Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters
Tetrahedron Letters 46 (2005) 4511–4514

Solvent-free biocatalytic amidation of carboxylic acids

Ashok K. Prasad,[a,*] Mofazzal Husain,[a,b] Brajendra K. Singh,[a] Rajinder K. Gupta,[b] Vijay K. Manchanda,[c] Carl E. Olsen[d] and Virinder S. Parmar[a,*]

[a]*Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi 100 007, India*
[b]*School of Biotechnology, GGSIP University, Kashmere Gate, Delhi 110 006, India*
[c]*Radiochemistry Division, Bhabha Atomic Research Center, Mumbai 400 085, India*
[d]*Chemistry Department, Royal Veterinary and Agricultural University, Frederiksberg C, DK-1871 Copenhagen, Denmark*

Received 20 December 2004; revised 6 April 2005; accepted 15 April 2005

Abstract—Lipase-catalyzed enantioselective amidation was performed by reacting the *racemic* amine with aliphatic acids in nonsolvent system. The reaction equilibrium was shifted towards amide synthesis by the removal of water under reduced pressure. This methodology avoids the use of activating agents and hazardous solvents.

1. Introduction

The synthesis of optically pure amides is an area of growing interest in synthetic chemistry,[1] amines and their derived amides are important compounds in organic synthesis because of the presence of these functional groups in many pharmacologically active compounds.[2–6] Synthesis of these compounds have mainly been achieved by classical chemical reactions, which generally involve the generation of a reactive carboxy derivative, either an acid chloride or anhydride, followed by aminolysis with amine.[7] Also, the conversion of esters to amides has some limitations as the commonly used reagents, that is, sodium methoxide, sodium hydride, sodium metal or butyl lithium often interfere with other functional groups present in the reacting species.[8–13]

Enzyme-catalyzed organic reactions have provided a great impetus to organic synthesis during the last two decades. Enzymes, especially lipases are known for their low cost and great tolerance towards their substrates. In recent past, we have used different lipases, viz. from porcine pancreas (PPL), *Candida rugosa* (CRL), *Candida antarctica* (CAL) and *Pseudomonas* sp. for carrying out the selective protection/deprotection of hydroxyl groups in different classes of compounds, for example, aryl alkyl ketones,[14,15] hydroxymethylated phenolic compounds,[16] triazolylsugars,[17,18] benzoxazines,[19] dihydrocoumarins[20] and chromanones.[21] The design of efficient methods for the preparation of optically active amines and amides is of special interest. Among the resolution-based procedures, the enzymatic methods are emerging as a useful alternative. Thus, lipase B from *C. antarctica* (CAL-B) has proven to be the most efficient catalyst for aminolysis reactions in organic solvents, allowing the preparation of variety of optically active primary amines and amides.[22–28] Environmentally benign character of the enzymatic processes is desirable for large scale industrial applications.[29] We report herein the lipase-catalyzed amidation of free carboxylic acids in bulk (under solvent-free conditions).

It would often be convenient to prepare chiral amides directly from carboxylic acids, but a straightforward reaction of acid and amine is not feasible. We envisaged to develop a one-pot biocatalytic amidation procedure by using lipase as catalyst. In this report, we have carried out *C. antarctica* lipase (CAL-B) catalyzed enantioselective amidation of aliphatic acids by *racemic* 2-ethylhexyl amine in bulk (without solvent) at 90 °C.

2. Results and discussion

We carried out the amidation of aliphatic acids, namely propanoic acid (**1a**), butanoic acid (**1b**), 2-methylpropanoic

Keywords: Lipase; Enantioselective; Amidation; Bulk reaction; Chiral amide.
* Corresponding authors. Tel.: +91 11 27666555; fax: +91 11 27667206 (A.K.P.); e-mail: ashokenzyme@yahoo.com

