphenylcarbamate)[5] on silica gel [elution with hexane–propan-2-ol (49:1)]. [c] Optical rotation values of (**6**) were: $[\alpha]_D^{24}$ −129° (*c* 1.5, acetone) for R^1 = Me, R^2 = Ph; $[\alpha]_D^{24}$ −38° (*c* 2.0, acetone) for R^1 = Me, $R^2 = CH_2Ph$.



diol (**2b**) was prepared in the same way from the diester (**1b**).[6] Incubation of (±)-(**1b**) (0.5 g) with resting cells of *Trichoderma viride* at 25 °C for 48 h gave a 60:40 mixture of the recovered diester (**1b**) and the diol (**2b**), which was chromatographed to give (+)-(2*R*,3*R*)-(**1b**)[4] (250 mg), $[\alpha]_D^{25}$ +13.6° (MeOH) (61% e.e.) and (−)-(2*S*,3*S*)-(**2b**)[4] (170 mg), m.p. 119—120 °C, $[\alpha]_D^{25}$ −118.7° (MeOH) (93% e.e.),§ respectively. Interestingly none of the isolated micro-organisms accumulated the possible monoester intermediate (<4% yield) but afforded the diol (**2**) directly.

Following the Sharpless epoxidation procedure,[7] a CH_2Cl_2 solution of a new chiral epoxidation reagent was prepared *in situ* from $Ti(OPr^i)_4$ and the optically active diol (**2**). The allylic alcohol (**3**) (1 equiv.) in dry CH_2Cl_2 was added to this reagent (1 equiv.) at −20 °C, and the whole mixture was stirred at this temperature for several minutes. Then, a solution of Bu^tOOH (1.1 equiv.) in dry CH_2Cl_2 was added dropwise to the stirred mixture over 10 min and stirred for 15 h at −15 to −20 °C. Routine work-up involving SiO_2 chromatography afforded the results summarized in Table 1.¶

In search for another use of this chiral auxiliary, our efforts were directed to the asymmetric oxidation of prochiral sulphides to sulphoxides. According to Kagan's procedure, [$Ti(OPr^i)_4$/(−)-(**2**)H_2O/Bu^tOOH, 1:2:1:1.1] in CH_2Cl_2 (−20 °C), cleanly oxidized prochiral sulphides to the optically active sulphides in high enantiomeric excess. Results for the asymmetric oxidations attempted are summarized in Table 2.

These results show that by using the optically active 1,2-bis(2-methoxyphenyl)ethane-1,2-diol (**2a**) the titanium(IV) catalyst exhibits good enantiomer selectivity towards the asymmetric epoxidation of allylic alcohols and the asymmetric oxidation of sulphides.

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¶ The chiral auxiliary (**2**) was recovered without any noticeable loss in yield or optical purity.