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Nitrile Biotransformations for Highly Efficient and Enantioselective Syntheses of Electrophilic Oxiranecarboxamides

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Abstract: Catalyzed by a nitrile hydratase/amidase-containing microbial *Rhodococcus* sp. AJ270 whole-cell catalyst, a number of racemic *trans*-2,3-epoxy-3-arylpropanenitriles **1** underwent rapid and efficient hydrolysis under very mild conditions to afford 2*R*,3*S*-2-arylglycidamides **2** in excellent yield with enantiomeric excess higher than 99.5%. The overall enantioselectivity of the biotransformations originated from the combined effects of a dominantly high 2*S*-enantioselective amidase and low 2*S*-enantioselective nitrile hydratase involved in the cell. The influence of the substrates on both reaction efficiency and enantioselectivity was also discussed in terms of steric and electronic effects.

Enantiomerically pure electrophilic epoxides are important and versatile intermediates in organic synthesis. Oxiranecarboxamides and oxiranecarboxylic acid esters, for example, are the key building blocks in the synthesis of natural products such as the Taxol side chain,[1] (−)-dehydroclausenamide,[2] (+)-neoclausenamide,[3] and (+)-clausenamide,[4] synthetic pharmaceuticals such as diltiazem,[1b,5] a potent coronary vasodilating agent, and SK&F 104353,[6] a potent and selective leukotriene antagonist. Selective chemical transformation and ring-opening reactions of electrophilic oxiranes also provide powerful and efficient routes to a variety of useful compounds including 2,3-epoxyketone,[7] aziridinecarboxylate,[8] and isoserine derivatives.[1c,9] It is also intriguing to note that the phenylglycidamide structure has recently been found to occur in natural products. Examples include SB-204900[10] and prebalamide,[11] which were isolated respectively from the plant *Clusena lansium* and *Clausena indica*, whose leaves and fruit have been used to treat asthma and viral hepatitis.

Although the preparation of enantiopure epoxide compounds has been well-developed by Sharpless and others, no general and single approach stands out for the synthesis of optically active electrophilic epoxides.[12] Jacobsen[1b] reported that the (salen)Mn(III)-catalyzed asymmetric epoxidation of substituted *cis*-cinnamate esters gave a mixture of *cis*- and *trans*-arylglycidic esters with enantiomeric excess values (ee) ranging from 41 to 97%, and the ratio of cis to trans isomers was governed by the nature of the ester group and by the substituent on the benzene ring. Epoxidation of *trans*-cinnamate esters with chiral dioxiranes and MCPBA localized in an egg phosphatidylcholine liposomal bilayer afforded *trans*-arylglycidic esters with moderate to good ee values.[13] The reactions between chiral sulfonium ylides and aldehydes[14] and between sulfonium ylides and chiral aldehydes[15] have been employed to prepare enantiomerically enriched oxiranecarboxamides but only moderate ee values and diastereomeric excess values (des) were obtained, respectively. Extended from their early findings of epoxidation of electrophilic alkenes with lithium *tert*-butylhydroperoxide, Meth-Cohn and co-workers have recently reported a diastereoselective epoxidation of *trans*-cinnamamides using prolinols or prolineanilide as a chiral auxiliary. Catalyzed by the lipase from *Candida cylindracea*, racemic *trans*-4-methoxyphenyl- and -phenylglycidic esters were hydrolyzed to give optically active 2*R*,3*S* esters in good yields,[18] while the kinetic resolution of racemic *trans*-arylglycidic acid amides catalyzed by the

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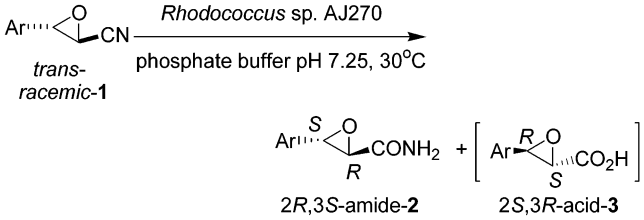
TABLE 1. Biotransformations of Racemic *trans*-2,3-Epoxy-3-arylpropanenitriles 1

