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Enzymatic synthesis of optically active 2-methyl- and 2,2-dimethylcyclopropanecarboxylic acids and their derivatives

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Abstract

Catalyzed by *Rhodococcus* sp. AJ270 microbial cells under very mild conditions, racemic 2,2-dimethylcyclopropanecarbonitrile (**1**) and its amide (**2**), and *trans*- and *cis*-2-methylcyclopropanecarboxamides (**4**) and (**7**) underwent enantioselective hydrolysis to give the corresponding optically active amides and acids.

Keywords: *Rhodococcus* sp.; Optically active; Racemic nitriles; Nitrile hydratase; Amidase; Enantioselectivity; 2-Methylcyclopropanecarboxylic acid; 2,2-Dimethylcyclopropanecarboxylic acid

1. Introduction

Nitrile is an important intermediate in organic synthesis because of its easy preparations and versatile transformations [1]. Chemical hydrolyses of nitriles, for instance, are frequently used in both academic and industry to synthesize amides and acids. Unfortunately, these applications are restricted to structurally simple nitriles containing no labile groups for chemical processes often require harsh conditions such as using strong acids or bases, and give poor selectivities. In contrast, biotransformations of nitriles into the corresponding amides and acids proceed with excellent selectivities under very mild conditions. So far a large number of nitrile-hydrolyzing microorganisms have been isolated and they have been reported to catalyze a direct transformation of nitrile into an acid through a nitrilase and/or a hydration reaction of nitrile via a nitrile hydratase followed by a hydrolysis of amide with an amidase (for useful reviews of nitrile biotransformations see [2–6]).

Rhodococcus sp. AJ270, a novel isolate from a soil sample [7], appears as a robust and useful nitrile hydratase/amidase-containing biocatalyst. Compared with other microbes reported, it displays broad enzymatic activity against almost all types of nitriles including aromatic, heterocyclic and aliphatic ones, and both amides and acids can be obtained in high yields from appropriate nitriles [8]. It shows excellent regioselectivity in hydrolyzing aromatic dinitriles and a variety of aliphatic dinitriles bearing a suitably placed second chelating moiety [9]. It has been demonstrated recently that *Rhodococcus* sp. AJ270 is an efficient enantioselective biocatalytic system able to transform some racemic nitriles such as α-methyl-, α-ethyl- [10], α-isopropylphenylacetonitriles [11] and α-amino nitriles [12] into the corresponding amides and acids in enantiopure forms. Very recently, we have also found that *Rhodococcus* sp. AJ270 effectively catalyzes enantioselective hydrolysis of both *trans*- and *cis*-2-arylcyclopropanecarbonitriles [13,14]. Encouraged by these studies, we undertook

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the investigation of *Rhodococcus* sp. AJ270-catalyzed biotransformations of 2-methyl- and 2,2-dimethylcyclopropanecarbonitriles and their amides, envisaging the simple synthesis of enantiomerically enriched 2-methyl- and 2,2-dimethylcyclopropanecarboxylic acid derivatives, that are the key segments of curacin A [15], a potent antimitotic agent isolated from *Lyngbya majuscula*, and of cilastatin [16], an inhibitor of dehydropeptidase, respectively.

Though the asymmetric cyclopropanation reactions have been advanced tremendously in the past decades [17,18], no direct asymmetric synthesis of 2-methyl- and of 2,2-dimethylcyclopropanecarboxylic acid derivatives have been reported. Optically active 2-methylcyclopropanecarboxylic acid and its amide derivative have been prepared either from the optical resolution [19] or through the multistep transformations [20–22]. *S*-(+)-2,2-Dimethylcyclopropanecarboxamide has been obtained from kinetic resolution of racemic 2,2-diemthylcyclopropanecarboxamide using amidase-containing microbes or the amidases, a process has been developed into industrial operation in Lonza [23,24].