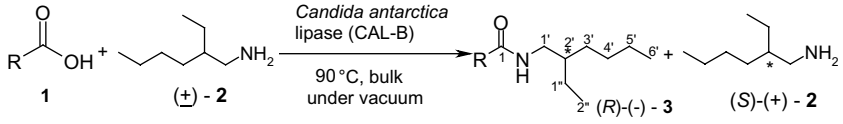
0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.04.121

acid (**1c**), pentanoic acid (**1d**), hexanoic acid (**1e**) and octanoic acid (**1f**) with *racemic* 2-ethylhexyl amine (**2**) to obtain the corresponding highly enantiomerically enriched amides, that is, (*R*)-(−)-*N*-2-ethylhexylpropanamide (**3a**), (*R*)-(−)-*N*-2-ethylhexylbutanamide (**3b**), (*R*)-(−)-*N*-2-ethylhexyl (2-methyl)propanamide (**3c**), (*R*)-(−)-*N*-2-ethylhexylpentanamide (**3d**), (*R*)-(−)-*N*-2-ethylhexylhexanamide (**3e**) and (*R*)-(−)-*N*-2-ethylhexyloctanamide (**3f**) (Scheme 1).

The best conversion of acids to amides was observed by using CAL-B in bulk (without solvent) at 90 °C under vacuum, no reaction occurred in organic solvents, that is, diisopropyl ether, tetrahydrofuran and acetonitrile. PPL and CRL did not catalyze the amidation reaction. As all the amides as well as the unreacted amine were found to be optically active (Table 1), it is indicated that the CAL-B-catalyzed amidation is enantioselective. It is noteworthy to mention that no amidation was observed when these reactions were carried out under identical conditions, but without the addition of CAL-B.

First, the feasibility of a nonsolvent system was investigated. The reactions with one mole of amine **2** and half mole of carboxylic acid (Scheme 1) were performed. The reaction mixture was very viscous and the reaction temperature had to be raised up to 90 °C in order to achieve an efficient stirring in the system. Recently Irimescu and Katu[30] reported lipase catalyzed amide synthesis. They have used equimolar amounts of amine and carboxylic acid and heated it up to 55 °C, but the reaction did not go to completion as some unreacted acid and amine remained in the reaction mixture in salt form even after incubating the mixture for longer times. In our study, we have overcome this problem by heating the reaction mixture up to 90 °C under reduced pressure and found 100% conversion of acids obtaining corresponding amides in 80–91% isolated yields. The unreacted amine and amide were separated by column chromatography and both were found to be optically active (Table 1).

The chiral amides **3a**–**f** and amine **2** were fully characterized from their spectral data, the six amides **3a**–**f** have been synthesized for the first time. The ee value of unreacted amine **2** in all the six amidation reactions was calculated by comparing the sign and specific rotation value of the unreacted amine **2** with that of commercially available optically pure (*R*)-(−)-2-ethylhexyl



Compounds 1 & 3	R
a	CH_2CH_3
b	$CH_2CH_2CH_3$
c	$CH(CH_3)CH_3$
d	$CH_2(CH_2)_2CH_3$
e	$CH_2(CH_2)_3CH_3$
f	$CH_2(CH_2)_5CH_3$

Scheme 1.

Table 1. *Candida antarctica* lipase (CAL-B) catalyzed enantioselective amidation of aliphatic acids with *racemic* 2-ethylhexyl amine in bulk[a]

Acid	Amine	Reaction time[b] (h)	(*R*)-(−)-Amide[c]		Unreacted (*S*)-(+)-2-ethylhexyl amine (**2**) (ee >99%)[c]	
			Compound[d]	% Yield	% Yield	$[\alpha]_D$[e]
1a	(±)-2	11	**3a**	85	45	+16.4 (*c* 0.48)
1b	(±)-2	12	**3b**	88	43	+15.0 (*c* 0.55)
1c	(±)-2	20	**3c**	80	40	+15.2 (*c* 0.50)
1d	(±)-2	12	**3d**	91	43	+14.0 (*c* 0.50)
1e	(±)-2	14	**3e**	88	46	+13.5 (*c* 0.60)
1f	(±)-2	16	**3f**	85	42	+14.0 (*c* 0.43)

[a] All these reactions, when performed under identical conditions but without adding CAL-B, did not yield any product.
[b] Reaction mixture was quenched after 50% conversion of 2-ethylhexyl amine in all the cases.
[c] Absolute configuration and ee values were determined by comparing the sign and specific rotation value of the unreacted amine **2** with that of enantiomerically pure (*R*)-(−)-2-ethylhexyl amine, which is commercially available (Norse Lab, CA, USA).
[d] Optical rotation values of compounds **3a**–**f** have not been mentioned in the table because they are already given in Section 4.
[e] Optical rotation values were recorded in $CHCl_3$ at 20 °C.

amine and was found to be more than 99% in all the six cases. So we believe that the ee of optically enriched amides **3a**–**f** is 99%, or more as well.