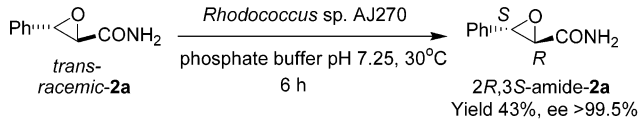
				2	
entry	1	Ar	reaction conditions[a]	yield (%)[b]	ee (%)[c]
1	**1a**	C_6H_5	2 mmol, 25 mL of buffer (pH 7.0), 5.3 h	42	96.4
2	**1a**	C_6H_5	2 mmol, 25 mL of buffer (pH 7.0), 25 mL of hexane, 5.2 h	42	99.5
3	**1a**	C_6H_5	2 mmol, 50 mL of buffer (pH 7.25), 27 min	76[d]	19.5[d]
4	**1a**	C_6H_5	2 mmol, 50 mL of buffer (pH 7.25), 6.5 h	45	>99.5
5	**1b**	4-Me-C_6H_4	1 mmol, 50 mL of buffer (pH 7.25), 3 h	47	>99.5
6	**1b**	4-Me-C_6H_4	2 mmol, 25 mL of buffer (pH 7.25), 5 h	47	>99.5
7	**1c**	2-Me-C_6H_4	2 mmol, 50 mL of buffer (pH 7.25), 24 h	60	39.9
8	**1d**	4-F-C_6H_4	2 mmol, 50 mL of buffer (pH 7.25), 6 h	47	>99.5
9	**1e**	4-Cl-C_6H_4	2 mmol, 50 mL of buffer (pH 7.25), 10 h	49	>99.5
10	**1f**	3-Cl-C_6H_4	2 mmol, 50 mL of buffer (pH 7.25), 80 h	61	31.3

[a] *Rhodococcus* sp. AJ270 cells (2 g wet weight) were used. [b] Isolated yield. [c] Determined by HPLC analysis with use of a Chiralcel OD column. [d] 2*R*,3*S*-Nitrile **1a** (9% yield, 55.1% ee) was recovered.

SCHEME 1. Biotransformations of Racemic *trans*-2,3-Epoxy-3-arylpropanenitriles 1



SCHEME 2. Biocatalytic Kinetic Resolution of Racemic *trans*-2,3-Epoxy-3-arylpropanamide (2a)



amidase led to optically active amides with varied enantiomeric purity.[5c]

Biotransformations of nitriles, either through a direct conversion from a nitrile to a carboxylic acid catalyzed by a nitrilase[19] or through the nitrile hydratase-catalyzed hydration of a nitrile followed by the amide hydrolysis catalyzed by the amidase,[20] are effective and environmentally benign methods for the production of carboxylic acids and their amide derivatives. The microbial hydration of acrylonitrile to acrylamide, for instance, is one of the largest industrial biotransformations in the world.[21] Recent studies[22,23] have demonstrated that biotransformations of nitriles also complement the existing asymmetric chemical and enzymatic synthetic methods for carboxylic acids and their derivatives. The distinct features of enzymatic transformations of nitriles are the formation of enantiopure carboxylic acids, and the straightforward generation of enantiopure amides, which are valuable organonitrogen compounds in synthetic chemistry. Our interests[23] in enantioselective biotransformations of nitriles using microbial cells and in utilizing this methodology to create unique and versatile chiral organonitrogen compounds have led us to investigate the biotransformation of oxiranecarbonitriles. In this paper we report highly efficient and convenient synthesis of enantiopure electrophilic oxiranecarboxamides.

