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Regio- and Stereoselective Concurrent Oxidations with Whole Cell Biocatalyst: Simple and Green Syntheses of Enantiopure 1,2-Diols via Oxidative Kinetic Resolution

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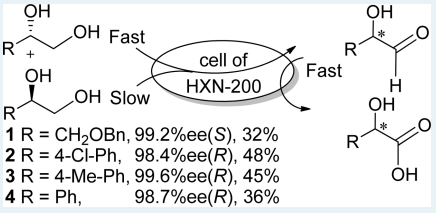
Supporting Information

ABSTRACT: A simple and green method for preparing several enantiopure 1,2-diols was developed, for the first time, via regio- and stereoselective concurrent oxidations of the racemates with microbial cells. *Sphingomonas* sp. HXN-200 was found to catalyze the regio- and stereoselective oxidations of 3-*O*-benzylglycerol **1** to the corresponding α-hydroxy aldehyde **5** and then to the α-hydroxy carboxylic acid **6**. Concurrent biooxidations of racemic 3-*O*-benzylglycerol **1** with resting cells of *Sphingomonas* sp. HXN-200 gave (*S*)-**1** in 99.2% enantiomeric excess (ee) and 32% yield. Similar biooxidations of racemic 1-(4-chlorophenyl)-1,2-ethanediol **2**, 1-(4-methylphenyl)-1,2-ethanediol **3**, and phenyl-1,2-ethanediol **4** gave (*R*)-**2** in 98.4% ee and 48% yield, (*R*)-**3** in 99.6% ee and 45% yield, and (*R*)-**4** in 98.7% ee and 36% yield, respectively. These represent the best results known thus far for the enzymatic syntheses of the useful and valuable diols (*S*)-**1** and (*R*)-**2**−**4**.



KEYWORDS: enzyme catalysis, enantioselective synthesis, concurrent oxidations, enantiopure 1, 2-diols, *Sphingomonas* sp. HXN-200, tandem biocatalysis

1. INTRODUCTION

Enantiopure vicinal diols are useful and valuable intermediates for pharmaceutical production. For instances, (*S*)-3-*O*-benzylglycerol **1** (Scheme 1) is an intermediate for the syntheses of antiherpesvirus agent Vistide,[1,2] migrastatin analogues for treating colon and/or ovarian cancer,[3] and subtype-selective LPA3 receptor antagonist;[4] (*R*)-1-(4-chlorophenyl)-1,2-ethanediol **2** is useful for the preparation of a NMDA receptor antagonist (*R*)-(-)-Eliprodil[5] and an anticonvulsant agent;[6] (*R*)-1-(4-methylphenyl)-1,2-ethanediol **3** is an intermediate in the syntheses of several important enantiopure compounds such as 3-substituted 3,4-dihydro-isocoumarins;[7] (*R*)-phenyl-1,2-ethanediol **4** is used in the syntheses of arylalkylamine calcimimetics (*R*)-(+)-NPS R-568,[8] NK-1 receptor antagonists (+)-CP-99,994 and (+)-CP-122,721,[9] and nucleoside analogues harboring an antiviral activity.[10] Several chemical methods have been developed for the enantioselective syntheses of these 1,2-diols, including Sharpless asymmetric dihydroxylations of olefins,[7,11−13] asymmetric hydrogenations of hydroxy-ketones,[14] and enantioselective hydrolysis of epoxides.[15,16] However, they all require the use of toxic metal catalysts.