To our knowledge, the results presented in this study demonstrate for the first time the chiral amide synthesis in nonsolvent system by the direct lipase-catalyzed reaction of amines with carboxylic acids and this study may find applications in the kinetic resolution of primary amines. The present enzymatic procedure offers some important advantages over the chemical one for the application in industrial processes. In addition, the enantioselectivity of lipase allows the kinetic resolution of chiral substrates. In comparison to other lipase-catalyzed systems used to date, the reaction rates and conversions are comparable to the reactions employing other more expensive acyl donors such as esters or carbonates.[31]

3. Conclusion

We have developed a novel, efficient and environmentally benign method affording optically enriched amides. This method may find general utility towards the synthesis of analogous compounds in optically enriched form as it is difficult to synthesize amides directly from carboxylic acids and amines by purely chemical means in enantoimerically pure form. The highly optically enriched amides (ee's >99%) were exclusively obtained in high yields (80–91%).

4. Experimental

The IR spectra were recorded either on a Perkin–Elmer 2000 FT-IR or RXI FT-IR spectrophotometer. The optical rotations were measured with Bellingham Stanley AD 220 polarimeter. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 Avance spectrometer at 300 and at 75.5 MHz, respectively, using TMS as internal standard. The chemical shifts values are on δ scale and the coupling constants (J) are in Hertz. The FAB-HRMS spectra of all the compounds to measure their accurate masses were recorded on a JEOL JMS-AX505W high-resolution mass spectrometer in positive mode using the matrix HEDS (bishydroxyethylsulfide) doped with sodium acetate. The *C. antarctica* lipase, immobilized on accurel was gifted by Novo Nordisk Co. and used after storing in vacuo over P_2O_5 for 30 h. Analytical TLCs were performed on pre-coated Merck silica gel $60F_{254}$ plates; the spots were detected by treating the TLC plate with iodine. Silica gel (100–200 mesh) was used for column chromatography.

4.1. General method for the amidation of acids using *C. antarctica* lipase

To a mixture of the acid (**1a**–**f**, 2.5 mmol) and *racemic* 2-ethylhexyl amine (**2**, 5.0 mmol), CAL-B (300 mg) was added. The reaction mixture was heated at 90 °C under vacuum with stirring and progress of reaction was monitored by IR spectra. When the acid was consumed completely, the reaction mixture was diluted with dichloromethane and quenched by filtering off the enzyme. The organic solvent was evaporated under vacuo and the residue was subjected to column chromatography using petroleum ether/ethyl acetate as eluent to afford the pure amide and the unreacted amine in optically enriched forms.

4.1.1. (*R*)-(−)-*N*-2-Ethylhexylpropanamide (3a). It was obtained as viscous oil (393 mg) in 85% yield. R_f: 0.47 (ethyl acetate–petroleum ether, 2:8); $[\alpha]_D^{20}$ −11.12 (*c* 0.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (6H, t, J = 7.2 Hz, C-6′H and C-2″H), 1.16 (3H, t, J = 7.61 Hz, C-3H), 1.27–1.34 (8H, m, C-3′H, C-4′H, C-5′H and C-1″H), 1.36–1.43 (1H, m, C-2′H), 2.20 (2H, q, J = 7.57 Hz, C-2H), 3.19 (2H, t, J = 5.95 Hz, C-1′H) and 5.56 (1H, br s, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.84 (C-2″), 10.72 (C-6′), 13.86 (C-3), 22.85, 24.15, 28.76 and 29.69 (C-3′, C-4′, C-5′ and C-1″), 30.90 (C-2), 39.30 (C-2′), 42.24 (C-1′) and 173.65 (C=O); IR (Nujol) cm^{-1}: 3297 (NH), 1647 (C=O), 1556, 1462, 1377, 1272, 1238, 1144 and 1051; FAB-HRMS: *m*/*z* 186.1856 ($[M+H]^+$, $C_{11}H_{23}NO$+H calcd 186.1858).