We first examined the reaction of racemic *trans*-2,3-epoxy-3-phenylpropanenitrile (**1a**).[24] Catalyzed by the *Rhodococcus* sp. AJ270, a nitrile hydratase/amidase-containing microbial whole cell catalyst,[25] under very mild conditions, nitrile **1a** was converted efficiently into the optically active 2*R*,3*S*-2-phenylglycidamide (**2a**).[5c] The corresponding phenylglycidic acid **3a** was not obtained because it underwent spontaneous decomposition to phenylacetaldehyde under the reaction conditions as reported in the literature[18] (Scheme 1). As indicated in Table 1, although the biotransformation of **1a** took place effectively under various conditions such as in aqueous phosphate buffer with pH 7.0 (entry 1) or in a biphasic system of phosphate buffer (pH 7.0) with hexane (entry 2), the best chemical yield (45%) with highest enantiomeric excess (ee >99.5%) was obtained for **2a** when the reaction was conducted in phosphate buffer at pH 7.25 (entry 4). To understand the outcome of the stereochemistry of both the nitrile hydratase and the amidase involved in *Rhodococcus* sp. AJ270 cells, the reaction of **1a** was quenched in 27 min. The optically active 2*R*,3*S*-2-phenylglycidamide (**2a**, 76%) thus isolated and recovered 2*R*,3*S*-nitrile **1a** (9%) showed an enantiomeric excess value of 19.5 and 55.1%, respectively (entry 3). Chemical hydrolysis of 2*R*,3*S*-nitrile **1a** (ee 55.1%) recovered from biotransformation afforded 2*R*,3*S*-2-phenylglycidamide (**2a**, ee 57.1%) in 75% yield. We then investigated the biotransformation of racemic **2a** under the identical conditions, and found that (±)-**2a** was resolved after 6 h into enantiopure 2*R*,3*S*-2-phenylglycidamide (**2a**) in 43% yield (Scheme 2). This indicated clearly that the amidase

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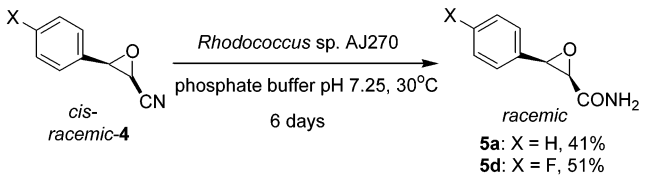
SCHEME 3. Biotransformations of Racemic *cis*-2,3-Epoxy-3-arylpropanenitriles 4



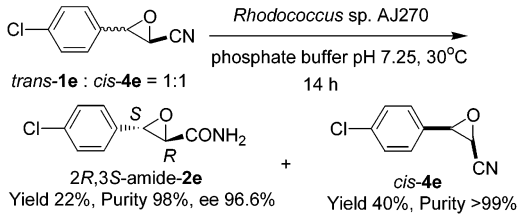
of *Rhodococcus* sp. AJ270 displays high 2*S*-enantioselectivity against *trans*-2-phenylglycidamide while the nitrile hydratase shows low 2*S*-enantioselectivity against nitrile. The excellent enantioselection of the biotransformation of nitrile **1a** originates from the combined effects of enantioselective nitrile hydratase and amidase, with the later being dominant.

To test the scope of the reaction and the influence of substituent on the efficiency and enantioselectivity of biotransformations, a number of racemic *trans*-2,3-epoxy-3-arylpropanenitriles **1** were prepared[24] and subjected to incubation with *Rhodococcus* sp. AJ270 (Scheme 1). It is interesting to note that it is the substitution pattern rather than the nature of the substituent on the benzene ring of the substrate that plays a crucial role in determining both the reaction rate and the enantioselectivity. As illustrated in Table 1, nitrile **1a** and all its para-substituted analogues **1b**,**d**,**e** underwent a very rapid hydrolysis to give an almost quantitative yield of amide in enantiomerically pure form. With a substituent at the ortho- or meta-position, substrates **1c** and **1f** took a longer incubation time to give amides **2c** and **2f**, respectively, with only moderate enantiomeric excesses. This suggested that the enzymes involved are very sensitive toward the steric effect of the substrates, even with a substituent being remote from the cyano or amido function group. The analogous phenomenon has been observed in the biohydrolysis of *trans*-2-arylcyclopropanecarbonitrile derivatives.[23i]

In contrast to the racemic *trans*-2,3-epoxy-3-arylpropanenitriles **1**, the biotransformation with the racemic *cis*-2,3-epoxy-3-arylpropanenitrile substrates **4** proceeded very sluggishly. Under the same reaction conditions as those for **1**, both 2,3-epoxy-3-phenyl- (**4a**) and -3-(4-fluorophenyl)propanenitrile (**4d**) compounds were not completely hydrated after 6 days of interaction with the whole cell catalyst, and about one-fourth of the optically inactive nitriles **4** was recovered. This indicated a steric restriction of the nitrile hydratase toward the nitrile substrates. More unexpectedly, the corresponding amides **5a** and **5d** obtained were optically inactive (Scheme 3)! A similar result for the very slow and nonenantioselective reaction was also obtained from the biohydrolysis employing racemic *cis*-2,3-epoxy-3-phenylpropanamide (±)-**5a** as the substrate. This is in sharp contrast to the biotransformation of *cis*-2-arylcyclopropanecarbonitriles,[23i] which led to excellent enantioselectivity in a similarly lengthy reaction time. The dramatic effect on the enantioselectivity of the amidase caused by the change of one carbon into the oxygen in the three-membered-ring structure remains unclear at the current stage though the change of polarity of the molecule may be important.