On the other hand, enzyme catalyses often provide with greener methods for efficient and enantioselective syntheses because of *non*-toxicity of biocatalysts and mild reaction conditions. Many enzymatic methods have thus been explored for the preparation of enantiopure 1,2-diols such as (*S*)-**1** and (*R*)-**2**−**4** (Scheme 1). Surprisingly, their enantioselectivity and efficiency are not satisfactory. Asymmetric dihydroxylation of styrene with dioxygenase gave (*R*)-**4** in only 80% enantiomeric excess (ee),[17,18] while asymmetric reduction of the hydroxyketone with Bakers' yeast gave (*S*)-**1** in 55%−92% ee with low yields.[19,20] Enzymatic resolution is often the method of choice for the preparation of enantiopure compound. However, lipase-catalyzed resolution of vicinal diol was less enantioselective. Thus, enantiopure diols such as (*R*)-**2** and (*R*)-**3** had to be prepared via lipase-catalyzed resolution of the corresponding hydroxyl monoesters followed by an additional hydrolysis step.[21] Epoxide hydrolase-catalyzed hydrolyses of racemic epoxides were also not enantioselective enough to give the corresponding vicinal diols in high ee.[22−24] Enantioconvergent hydrolysis[25−27] of epoxides with epoxide hydrolase(s) is elegant and afforded (*R*)-**4** in 86% ee and (*R*)-**2** in 96% ee. Nevertheless, the product ee needs to be further increased for pharmaceutical application. Resolution based on enantioselective oxidation is a useful approach; however, biooxidation of racemic **4** with a halohydrin dehydro-dehalogenase in the presence of phenazine methosulfate (PMS) as artificial electron acceptors gave 39.5% of (*R*)-**4** in 95.1% ee,[28] which suffers from both unsatisfied enantioselectivity and the use of costly auxiliary.

Scheme 1. Some Useful Enantiopure 1,2-Diols

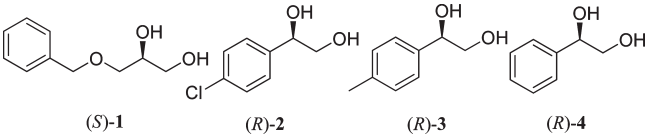


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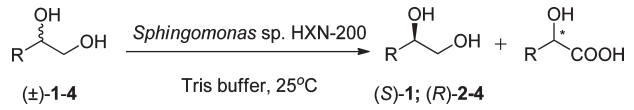
Table 1. Syntheses of (*S*)-1 and (*R*)-2−4 by Regio- and Stereoselective Concurrent Oxidations of (±)-1−4 with Resting Cells of *Sphingomonas* sp. HXN-200



(±)-**1**-**4** (*S*)-**1**; (*R*)-**2**-**4**

sub.	conc. (mM)	cells (g/L)	activity[a] (U/g cdw)	time (h)	prod.	ee (%)	yield (%)	*E*
(±)-**1**	5.8	10	4.2	3	(*S*)-**1**	99.9	26	13
(±)-**1**	10.8	10	3.5	6	(*S*)-**1**	99.6	26	10
(±)-**1**	19.4	10	2.5	15	(*S*)-**1**	99.2	32	13
(±)-**2**	9.4	7.9	2.5	10	(*R*)-**2**	98.8	47	72
(±)-**2**	18.0	7.9	1.4	18	(*R*)-**2**	98.4	48	82
(±)-**3**	7.9	14	3.4	4	(*R*)-**3**	99.6	45	87
(±)-**3**	17.3	14	4.1	10	(*R*)-**3**	97.6	47	65
(±)-**4**	5.1	17	0.5	21	(*R*)-**4**	98.7	36	17

[a] Activity was determined at 0.5 h for (±)-**1**, 3 h for (±)-**2**, and 1 h for (±)-**3** and (±)-**4**.

In this paper, we describe a new, simple, and efficient enzymatic method for the preparation of 1,2-diols (*S*)-**1** and (*R*)-**2**−**4** in high ee by regio- and stereoselective concurrent biooxidations of the racemic 1,2-diols with microbial cells containing the necessary tandem oxidative enzymes.

2. EXPERIMENTAL SECTION

2.1. Materials. 3-*O*-benzylglycerol **1** (>97%) was purchased from Fluka. 1-(4-Chlorophenyl)-1,2-ethanediol **2** (>98%) and 1-(4-methylphenyl)-1,2-ethanediol **3** (>98%) were obtained from Spectra Group Inc. Phenyl-1,2-ethanediol **4** (>97%), (*R*)-3-*O*-benzylglycerol **1** (99%), and (*S*)-Phenyl-1,2-ethanediol **4** (99%) were purchased from Aldrich. Chloroform (HPLC grad) and *n*-hexane (HPLC grad) are obtained from Fisher. (*S*)-(4-Chlorophenyl)-1,2-ethanediol **2** and (*S*)-1-(4-methylphenyl)-1,2-ethanediol **3** were synthesized by using a reported procedure.[29]

2.2. Analytic Methods. Optical rotations were measured on a Jasco spectropolarimeter. ^{1}H NMR spectrum was recorded on a Bruker Avance 500 (AV500) system.