4.1.2. (*R*)-(−)-*N*-2-Ethylhexylbutanamide (3b). It was obtained as viscous oil (434 mg) in 88% yield. R_f: 0.49 (ethyl acetate–petroleum ether, 2:8); $[\alpha]_D^{20}$ −10.25 (*c* 0.47, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (9H, t, J = 7.2 Hz, C-4H, C-6′H, C-2″H), 1.27–1.33 (8H, m, C-3′H, C-4′H, C-5′H and C-1″H), 1.36–1.43 (1H, m, C-2′H), 1.62–1.70 (2H, m, C-3H), 2.15 (2H, t, J = 7.30 Hz, C-2H), 3.19 (2H, t, J = 5.87 Hz, C-1′H) and 5.55 (1H, br s, NH); ^{13}C NMR (75.5 MHz $CDCl_3$): δ 10.90 (C-2″), 13.79 and 14.05 (C-4 and C-6′), 19.31, 23.04, 24.33 and 28.94 (C-3′, C-4′, C-5′ and C-1″), 31.09 (C-3), 38.91 (C-2), 39.49 (C-2′), 42.36 (C-1′) and 173.06 (C=O); IR (Nujol) cm^{-1}: 3299 (NH), 1645 (C=O), 1556, 1470, 1381, 1246 and 1095; FAB-HRMS: *m*/*z* 200.2019 ($[M+H]^+$, $C_{12}H_{25}NO$+H calcd 200.2014).

4.1.3. (*R*)-(−)-*N*-2-Ethylhexyl (2-methyl)propanamide (3c). It was obtained as viscous oil (393 mg) in 80% yield. R_f: 0.50 (ethyl acetate–petroleum ether, 2:8); $[\alpha]_D^{20}$ −13.12 (*c* 0.47, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (6H, t, J = 7.2 Hz, C-6′H and C-2″H), 1.15 (6H, d, J = 6.9 Hz, $CH(CH_3)_2$), 1.27–1.35 (8H, m, C-3′H, C-4′H, C-5′H and C-1″H) 1.41–1.45 (1H, m, C-2′H), 2.30–2.37 (1H, m, C-2H), 3.18 (2H, t, J = 5.97 Hz, C-1′H) and 5.51 (1H, br s, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.24 (C-2″), 14.34 (C-6′), 20.04 ($CH(CH_3)_2$), 23.33, 24.68, 29.24 and 31.40 (C-3′, C-4′, C-5′ and C-1″), 36.15 (C-2), 39.82 (C-2′), 42.58 (C-1′) and 177.30 (C=O); IR (Nujol) cm^{-1}: 3300 (NH), 1646 (C=O), 1554, 1468, 1379, 1244 and 1096; FAB-HRMS: *m*/*z* 200.2024 ($[M+H]^+$, $C_{12}H_{25}NO$+H calcd 200.2014).

4.1.4. (*R*)-(−)-*N*-2-Ethylhexylpentanamide (3d). It was obtained as viscous oil (483 mg) in 91% yield. R_f: 0.52 (ethyl acetate–petroleum ether, 2:8); $[\alpha]_D^{20}$ −11.86 (*c* 0.50, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (9H, t, J = 7.53 Hz, C-5H, C-6′H and C-2″H), 1.27–1.38 (10H, m, C-3H, C-3′H, C-4′H, C-5′H and

C-1″H), 1.40–1.43 (1H, m, C-2′H), 1.58–1.64 (2H, m, C-4H), 2.18 (2H, t, $J = 7.47$ Hz, C-2H), 3.18 (2H, t, $J = 5.95$ Hz, C-1′H) and 5.75 (1H, br s, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.15 (C-2″), 14.07 and 14.31 (C-5 and C-6′), 22.72, 23.31, 24.59, 28.30 and 29.21 (C-3, C-3′, C-4′, C-5′ and C-1″), 31.35 (C-4), 36.94 (C-2), 39.74 (C-2′), 42.67 (C-1′) and 173.54 (C=O); IR (Nujol) cm^{-1}: 3294 (NH), 1645 (C=O), 1556, 1463, 1379, 1271, 1235, 1202, 1144 and 1114; FAB-HRMS: *m/z* 214.2190 ($[M+H]^+$, $C_{13}H_{27}NO+H$ calcd 214.2171).