To take advantage of the huge difference in hydration reaction rate between *trans*- and *cis*-nitrile isomers, a

SCHEME 4. Biotransformations of a Mixture of Racemic *trans*- and *cis*-2,3-Epoxy-3-arylpropanenitriles



mixture of *trans*- and *cis*-2,3-epoxy-3-(4-chlorophenyl)-propanenitriles (**1e** and **4e**), obtained directly from the Darzens reaction,[24] was subjected to biocatalysis, with the hope of achieving asymmetric synthesis of enantiopure glycidamide and the easy separation of pure *cis*-nitrile in one operation. To our delight, biotransformation did produce optically active amide **2e** in both excellent chemical yield (88% based on theoretical yield) and enantiomeric purity (ee 96.6%) after quenching the reaction in 14 h. Pure *cis*-nitrile **4e** was also readily obtained in high yield (80% based on theoretical yield) (Scheme 4). The successful reaction allowed us to prepare enantiomerically enriched amides **2** while avoiding the somewhat tedious chromatographic separation of trans- and cis-isomers of nitriles prior to biotransformations.

In summary, a highly efficient and convenient synthesis of enantiopure 2*R*,3*S*-2-arylglycidamides has been developed with the biotransformations of racemic nitriles with use of a *Rhodococcus* sp. AJ270 whole cell catalyst under very mild conditions. The overall enantioselectivity of the biotransformations originated from the combined effects of a dominantly high 2*S*-enantioselective amidase and low 2*S*-enantioselective nitrile hydratase involved in the cell. We have also shown that both the nitrile hydratase and the amidase are sensitive toward the structure of the substrates. The enantiopure electrophilic 2*R*,3*S*-2-arylglycidamides, hardly accessible by other methods, can serve as versatile chiral synthons, and their applications in synthesis are actively investigated in this laboratory.

Experimental Section

General. Both melting points and boiling points are uncorrected. Elemental analyses were performed at the Analytical Laboratory of the Institute. The enantiomeric excesses of all compounds were obtained with a Shimadzu LC-10AVP HPLC system, using a Chiracel OD column. A mixture of hexane:2-propanol [9:1] as the mobile phase at a flow rate of 0.8 mL/min was employed.

The starting nitriles were prepared following a literature method.[24] The racemic amides were prepared from chemical hydrolysis of nitriles.[26]

General Procedure for the Biotransformations of Nitriles or Amides. To an Erlenmeyer flask (150 mL) with a screw cap was added *Rhodococcus* sp. AJ270 cells[25] (2 g wet weight) and potassium phosphate buffer (0.1 M, pH 7.25, 50 mL), and the resting cells were activated at 30 °C for 0.5 h with orbital shaking. Racemic nitriles **1** or **4** or amides **2a** or **5a** as fine powder were added in one portion to the flask and the mixture was incubated at 30 °C with use of an orbital shaker (200 rpm). The reaction, monitored by TLC and HPLC, was

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quenched after a specified period of time (see Table 1 and text) by removing the biomass through a Celite pad filtration. The resulting aqueous solution was extracted with ethyl acetate (3 × 75 mL). After the solution was dried ($MgSO_4$) and the solvent removed under vacuum, the residue was chromatographied on a silica gel column with a mixture of petroleum ether and ethyl acetate as the mobile phase to give pure product **2** or **5**, respectively. All products were characterized by their spectra data and comparison of the melting points and optical rotary power with that of the known compounds, which are listed as follows, or by full characterization.