Concentrations of diols **1**−**4** were determined by using a Shimadzu Prominence HPLC on an Agilent Zorbax Eclipse Rx-phenyl column (2.1 × 150 mm, 5 μm). Detection: UV at 210 nm; Eluent: ACN:H_2O (1:9); Flow rate: 0.25 mL/min; Retention time: 9.5 min for benzyl alcohol, internal standard; 12.8 min for 3-*O*-benzylglycerol **1**; 19.9 min for 1-(4-chlorophenyl)-1,2-ethanediol **2**; 12.0 min for 1-(4-methylphenyl)-1,2-ethanediol **3**; and 6.7 min for phenyl-1,2-ethanediol **4**.

The ee of diols **1**−**4** was determined by using a Shimadzu Prominence HPLC on a chiral column (Chiral Technologies, 250 × 4.6 mm, 5 μm) with a PDA detector. 3-*O*-Benzylglycerol **1**: column: Chiralcel OD-H, eluent: *n*-hexane:i-PrOH (9:1), flow rate:0.9 mL/min, retention time: 13.8 min for (*R*)-**1**, 16.8 min for (*S*)-**1**. 1-(4-Chlorophenyl)-1,2-ethanediol **2**: Chiralcel OD-H, eluent: *n*-hexane:i-PrOH (95:5), flow rate:1.0 mL/min, retention time: 17.3 min for (*R*)-**2**, 19.3 min for (*S*)-**2**. 1-(4-Methylphenyl)-1,2-ethanediol **3**: Chiralpak AS-H, eluent: *n*-hexane:i-PrOH (95:5), flow rate:1.0 mL/min, retention time: 20.4 min for (*S*)-**3**, 23.4 min for (*R*)-**3**. Phenyl-1,2-ethanediol **4**: Chiralcel OB-H, eluent: *n*-hexane:i-PrOH (9:1), flow rate:1.0 mL/min, Retention time: 7.9 min for (*R*)-**4**, 9.7 min for (*S*)-**4**.

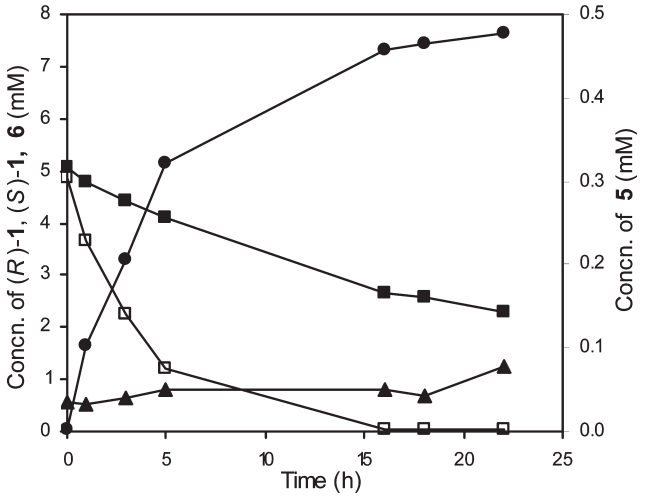


Figure 1. Time course of regio- and stereoselective concurrent oxidations of 10 mM (±)-**1** with resting cells of *Sphingomonas* sp. HXN-200 (8.6 g cdw/L) in 10 mL of 50 mM Tris buffer (pH = 7.5). (□ for (*R*)-**1**, ■ for (*S*)-**1**, ▲ for **5**, and ● for **6**.

The concentrations and structures of bioproduct **5** and **6** were analyzed by using an Agilent 1100 LC-MS system with UV detection at 210 nm and APCI MS detection (negative) at 70 eV. An Agilent Zorbax Eclipse Rx-phenyl column (Agilent, 2.1 × 150 mm, 5 μm) was employed. HPLC analysis condition: eluent: ACN:H_2O (5:95); flow rate: 0.3 mL/min; retention time: 21.6 min for compound **1**, 17.6 min for compound **5**, and 2.3 min for compound **6**.