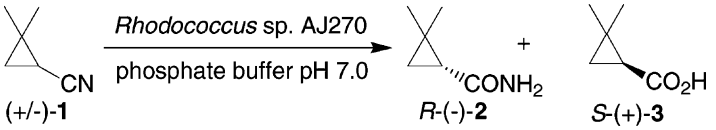
2. Results and discussion

Incubation of 2,2-dimethylcyclopropanecarbonitrile (**1**) with *Rhodococcus* sp. AJ270 cells at 30 °C led to the rapid formation of *R*-(−)-2,2-dimethylcyclopropanecarboxamide (**2**) and *S*-(+)-2,2-dimethylpropanecarboxylic acid (**3**), with enantiomeric excesses being 76 and 82%, respectively (Scheme 1). Attempts were made to increase the enantioselectivity by lowering the reaction temperature [25]. Although the reaction became slower at 20 °C, the enantioselectivity did improve, as the enantiomeric ratio (*E*) [26,27][1] increased from 23 to around 32. At the expense of the chemical yield, the enantiomeric excess of **3** reached as high as 90% (Table 1). To gain a better understanding of the stereochemistry of this biotransformation, the racemic 2,2-dimethylcyclopropanecarboxamide (**2**) was subjected to *Rhodococcus* sp. AJ270 (Scheme 2). The hydrolysis was found to proceed effectively. After quenching the reaction in 3 h, excellent chemical yields were obtained for *R*-amide (**2**) and *S*-acid (**3**) with an *E* value of 11 (Table 1).

Since the mixture of *trans*- and *cis*-2-methylcyclopropanecarbonitriles are not separable, we then turned our attention to the biotransformations of *trans*-2-methylcyclopropanecarboxamide (**4**) and its *cis*-isomer **7** which are readily prepared according to the different methods reported in the literature [19,28]. As shown in Table 2, the hydrolysis of *trans*-2-methylcyclopropanecarboxamide (**4**) proceeded very rapidly, and a complete transformation of amide (**4**) into optically inactive acid **6** finished within 40 min (Entry 3). At about 50% conversion, the reaction afforded the optically active 1*R*,2*R*-(−)-2-methylcyclopropanecarboxamide (**5**) and 1*S*,2*S*-(+)-2-methylcyclopropanecarboxylic acid (**6**) with moderate enantiomeric excesses ($E = 3.6$) (Entry 1). Differed from its *trans*-isomer **4**, the biotransformation of *cis*-2-methylcyclopropanecarboxamide (**7**) took a longer period time. Only after 15 h, did the reaction go to completion to give racemic acid **9** (Entry 7). A less efficient kinetic resolution ($E = 2.7$) was obtained when the reaction was quenched after half way (Entry 5). The highly enantiopure amides 1*R*,2*R*-**5** and 1*R*,2*S*-**8** could be obtained at the expense of chemical yield (Entries 2 and 6) (Schemes 3 and 4).

The outcomes obtained indicated that *Rhodococcus* sp. AJ270 can efficiently catalyze the hydrolysis of 2,2-dimethylcyclopropanecarbonitrile and its amide, and of both *trans*- and *cis*-2-methylcyclopropanecarboxamides. The rate of the amide hydrolysis, however, is dependent upon the steric effect of the substrate, as demonstrated by the fact that the presence of a *cis*-methyl group to amido function slows down the hydrolysis. The similar *cis*-substituent effect has been observed in the biocatalytic hydrolysis of 2-arylcyclopropanecarbonitriles [14] and in the chemical hydrolysis of 2-ethylcyclopropane-1,1-dicarboxylate [29]. It should be noted that the biotransformations did not give a fully recovery of crude material probably due to further metabolism of the substrate and/or the product by the microbe. The formation of optically active 1*R*-amides **2**, **5** and **8** and 1*S*-acids **3**, **6** and **9**, the configurations being assigned by the comparison of the optical rotations with those of authentic samples in literature (see Section 3), shows clearly that the amidase involved in *Rhodococcus* sp. AJ270 is 1*S*-selective. The higher enantiomeric

[1] E was calculated using a program selectivity.

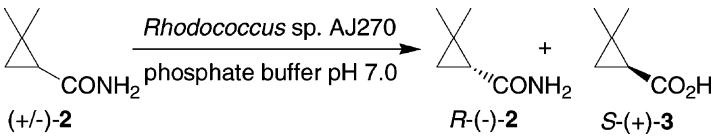


Scheme 1.