4.1.5. (*R*)-(−)-*N*-2-Ethylhexylhexanamide (3e). It was obtained as viscous oil (500 mg) in 88% yield. R_f: 0.56 (ethyl acetate–petroleum ether, 2:8); $[\alpha]_D^{20}$ −10.12 (*c* 0.60, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (9H, t, $J = 7.25$ Hz, C-6H, C-6′H and C-2″H), 1.27–1.33 (12H, m, C-3H, C-4H, C-3′H, C-4′H, C-5′H and C-1″H), 1.36–1.43 (1H, m, C-2′H), 1.60–1.65 (2H, m, C-5H), 2.17 (2H, t, $J = 7.35$ Hz, C-2H), 3.18 (2H, t, $J = 5.95$ Hz, C-1′H) and 5.17 (1H, br s, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.17 (C-2″), 14.24 and 14.34 (C-6 and C-6′), 22.74, 23.34, 24.59, 25.91, 29.22, 31.36 and 31.82 (C-3, C-4, C-5, C-3′, C-4′, C-5′ and C-1″), 37.21 (C-2), 39.75 (C-2′), 42.67 (C-1′) and 173.55 (C=O); IR (Nujol) cm^{-1}: 3296 (NH), 1645 (C=O), 1555, 1464, 1380, 1273, 1235, 1202, 1144 and 1113; FAB-HRMS: *m/z* 228.2336 ($[M+H]^+$, $C_{14}H_{29}NO+H$ calcd 228.2327).

4.1.6. (*R*)-(−)-*N*-2-Ethylhexyloctanamide (3f). It was obtained as viscous oil (541 mg) in 85% yield. R_f: 0.60 (ethyl acetate–petroleum ether, 2:8); $[\alpha]_D^{20}$ −9.25 (*c* 0.50, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (9H, t, $J = 7.25$ Hz, C-8H, C-6′H and C-2″H), 1.20–1.28 (16H, m, C-3H, C-4H, C-5H, C-6H, C-3′H, C-4′H, C-5′H and C-1″H), 1.34–1.40 (1H, m, C-2′H), 1.52–1.55 (2H, m, C-7H), 2.09 (2H, t, $J = 7.52$ Hz, C-2H), 3.11 (2H, t, $J = 5.95$ Hz, C-1′H) and 5.66 (1H, br s, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.86 (C-2″), 13.02 (C-8 and C-6′), 21.60, 22.02, 23.28, 24.93, 27.91, 28.06, 28.30, 30.05 and 30.73 (C-3, C-4, C-5, C-6, C-7, C-3′, C-4′, C-5′ and C-1″), 35.94 (C-2), 38.94 (C-2′), 41.36 (C-1′) and 172.25 (C=O); IR (Nujol) cm^{-1}: 3293 (NH), 1644 (C=O), 1555, 1463, 1379, 1271, 1144 and 1118; FAB-HRMS: *m/z* 256.2668 ($[M+H]^+$, $C_{16}H_{33}NO+H$ calcd 256.2640).

Acknowledgements

We thank the Board for Research in Nuclear Sciences (BRNS, DAE, Government of India) for financial assistance.