2.3. Cell Growth of *Sphingomonas* sp. HXN-200. *Sphingomonas* sp. HXN-200[30−33] was grown on *n*-octane vapor in 2 L of E2 medium in a fermentor at 30 °C.[30] The cells were harvested at the late exponential phase and washed with potassium phosphate buffer. The cell pellets were stored at −80 °C.

2.4. General Procedure for Sequential Oxidations of (±)-1−4 with Microbial Cells to Prepare (*S*)-1 and (*R*)-2−4. To a 10 mL suspension of cells of *Sphingomonas* sp. HXN-200 (10 g cdw/L) in 50 mM Tris-buffer (pH = 7.5) was added diols **1**, **2**, **3**, or **4** (5.1−19.4 mM), and the mixture was shaken at 25 °C and 300 rpm. The reaction was followed by taking samples at different reaction time points and analyzing the samples by HPLC. Once the ee of the remaining diol reached >98%, the reaction was stopped (at 3−12 h). The results are summarized in Table 1, Figure 1, and Figure 2. For preparation of samples for HPLC analysis to determine product concentration: 200 μL sample taken from biotransformation were centrifuged to remove cells; the supernatant was separated and then diluted with ACN (1:1) containing 2 mM benzyl alcohol as internal standard. For preparation of samples for ee analysis by chiral HPLC: 200 μL sample taken from biotransformation was centrifuged to remove the cells; the separated supernatant was then extracted with chloroform (1:1); the separated organic phase was evaporated; and the residue was dissolved in *n*-hexane.

2.5. Preparation and Identification of Hydroxy Acid 6 in Sequential Oxidation of (±)-1 with Resting Cells of *Sphingomonas* sp. HXN-200. To a 50 mL suspension of cells of *Sphingomonas* sp. HXN-200 (10 g cdw/L) in 50 mM Tris-buffer (pH = 7.5) was added 3-*O*-benzylglycerol **1** to a concentration of 20 mM. The mixture was shaken at 25 °C and 300 rpm, and the