Table 1
Enantioselective biotransformations of 2,2-dimethylcyclopropanecarbonitrile (**1**) and 2,2-dimethylcyclopropanecarboxamide (**2**)

Entry	Substrates	Reaction conditions[a]	Amide (%)[b]	e.e. (%)[c]	Acid (%)[b]	e.e. (%)[d]	E[e]
1	**1**	30 °C, 3 h	*R*-**2** (46)	76	*S*-**3** (39)	82	23
2	**1**	20 °C, 3 h	*R*-**2** (66)	32	*S*-**3** (26)	90	37
3	**1**	20 °C, 4.5 h	*R*-**2** (50)	70	*S*-**3** (44)	88	32
4	**2**	30 °C, 3 h	*R*-**2** (41)	88	*S*-**3** (47)	62	11

[a] Racemic nitrile **1** or amide **2** (1 mmol) was used in all cases.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis of the corresponding *N*,*N*-dibenzyl amide.
[d] Determined by chiral HPLC analysis of the corresponding *N*-benzyl amide.
[e] E was calculated on the basis of e.e. values. See [27].

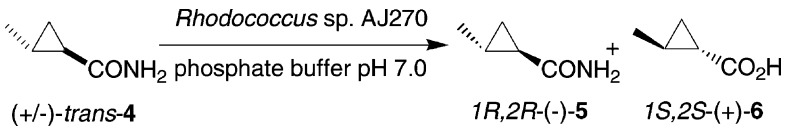


Scheme 2.

Table 2
Enantioselective biotransformations of *trans*- and *cis*-2-methylcyclopropanecarboxamides (**4**) and (**7**)

Entry	Substrates	Reaction conditions[a]	Amide (%)[b]	e.e. (%)[c]	Acid (%)[b]	e.e. (%)[d]
1	**4**	30 °C, 10 min	**5** (41)	53	**6** (54)	38
2	**4**	30 °C, 20 min	**5** (15)	90	**6** (83)	19
3	**4**	30 °C, 40 min	**5** (trace)	n.d.[e]	**6** (90)	0
4	**7**	30 °C, 1 h	**8** (66)	14	**9** (22)	43
5	**7**	30 °C, 4 h	**8** (48)	40	**9** (45)	31
6	**7**	30 °C, 9 h	**8** (18)	>99	**9** (73)	7
7	**7**	30 °C, 15 h	–	–	**9** (86)	0

[a] Racemic amides **4** and **7** (1 mmol) were used in all cases.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis of the corresponding *N*,*N*-dibenzyl amide.
[d] Enantiomeric excess of **6** was determined by chiral HPLC analysis of the corresponding benzyl ester while that of **9** was determined by HPLC analysis of the corresponding *N*,*N*-dibenzyl amide.
[e] Not determined.



Scheme 3.

Scheme 4.

ratio observed for the biotransformation of nitrile **1** than that of amide **2** suggested that the enantioselectivity of the former reaction resulted from the combined effect of the nitrile hydratase and the amidase. In other word, the biotransformation of nitrile is similar to a sequential kinetic resolution [30] cascaded with the enantioselective nitrile hydratase and amidase actions. To synthesize the highly enantiomerically enriched *S*-(+)-2,2-dimethylcyclopropanecarboxylic acid (**3**) and 1*R*,2*S*-(+)-2-methylcyclopropanecarboxamide (**8**), the concise building segments for cilastatin [16] and curacin A [20], respectively, it appears essential to monitor the biotransformations carefully.

3. Experimental

Both melting points, which were determined using a Reichert Kofler hot-stage apparatus, and boiling points are uncorrected. IR spectra were obtained on a Perkin-Elmer 782 instrument as liquid films or KBr discs. NMR spectra were recorded on a Bruker AM 300 spectrometer. Chemical shifts are reported in ppm, and coupling constants are given in Hz. Mass spectra were measured on an AEI MS-50 mass spectrometer, and microanalyses were carried out by the Analytical Laboratory of the Institute.