2*R*,3*S*-(−)-3-Phenylglycidamide (2a): 6.5 h; yield 45.4%; mp 157−158 °C; $[\alpha]^{25}_D$ −160° (*c* 0.5, CH_3OH); ee >99.5% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.26−7.41 (m, 5H), 6.20 (s, br, 1H), 5.67 (s, br, 1H), 3.97 (d, J = 1.5 Hz), 3.51 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 170.2, 134.7, 129.1, 128.7, 125.8, 59.0, 58.6; IR (KBr) ν 3380, 3195 ($CONH_2$), 1670, 1643 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 163 (16) [M$^+$], 107 (37), 106 (100), 92 (22), 91 (98). Anal. Calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58. Found: C, 65.88; H, 5.47; N, 8.38. When the reaction was quenched in 27 min, optically active amide **2a** [ee 19.5% (chiral HPLC analysis)] and nitrile **1a** [ee 55.1% (chiral HPLC analysis)] were isolated in 76% and 9% yield, respectively. Biocatalytic kinetic resolution of (±)-**2a** gave, after 6 h, 2*R*,3*S*-(−)-3-phenylglycidamide (**2a**) in 43% yield with >99.5% ee (chiral HPLC analysis). Chemical hydrolysis of optically active nitrile **1a** (24 mg, ee 55.1%) under alkaline conditions in the presence of H_2O_2 (30%) gave 2*R*,3*S*-(−)-3-phenylglycidamide (**2a**) in 75% yield with 57.1% ee (chiral HPLC analysis).

2*R*,3*S*-(−)-3-(4-Methylphenyl)glycidamide (2b): 5 h; yield 47.2%; mp 190−191 °C; $[\alpha]^{25}_D$ −136° (*c* 0.5, CH_3OH) {lit.[5c] $[\alpha]^{25}_D$ +158° (*c* 0.5, CH_3OH) 2*S*,3*R*-(+)-3-(4-methylphenyl)glycidamide}; ee >99.5% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.15 (s, 4H), 6.20 (s, br, 1H), 5.59 (s, br, 1H), 3.93 (d, J = 1.8 Hz, 1H), 3.51 (s, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.1, 138.9, 131.5, 129.2, 125.6, 58.8, 58.3, 21.0; IR (KBr) ν 3400, 3207 ($CONH_2$), 1667 (sh), 1641 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 177 (29) [M$^+$], 160 (20), 132 (29), 121 (33), 120 (96), 105 (100). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.48; H, 6.00; N, 7.79.

2*R*,3*S*-(−)-3-(2-Methylphenyl)glycidamide (2c): 24 h; yield 60.0%; mp 181−182 °C; $[\alpha]^{25}_D$ −24.5° (*c* 1.0, CH_3OH); ee 39.9% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.18−7.27 (m, 4H), 6.26 (s, br, 1H), 5.74 (s, br, 1H), 4.11 (d, J = 1.8 Hz, 1H), 3.42 (s, 1H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.3, 136.4, 133.2, 130.1, 128.6, 126.2, 124.2, 57.8, 57.2, 18.8; IR (KBr) ν 3426, 3158 ($CONH_2$), 1693, 1645 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 177 (38) [M$^+$], 132 (20), 121 (32), 120 (100), 105 (97), 104 (72). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.81; H, 6.12; N, 8.00.

2*R*,3*S*-(−)-3-(4-Fluorophenyl)glycidamide (2d): 6 h; yield 47.3; mp 163−164 °C; $[\alpha]^{25}_D$ −140° (*c* 0.5, CH_3OH); ee >99.5% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.26 (t, J = 8.6 Hz, 2H), 7.07 (t, J = 8.6 Hz, 2H), 6.20 (s, br, 1H), 5.81 (s, br, 1H), 3.96 (d, J = 1.1 Hz), 3.47 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 170.0, 164.8, 161.6, 130.5, 127.6, 127.5, 116.0, 115.7, 58.6, 58.4; IR (KBr) ν 3370, 3187 ($CONH_2$), 1669, 1645 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 181 (11) [M$^+$], 125 (42), 124 (94), 109 (100), 108 (63). Anal. Calcd for $C_9H_8FNO_2$: C, 59.67; H, 4.45; N, 7.73. Found: C, 59.53; H, 4.64; N, 7.75.