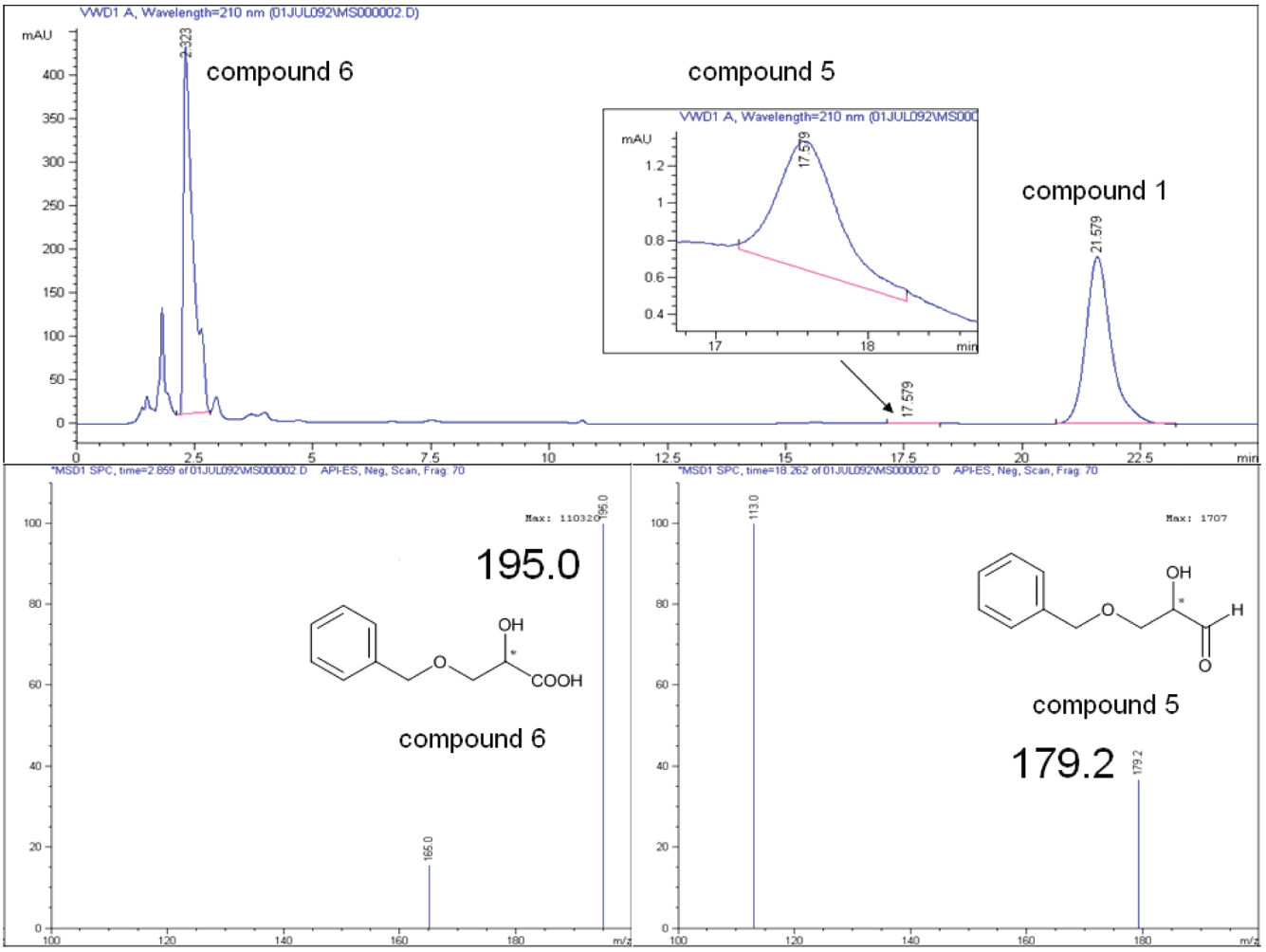


Figure 2. LC-MS analysis of the sample taken at 5 h in the biotransformation of 10 mM (±)-**1** with resting cells of *Sphingomonas* sp. HXN-200 (8.6 g cdw/L) in 10 mL of 50 mM Tris buffer (pH = 7.5).

reaction was followed by periodical sampling and HPLC analysis. The reaction was stopped after 24 h at 72% conversion. The diol **1** was extracted into chloroform by 3 times extraction (1:1). The remaining solution was acidified with sulphuric acid and then extracted with chloroform (1:1). The carboxylic acid **6** in chloroform was concentrated by evaporation at reduced pressure and purified by flash chromatography on a silica gel column (R_f 0.27, *n*-hexane:EtOAc 1:2). This gave the carboxylic acid **6** as white powder in 28.2% yield. HPLC-MS analysis: >98% purity; MS, 195.1 [M − 1]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.77−3.84 (*m*, 2H), δ 4.37 (*t*, 1H), δ 4.57−4.60(*m*, 2H), δ 7.26−7.37 (*m*, 5H).

3. RESULTS AND DISCUSSION

3.1. Discovery and Mechanistic Investigation of *Sphingomonas* sp. HXN-200 for Regio- and Stereoselective Concurrent Biooxidations of 1,2-diol (±)-1. The enantioselective oxidative resolution of (±)-3-*O*-benzylglycerol **1** was chosen as the initial target reaction, and 70 microorganisms that can grow on *n*-octane as sole carbon source were screened for this reaction by using previously established microtiter plate screening system[31] coupled with HPLC analysis. The strains degrading *n*-octane often contain oxygenase catalyzing the hydroxylation of *n*-octane to *n*-octanol as well as a set of other oxidative enzymes catalyzing the oxidation of *n*-octanol to *n*-octanoic acid. This set of enzymes might also be able to catalyze the oxidation of 1,2-diol (±)-**1** to the corresponding α-hydroxy acid **6** in an enantioselective way (Scheme 2). From screening experiments, *Sphingomonas* sp. HXN-200, an alkane degrading strain with known monooxygenase[31,32] and epoxide hydrolase activity,[33,30] was surprisingly found to catalyze the enantioselective oxidations of 1,2-diol (±)-**1**, leaving (*S*)-**1** in high ee as unreacted substrate in the reaction mixture.