Polarimetry was carried out using an optical activity AA-10R polarimeter, and the measurements were made at the sodium D-line with a 5 cm path length cell. Concentrations (*c*) are given in g/100 ml. Prior to chiral HPLC analysis with a Shimadzu LC-10AVP HPLC system, amides **2**, **5**, **8** were converted to their *N*,*N*-dibenzyl amide derivatives while acids **3** and **6** were derivatized into *N*-benzyl amide and benzyl ester, respectively. Acid **9** was also transformed chemically into its *N*,*N*-dibenzyl amide before chiral HPLC analysis.

The *Rhodococcus* sp. AJ270 cells were cultivated according to a literature procedure [7,8]. All the racemic substrates such as nitrile **1** [31] and amides **2** [31], **4** [28] and **7** [28] were synthesized according to the literature. The configurations of amides **2**, **5** and **7** and of acids **3**, **6** and **9** were determined by the comparison of the direction of optical rotation with that of authentic samples.

3.1. General procedure for the biotransformations of nitrile *1* and amides *2*, *4*, and *7*

To an Erlenmeyer flask (100 ml) with a screw cap was added *Rhodococcus* sp. AJ270 cells [8] (2 g wet weight) and the potassium phosphate buffer (0.1 M, pH 7.0, 50 ml) and the resting cells were activated at 30 or 20 °C for 0.5 h with orbital shaking. Nitrile **1** or amides **2**, **4** and **7** (1 mmol) was added in one portion to the flask and the mixture was incubated at 30 or 20 °C using an orbital shaker (200 rpm). The reaction, monitored by TLC, was quenched after a specified period of time (see Tables 1 and 2) by removing the biomass through a Celite pad filtration. The resulting aqueous solution was basified to pH 12 with aqueous NaOH (2 M). Extraction with diethyl ether gave, after drying ($MgSO_4$), concentration and purification, the amide. The aqueous solution was then acidified using aqueous HCl (2 M) to pH 2 and extracted with diethyl ether. Acid was obtained after removal of the solvent. All products were characterized by their spectra data and comparison of the melting points and optical rotary power with the known compounds, which are listed below.

3.1.1. Enzymatic hydrolysis of (±)-2,2-dimethylcyclopropanecarbonitrile (*1*)

3.1.1.1. R-(−)-2,2-Dimethylcyclopropanecarboxamide (2). The 3 h (46%), $[\alpha]_D^{25}$ − 76 (*c* 1.0, $CHCl_3$) [[32], $[\alpha]_D^{20}$ +82 (*c* 1.0, CH_3OH), *S*-(+)-2,2-dimethylcyclopropanecarboxamide], e.e. 76% (chiral HPLC analysis of the corresponding *N*,*N*-dibenzyl amide using a Chiralcel OD column with a mixture of hexane and 2-propanol (9:1) at a flow rate 0.4 ml/min

as the mobile phase, $t_{(-)}$ = 14.55 min, $t_{(+)}$ = 13.52 min). The mp, 130–132 °C ([19], 135–138 °C, *S*-(+)-2,2-dimethylcyclopropanecarboxamide); ν_{max}-(KBr) (cm^{-1}) 3350, 3178, 1660, 1624; δ_H 5.54 (br s, 1H, N*H*H), 1.90 (br s, 1H, NH*H*), 1.32 (dd, J = 7.8, 5.4, 1H), 1.20 (s, 3H), 1.15 (s, 3H), 1.10 (dd, J = 4.8, 4.7, 1H), 0.78 (dd, J = 7.9, 4.3, 1H); δ_C 173.7, 28.1, 26.9, 21.9, 20.5, 18.4; *m/z* (EI) 113 (M^+, 49%), 98 (24), 97 (27), 81 (12), 72 (45), 70 (75), 69 (45), 68 (23), 67 (23), 55 (61), 41 (100).