2*R*,3*S*-(−)-3-(4-Chlorophenyl)glycidamide (2e): 10 h; yield 49.0%; mp 190−191 °C; $[\alpha]^{25}_D$ −144° (*c* 0.5, CH_3OH); ee >99% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.32 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 6.15 (s, br, 1H), 5.60 (s, br, 1H), 3.93 (s, 1H), 3.44 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 167.8, 133.1, 131.4, 127.1, 125.3, 125.2, 56.7, 56.4; IR (KBr) ν 3410, 3245 ($CONH_2$), 1696, 1660 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 199 (7) [M$^+$ + 2], 197 (20) [M$^+$], 142 (34), 140 (99), 127 (25), 125 (79), 91 (26), 89 (100). Anal. Calcd for $C_9H_8ClNO_2$: C, 54.70; H, 4.08; N, 7.09. Found: C, 54.54; H, 4.27; N, 7.02.

2*R*,3*S*-(−)-3-(3-Chlorophenyl)glycidamide (2f): 80 h; yield 61.2; mp 122−124 °C; $[\alpha]^{25}_D$ −52° (*c* 1.0, CH_3OH); ee 31% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.15−7.31 (m, 4H), 6.14 (s, br, 1H), 5.43 (s, br, 1H), 3.93 (d, J = 1.4 Hz, 1H), 3.45 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 169.9, 136.9, 134.8, 130.0, 129.3, 125.8, 124.1, 58.6, 58.1; IR (KBr) ν 3416, 3172 ($CONH_2$), 1696, 1663 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 199 (12) [M$^+$ + 2], 197 (30) [M$^+$], 142 (26), 140 (68), 127 (18), 125 (62), 91 (41), 89 (100). Anal. Calcd for $C_9H_8ClNO_2$: C, 54.70; H, 4.08; N, 7.09. Found: C, 54.63; H, 4.12; N, 7.04.

cis-(±)-3-Phenylglycidamide (4a): 5 d, yield 73%; 6 d, yield 41%; mp 140−141 °C; $[\alpha]^{25}_D$ 0° (*c* 1.0, CH_3OH); ee 0% (chiral HPLC analysis); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.33−7.36 (m, 5H), 5.78 (s, br, 1H), 5.19 (s, br, 1H), 4.34 (d, J = 4.8 Hz, 1H), 3.74 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 168.6, 132.7, 128.3, 126.2, 57.0, 56.0; IR (KBr) ν 3410, 3172 ($CONH_2$), 1687, 1663 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 163 (11) [M$^+$], 107 (37), 106 (100), 91 (73), 90 (63). Anal. Calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.16; H, 5.54; N, 8.33. Biotransformation starting from racemic *cis*-(±)-3-phenylglycidamide **4a**, after 5 d, gave optically inactive **4a** in 71% yield.

***cis*-(±)-3-(4-Fluorophenyl)glycidamide (4d):** 6 d; yield 44%; mp 142−143 °C; $[\alpha]^{25}_D$ 0° (*c* 1.0, CH_3OH); ee 0%; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.36 (dd, J = 8.3, 5.1 Hz, 2H), 7.05 (t, J = 8.5 Hz, 2H), 5.80 (s, br, 1H), 5.35 (s, br, 1H), 4.31 (d, J = 4.7 Hz, 1H), 3.77 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 168.4, 164.1, 160.8, 128.6, 128.1, 128.0, 115.5, 57.2, 56.0; IR (KBr) ν 3418, 3289 ($CONH_2$), 1704, 1668 cm^{-1} (C═O); MS (EI) *m*/*z* (%) 181 (10) [M$^+$], 125 (52), 124 (100), 109 (83), 108 (70), 107 (54). Anal. Calcd for $C_9H_8FNO_2$: C, 59.67; H, 4.45; N, 7.73. Found: C, 59.66; H, 4.32; N, 7.49.

Biotransformations of a Mixture of Racemic *trans*- and *cis*-2,3-Epoxy-3-(4-chlorophenyl)propanenitriles (2e and 4e). Following the general procedure described above, incubation of a mixture of (±)-**2a** and (±)-**4a** (1 mmol each) with *Rhodococcus* sp. AJ270 cells in 14 h gave 2*R*,3*S*-(−)-3-(4-chlorophenyl)-glycidamide (**2e**) in 21.5% yield with 96.6% ee and *cis*-(±)-2,3-epoxy-3-(4-chlorophenyl)propanenitrile (**4e**) in 40.4% yield. The purity of products 2*R*,3*S*-(−)-**2e** and *cis*-(±)-**4e**, determined by ^{1}H NMR, was 98% and >99%, respectively.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of amides; HPLC analysis of amides. This material is available free of charge via the Internet at http://pubs.acs.org.

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