To further investigate this reaction, cells of *Sphingomonas* sp. HXN-200 were produced in a large amount by growing on *n*-octane in E2 medium in a bioreactor.[30] The resting cells were used as biocatalysts for the oxidative resolution of (±)-**1**. Bioconversion was performed with 9.9 mM (±)-**1** at a cell density of 8.6 g cdw/L (cdw: cell dry weight) in 10 mL of 50 mM Tris buffer (pH = 7.5). To explore the possible mechanism of this biotransformation, samples were taken at different time points and analyzed by HPLC to determine the concentration and ee of the remaining diol as well as the concentrations of all products generated during biotransformation. The course of the biotransformation is shown in Figure 1. The concentration of (*R*)-**1** decreased at a higher rate than that of (*S*)-**1**, thus the bioconversion of (*R*)-**1** is faster than that of (*S*)-**1**. The aldehyde intermediate **5**[34] and the carboxylic acid **6**[35] were produced

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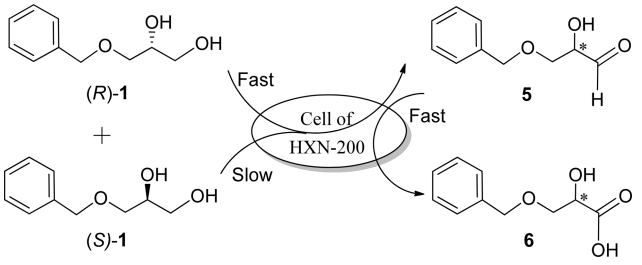
Scheme 2. Regio- and Stereoselective Concurrent Oxidations of (±)-1 with Resting Cells of *Sphingomonas* sp. HXN-200[a]



[a] (*R*)-**1** is preferentially oxidized by the cells to give **5** which is then further oxidized by the cells to afford **6**, leaving unreacted (*S*)-**1** in high ee.

during the biotransformation, evidenced by HPLC-MS analysis (Figure 2). The structures of the aldehyde intermediate **5** and the carboxylic acid **6** were confirmed based on the desired M-1 peaks (Figure 2). No other intermediates such as the 2-keto alcohol were observed in HPLC-MS analysis, thus confirming the clean transformation as well as the mechanism involving regio- and stereoselective concurrent oxidation of terminal hydroxy group of diol (±)-**1** to the hydroxy aldehyde **5** and then to the hydroxy carboxylic acid **6** (Scheme 2). During the whole reaction period (Figure 1), the concentration of aldehyde intermediate **5** was very low, indicating the fast oxidation of **5** to **6**. On the other hand, the concentration of **6** increased at a higher rate at 0−5 h, possibly because of the faster oxidation of (*R*)-**1** to **5** which was then quickly oxidized to the acid **6.** The formation of **6** became slower at later stage (16−22 h) because of the lower rate for the oxidation of (*S*)-**1** to **5**, and no (*R*)-**1** remained in the system in this period. Interestingly, the acid **6** was not further degraded with the resting cells of *Sphingomonas* sp. HXN-200. The total concentrations of **1**, **5**, and **6** were well balanced at each reaction time points, suggesting no formation of other products.

To further confirm the proposed mechanism, oxidative resolution of 20 mM (±)-**1** was carried out on a 50 mL-scale to prepare α-hydroxy carboxylic acid **6**. The reaction was stopped when (*R*)-**1** was completely converted. The reaction product was isolated under unoptimized conditions, by acidification and extraction with organic solvent followed by flash chromatography, to give α-hydroxy carboxylic acid **6** in 28% yield. The structure of this acid product was confirmed by ^{1}H NMR and MS analyses.

3.2. Whole Cell-Based Regio- and Stereoselective Concurrent Biooxidations of 1,2-Diols to Prepare (*S*)-1 and (*R*)-2−5. The oxidative resolution of (±)-**1** was explored with resting cells of *Sphingomonas* sp. HXN-200 at 10 g cdw/L as catalysts at different substrate concentrations. As shown in Table 1, biotransformation of 5.8 mM (±)-**1** for 3 h gave (*S*)-**1** as the sole product in 99.9% ee and 26% yield, with an enantiomeric ratio (*E*) of 13. The specific activity reached 4.2 U/g cdw (U = μmol/min). Further increase of substrate concentrations to 19.4 mM (±)-**1** for the same oxidative resolution afforded (*S*)-**1** in 99.2% ee and 32% yield after 15 h, with the same enantioselectivity.