*3.1.1.2. S-(+)-2,2-Dimethylcyclopropanecarboxylic acid (**3**).* The 3 h, 20 °C (26%), $[\alpha]_D^{25}$ + 130.7 (*c* 1.5, $CHCl_3$) ([33], $[\alpha]_D^{27}$ + 38.89 (*c* 1.01, $CHCl_3$) e.e. 90% (chiral HPLC analysis of the corresponding *N*-benzyl amide using a Chiralcel OJ column with a mixture of hexane and 2-propanol (9:1) at a flow rate 0.8 ml/min as the mobile phase, $t_{(-)}$ = 10.85 min, $t_{(+)}$ = 9.28 min). Oil; ν_{max}(KBr) (cm^{-1}) 2260–3600, 1695; δ_H 11.82 (br s, 1H), 1.50 (dd, J = 7.9, 5.5, 1H), 1.26 (s, 3H), 1.18 (s, 3H), 1.13 (dd, J = 4.9, 4.7, 1H), 0.93 (dd, J = 7.9, 4.3, 1H); δ_C 179.3, 26.8, 26.5, 24.2, 22.7, 18.6; *m/z* (EI) 114 (M^+, 51%), 99 (32), 81 (20), 69 (87), 59 (83), 44 (53), 41 (100).

*3.1.2. Enzymatic hydrolysis of (±)-2,2-dimethylcyclopropanecarboxamide (**2**)*

*3.1.2.1. R-(−)-2,2-Dimethylcyclopropanecarboxamide (**2**).* The 3 h, 30 °C (41%), e.e. 88%.

*3.1.2.2. S-(+)-2,2-Dimethylcyclopropanecarboxylic acid (**3**).* The 3 h, 30 °C (47%), e.e. 62%.

*3.1.3. Enzymatic hydrolysis of (±)-trans-2-methylcyclopropanecarboxamide (**4**)*

*3.1.3.1. (1R,2R)-(−)-2-Methylcyclopropanecarboxamide (**5**).* The 10 min (41%), $[\alpha]_D^{25}$ − 48.9 (*c* 1.9, $CHCl_3$), e.e. 53%, mp 99–100 °C; 20 min (15%), $[\alpha]_D^{25}$ − 109.3 (*c* 0.75, $CHCl_3$), e.e. 90% (chiral HPLC analysis of the corresponding *N*,*N*-dibenzyl amide using a Chiralcel OJ column with a mixture of hexane and 2-propanol (9:1) at a flow rate 0.6 ml/min as the mobile phase, $t_{(-)}$ = 11.44 min, $t_{(+)}$ = 10.08 min), mp 95–96 °C ([28], mp 111.3–112 °C, DL form). ν_{max}(KBr) (cm^{-1}) 3351, 3181, 1662, 1623; δ_H 7.00 (br s, 2H), 1.39–1.51 (m, 1H), 1.28–1.34 (m, 1H), 1.20–1.26 (m, 1H), 1.12 (d, J 6.0 Hz, 3H), 0.70–0.76 (m, 1H); *m/z* (EI) 99 (M^+, 23%), 98 (54), 82 (20), 56 (100), 55 (46), 44 (38).

*3.1.3.2. (1S,2S)-(+)-2-Methylcyclopropanecarboxylic acid (**6**).* The 10 min (54%), $[\alpha]_D^{25}$ + 32.2 (*c* 2.7, $CHCl_3$) ([34], $[\alpha]_D^{20}$ + 77.8, e.e. 78.2%) e.e. 38% (chiral HPLC analysis of the corresponding benzyl ester using a Chiralcel OJ column with a mixture of hexane and 2-propanol (9:1) at a flow rate 0.6 ml/min as the mobile phase, $t_{(-)}$ = 8.77 min, $t_{(+)}$ = 9.65 min). Oil: ν_{max}(KBr) (cm^{-1}) 3500–2500, 1690; δ_H 10.06 (br s, 1H), 1.39–1.50 (m, 1H), 1.29–1.35 (m, 1H), 1.20–1.26 (m, 1H), 1.12 (d, J = 6.0 Hz, 3H), 0.72–0.78 (m, 1H); *m/z* (EI) 100 (M^+, 47%), 82 (21), 73 (8), 56 (24), 55 (100), 54 (31), 53 (20), 45 (33), 43 (23), 41 (31), 39 (44).

*3.1.4. Enzymatic hydrolysis of (±)-cis-2-methylcyclopropanecarboxamide (**7**)*

*3.1.4.1. 1R,2S-(+)-2-Methylcyclopropanecarboxamide (**8**).* The 4 h (48%), mp 117–119 °C, $[\alpha]_D^{25}$ + 3.4 (*c* 2.35, $CHCl_3$), e.e. 40%; 9 h (18%), $[\alpha]_D^{25}$ + 10 (*c* 0.8, $CHCl_3$), e.e. >99% [chiral HPLC analysis of the corresponding *N*,*N*-dibenzyl amide using a Chiralpak AD column with a mixture of hexane and 2-propanol (9:1) at a flow rate 0.6 ml/min as the mobile phase, $t_{(-)}$ = 10.99 min, $t_{(+)}$ = 12.32 min] ([20] $[\alpha]_D^{20}$ + 6.6 (*c* 0.97, $CHCl_3$), mp 100–101 °C ([20], mp 117.5–118 °C). ν_{max}(KBr) (cm^{-1}) 3357, 3193, 1659, 1625; δ_H 7.06 (br s, 2H), 1.64–1.71 (m, 1H), 1.32–1.43 (m, 1H), 1.20 (d, J = 6.1 Hz, 3H), 1.04–1.09 (m, 1H), 0.96–1.02 (m, 1H); *m/z* (EI) 99 (M^+, 12%), 98 (25), 82 (13), 56 (100), 55 (35), 44 (27).

*3.1.4.2. (1S,2R)-(+)-2-Methylcyclopropanecarboxylic acid (**9**).* The 1 h (22%), $[\alpha]_D^{25}$ + 24 (*c* 0.85, $CHCl_3$), e.e. 43%; 4 h (45%), $[\alpha]_D^{25}$ + 12.8 (*c* 2.25, $CHCl_3$), e.e. 31% (chiral HPLC analysis of the corresponding *N*,*N*-dibenzyl amide using a Chiralpak AD column with a mixture of hexane and 2-propanol (9:1) at a flow rate 0.6 ml/min as the mobile phase) ([35], $[\alpha]_D^{20}$ +8.0 (*c* 0.8). Oil: ν_{max}(KBr) (cm^{-1}) 3500–2500, 1685; δ_H 10.0 (br, 1H), 1.64–1.71 (m, 1H), 1.13–1.43

(m, 1H), 1.23 (d, $J = 6.2$ Hz, 3H), 1.05–1.14 (m, 1H), 0.91–0.96 (m, 1H); *m/z* (EI) 100 (M^+, 32%), 82 (27), 73 (10), 56 (60), 55 (100), 54 (34), 53 (21), 45 (29), 43 (28), 41 (33), 39 (37), 32 (31).

4. Conclusion

Rhodococcus sp. AJ270 efficiently catalyzes the enantioselective hydrolysis of 2,2-dimethylcyclopropanecarbonitrile and 2,2-dimethyl- and 2-methylcyclopropanecarboxamides under very mild conditions. The amidase involved in the microbial cells displays 1*S*-enantioselectivity against all amides tested. By controlling the reaction conditions of biotransformations, highly enantiomerically enriched *S*-(+)-2,2-dimethylcyclopropanecarboxylic acid and 1*R*,2*S*-(+)-2-methylcyclopropanecarboxamide, the concise building blocks for cilastatin and curacin A, respectively, are conveniently synthesized.