To further explore the application potential of this catalytic system and the method, aryl 1,2-ethanediol (±)-**2**−**4** (Scheme 1) were subjected to oxidative resolution with the resting cells of *Sphingomonas* sp. HXN-200. As shown in Table 1, 1,2-diols **2**−**4** were all regio- and stereoselectively oxidized, leaving the unreacted

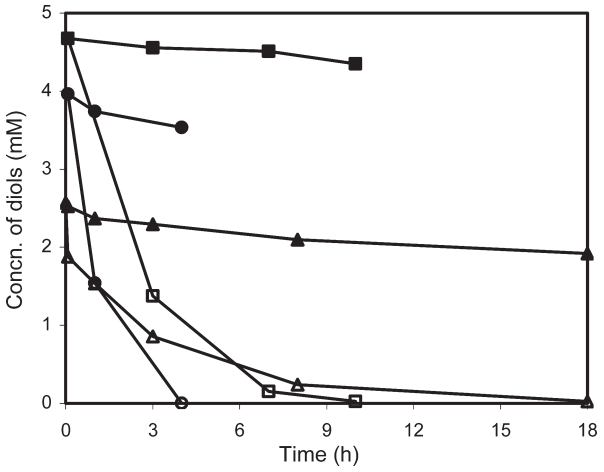


Figure 3. Time course of regio- and stereoselective concurrent oxidations of 9.4 mM (±)-**2** at cell density of 7.9 g cdw/L, 7.9 mM (±)-**3** at cell density of 14 g cdw/L, and 5.1 mM (±)-**4** at cell density of 16.9 g cdw/L, respectively. ■ for (*R*)-**2**, ● for (*R*)-**3**, ▲ for (*R*)-**4**, □ for (*S*)-**2**, ○ for (*S*)-**3**, and Δ for (*S*)-**4**.

(*R*)-1,2-diols in high ee. The preference for the enantioselective oxidations of (*S*)-**2**−**4** with the cells of *Sphingomonas* sp. HXN-200 is the same as that for the enantioselective oxidations of (*R*)-**1**, since the configurations of (*S*)-**2**−**4** are actually the same as that of (*R*)-**1** but named differently based on CIP rules.

Remarkably, higher enantioselectivities were observed for the oxidations of (±)-**2** and (±)-**3**. For instance, oxidative resolution of 18.0 mM (±)-**2** via concurrent biooxidations with cells of *Sphingomonas* sp. HXN-200 at 7.9 g cdw/L for 18 h gave (*R*)-**2** in 98.4% ee and 48% yield, which corresponds to an *E* of 82. Biotransformation of 7.9 mM (±)-**3** with HXN-200 cells at 14 g cdw/L for 4 h afforded (*R*)-**3** in 99.6% ee and 45% yield, giving rise to an *E* of 87. Increase of the concentration of (±)-**3** to 17.3 mM gave (*R*)-**3** still in high ee (97.6%) with 47% yield after 10 h reaction. The enantioselectivities showed here from the resolution based on concurrent biooxidations are much higher than those obtained in lipase-catalyzed resolution of the diol monoesters.[21] In comparison with (±)-**2**−**3**, the enantioselectivity for the oxidative resolution of (±)-**4** is moderate, with an *E* of 17. Nevertheless, biotransformation of 5.1 mM (±)-**4** with cells of *Sphingomonas* sp. HXN-200 at 17 g cdw/L for 21 h gave (*R*)-**4** in 98.7% ee and 36% yield.

Typical time-courses of concurrent oxidations of (±)-**2**−**4** were given in Figure 3. Bioconversions of (*S*)-**2**−**3** were much faster than that for (*R*)-**2**−**3**. (*R*)-**2** and (*R*)-**3** were thus obtained in high ee at 10 and 4 h, respectively, with a specific activity of 2.5 and 3.4 U/g cdw, respectively. Similarly, it was shown in Figure 2 that the oxidation of (*S*)-**4** was also faster than that of (*R*)-**4**. In comparison with (±)-**2**−**3**, the catalytic activity for the oxidation of (±)-**4** was lower: it took 21 h to reach high ee value for (*R*)-**4**. These results suggested that a substituent at *p*-position of the aromatic ring in the diols substrate increased the activity for the biooxidation with HXN-200 cells. Moreover, a substituent at *p*-position of the aromatic ring in the diols substrate could also facilitate the discrimination between the two enantiomers of diols, leading to higher enantioselectivity. On the other hand, different type of substituents (chloro vs methyl; Table 1, entry 4 vs 6) does not result in significant difference in either enantioselectivity or activity.