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References

[1] Z. Rappoport, The Chemistry of Cyano Group, Wiley/Interscience, New York, 1970.
[2] D. Evgred, S. Harnett, in: Proceedings of the Ciba Foundation Symposium 140 on Cyanide Compounds in Biology, Wiley, Chichester, 1988.
[3] J.-C. Jallegeas, A. Arnaud, P. Galzy, Adv. Biochem. Eng. 12 (1980) 1.
[4] J.L. Legras, G. Chuzel, A. Arnaud, P. Galzy, World J. Microbiol. Biotechnol. 6 (1990) 83.
[5] T. Sugai, T. Yamazaki, M. Yokoyama, H. Ohta, Biosci. Biotechnol. Biochem. 61 (1997) 1419.
[6] J. Crosby, J. Moiliet, J.S. Parratt, N.J. Turner, J. Chem. Soc., Perkin Trans. 1 (1994) 1679.
[7] A.J. Blakey, J. Colby, E. Williams, C. O'Reilly, FEMS Microbiol. Lett. 129 (1995) 57.
[8] O. Meth-Cohn, M.-X. Wang, J. Chem. Soc., Perkin Trans. 1 (1997) 1099.
[9] O. Meth-Cohn, M.-X. Wang, J. Chem. Soc., Perkin Trans. 1 (1997) 3197.
[10] M.-X. Wang, G. Lu, G.-J. Ji, Z.-T. Huang, O. Meth-Cohn, J. Colby, Tetrahedron: Asymmetry 11 (2000) 1123.
[11] M.-X. Wang, J.-J. Li, G.-J. Ji, J.-S. Li, J. Mol. Cat. B: Enzy. 14 (2001) 77.
[12] M.-X. Wang, S.-J. Lin, Tetrahedron Lett. 42 (2001) 6925.
[13] M.-X. Wang, G.-Q. Feng, Tetrahedron Lett. 41 (2000) 6501.
[14] G.-Q. Feng, M.-X. Wang, Chin. J. Chem. 19 (2001) 113.
[15] W.H. Gerwick, P.J. Proteau, D.G. Nagle, E. Hamel, A. Blokhin, D.L. Slate, J. Org. Chem. 59 (1994) 1243.
[16] Q. Wang, F. Yang, H. Du, M.M. Hossain, D. Bennett, D.S. Grubisha, Tetrahedron: Asymmetry 9 (1998) 3971 (and references cited therein).
[17] M.P. Doyle, M.N. Protopopova, Tetrahedron 54 (1998) 7919.
[18] A.B. Charette, J.F. Marcoux, Synlett (1995) 1197.
[19] R.G. Bergman, J. Am. Chem. Soc. 91 (1969) 7405.
[20] H. Ito, N. Imai, S. Tanikawa, S. Kobayashi, Tetrahedron Lett. 37 (1996) 1795.
[21] T. Onoda, R. Shirai, N. Kawai, S. Iwasaki, Tetrahedron 52 (1996) 13327.
[22] J.D. White, T.-S. Kim, M. Nambu, J. Am. Chem. Soc. 119 (1997) 103 (and references cited therein).
[23] K. Robins, T. Gilligan, US Patent 5,273,903 (1993).
[24] T. Zimmermann, K. Robins, O.M. Birch, E. Böhlen, US Patent 5,427,934 (1995).
[25] T. Sakai, I. Kawabata, T. Kishimoto, T. Ema, M. Utaka, J. Org. Chem. 62 (1997) 4906.
[26] C.-S. Chen, Y. Fujimoto, G. Girdaukas, C.J. Sih, J. Am. Chem. Soc. 104 (1982) 7294.
[27] K. Faber, H. Hoenig (Eds.), http://www.cis.TUGraz.at/orgc/.
[28] D.E. Applequist, A.H. Peterson, J. Am. Chem. Soc. 82 (1960) 2372.
[29] T. Toshima, A. Ichihara, Biosci. Biotechnol. Biochem. 59 (1995) 497.
[30] Z.-W. Guo, S.-H. Wu, C.-S. Chen, G. Girdaukas, C.J. Sih, J. Am. Chem. Soc. 112 (1990) 4942.
[31] E.D. Nelson, M. Maienthal, L.A. Lane, A.A. Benderly, J. Am. Chem. Soc. 79 (1957) 3467.
[32] T. Fujisawa, T. Ito, S. Nishiura, M. Shimizu, Tetrahedron Lett. 39 (1998) 9735.
[33] A. Mori, I. Arai, H. Yamamoto, H. Naki, Y. Arai, Tetrahedron 42 (1986) 6447.
[34] R. Ebens, R.M. Kellogg, Recl. Trav. Chim. Pays-Bas 109 (1990) 11552.
[35] T. Aratani, Y. Nakanisi, H. Nozaki, Tetrahedron 26 (1970) 1675.