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Our method of resolution of 1,2-diols by regio- and stereoselective concurrent oxidations with whole cell biocatalyst is clearly novel, and it gives also the best results known thus far for the enzymatic syntheses of (*S*)-**1** and (*R*)-**2**−**4** in high ee. This method is also complementary to our previously developed dihydroxylation method using tandem biocatalysts for the preparation of (*S*)-**2** and (*S*)-**4**.[36] Previously, oxidations of several racemic 1,2-diols consisting of 3−4 carbons with a cell-free three-enzyme system containing an alcohol dehydrogenase, an aldehyde dehydrogenase, and a glutamic dehydrogenase[37,38] were known to give the corresponding (*S*)-hydroxyacids in high ee and 26−32% yields with the recycling of NADH for about 800 times. Theoretically, such a system might also be used for the resolution of 1,2-diols consisting of 3−4 carbons. However, the low TTN for the recycling of the expensive NADH, the high cost of these isolated enzymes, and the poor availability of these enzymes in large quantities make the system less attractive for practical synthesis of enantiopure 1,2-diols. Our method utilizes the easily available and cheap whole cells as biocatalysts for the oxidative resolution of 1,2-diols without additional recycling of the cofactor, thus being of significant advantages.

4. CONCLUSIONS

A simple and green method for the preparation of enantiopure 1,2-diols has been developed, for the first time, by regio- and stereoselective concurrent oxidations of racemic 1,2-diols using microbial cells as catalysts. Biooxidation of (±)-3-*O*-benzylglycerol **1** with resting cells of *Sphingomonas* sp. HXN-200 gave (*S*)-**1** in 99.2% ee and 32% yield. Biooxidation of (±)-1-(4-chlorophenyl)-1,2-ethanediol **2** and (±)-1-(4-methylphenyl)-1,2-ethanediol **3** with resting cells of *Sphingomonas* sp. HXN-200 gave (*R*)-**2** in 98.8% ee and 48% yield and (*R*)-**3** in 99.6% ee and 45% yield, respectively. Similarly, (*R*)-phenyl-1,2-ethanediol **4** was obtained in 98.7% ee and 36% yield from the biocatalytic oxidative resolution of (±)-**4**. While the biooxidation of (±)-**1** and (±)-**4** showed an enantiomeric ratio *E* of 13 and 17, respectively, the biooxidations of (±)-**2** and (±)-**3** demonstrated an enantiomeric ratio *E* of 82 and 87, respectively. In all cases, the concurrent oxidations with whole cells of *Sphingomonas* sp. HXN-200 demonstrated better enantioselectivity than any other known biocatalytic methods for the syntheses of (*S*)-**1** and (*R*)-**2**−**4**. The diol product can be easily separated from the carboxylic acid by extraction with organic solvent such as ethyl acetate.[25] The application scope of the whole cell biocatalyst for the oxidative resolution of 1,2-diols is currently under investigation. Future improvement of this method could involve the engineering of recombinant whole cells biocatalysts expressing the two necessary oxidative enzymes for even more efficient transformations. Moreover, protein engineering of these enzymes could be performed to further increase enantioselectivity and expand substrate range. This method might be generally applicable in the preparation of enantiopure 1,2-diols by the discovery and development of whole-cell based biocatalysts containing the appropriate tandem enzymes.

■ ASSOCIATED CONTENT

Supporting Information. Cell growth of *Sphingomonas* sp. HXN-200, ^{1}H NMR, and LC-MS (ESI) spectra of the hydroxy acid **6** prepared from biotransformation, reverse-phase HPLC chromatograms for biooxidations of compound **1**−**4** with resting cells of *Sphingomonas* sp. HXN-200, and Chiral HPLC chromatograms for analyzing the ee and purity of bioproduct **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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