References and notes

1. Copala, G. M.; Shuster, H. F. *Asymmetric Synthesis: Construction of Chiral Molecules Using Amino Acids*; Wiley: New York, 1987.
2. Chauvette, R. R.; Pennington, P. A.; Ryan, C. W.; Cooper, R. D.; Jose, F. L.; Wright, I. G.; van Heyningen, E. M.; Huffman, G. W. *J. Org. Chem.* **1971**, *36*, 1259.
3. Parmar, V. S.; Jain, S. C.; Gupta, S.; Talwar, S.; Rajwanshi, V. K.; Kumar, R.; Azim, A.; Malhotra, S.; Kumar, N.; Jain, R.; Sharma, N. K.; Tyagi, O. D.; Lawrie, S. J.; Errington, W.; Howarth, O. W.; Olsen, C. E.; Singh, S. K.; Wengel, J. *Phytochemistry* **1998**, *49*, 1069.
4. Henkel, T.; Brunne, R. M.; Muller, H.; Reichel, F. *Angew. Chem. Int. Ed.* **1999**, *38*, 643.
5. Parmar, V. S.; Jain, S. C.; Bisht, K. S.; Jain, R.; Taneja, P.; Jha, A.; Tyagi, O. D.; Prasad, A. K.; Wengel, J.; Olsen, C. E.; Boll, P. M. *Phytochemistry* **1997**, *46*, 597.
6. Brown, A. R.; Ress, D. C.; Rankovie, Z.; Morphy, J. R. *J. Am. Chem. Soc.* **1997**, *119*, 3288.
7. Philbrook, G. E. *J. Org. Chem.* **1954**, *19*, 623.
8. Russel, P. B. *J. Am. Chem. Soc.* **1950**, *72*, 1853.
9. Feo, R. J. D.; Strickler, P. D. *J. Org. Chem.* **1963**, *28*, 2915.
10. Singh, B. *Tetrahedron Lett.* **1971**, 321.
11. Stern, E. S. *Chem. Ind. (London)* **1956**, 277.
12. Yang, K. W.; Cannon, J. G.; Rose, J. G. *Tetrahedron Lett.* **1970**, 1791.
13. Evans, D. A. *Tetrahedron Lett.* **1969**, 1573.
14. Prasad, A. K.; Pati, H. N.; Azim, A.; Trikha, S.; Poonam *Bioorg. Med. Chem.* **1999**, *7*, 1973.
15. Kumar, R.; Azim, A.; Kumar, V.; Sharma, S. K.; Prasad, A. K.; Howarth, O. W.; Olsen, C. E.; Jain, S. C.; Parmar, V. S. *Bioorg. Med. Chem.* **2001**, *9*, 2643.
16. Parmar, V. S.; Prasad, A. K.; Pati, H. N.; Kumar, R.; Azim, A.; Roy, S.; Errington, W. *Bioorg. Chem.* **1999**, *27*, 119.
17. Prasad, A. K.; Himanshu; Bhattacharya, A.; Olsen, C. E.; Parmar, V. S. *Bioorg. Med. Chem.* **2002**, *10*, 947.
18. Bhattacharya, A.; Prasad, A. K.; Maity, J.; Himanshu; Poonam; Olsen, C. E.; Gross, R. A.; Parmar, V. S. *Tetrahedron* **2003**, *59*, 10269.
19. Shakil, N. A.; Dhawan, A.; Sharma, N. K.; Kumar, V.; Kumar, S.; Bose, M.; Raj, H. G.; Olsen, C. E.; Cholli, A. L.; Samuelson, L. A.; Kumar, J.; Watterson, A. C.; Parmar, V. S.; Prasad, A. K. *Indian J. Chem.* **2003**, *42B*, 1958.
20. Singh, I.; Prasad, A. K.; Sharma, A. K.; Saxena, R. K.; Olsen, C. E.; Cholli, A. L.; Samuelson, L. A.; Kumar, J.; Watterson, A. C.; Parmar, V. S. *Bioorg. Med. Chem.* **2003**, *11*, 529.
21. Poonam; Prasad, A. K.; Azim, A.; Kumar, R.; Jain, S. C.; Parmar, V. S.; Olsen, C. E.; Errington, W. *Tetrahedron* **2001**, *57*, 7395.
22. Gonzalez-Sabin, J.; Gotor, V.; Rebolledo, F. *Tetrahedron: Asymmetry* **2004**, *15*, 481.
23. Jacobsen, E. E.; Hoff, B. H.; Moen, A. R.; Anthonsen, T. J. *Mol. Catal. B: Enzymatic* **2003**, *21*, 55.
24. Skupinska, K. A.; McEachern, E. J.; Baird, I. R.; Skerlj, R. T.; Bridger, G. J. *J. Org. Chem.* **2003**, *68*, 3546.
25. Gonzalez-Sabin, J.; Gotor, V.; Rebolledo, F. *Tetrahedron: Asymmetry* **2002**, *13*, 1315.
26. Badjic, J. D.; Kadnikova, N. E.; Kostic, N. M. *Org. Lett.* **2001**, *3*, 2025.
27. Azim, A.; Sharma, S. K.; Olsen, C. E.; Parmar, V. S. *Bioorg. Med. Chem.* **2001**, *9*, 1345.
28. de Castro, M. S.; Dominguez, P.; Sinisterra, J. *Tetrahedron* **2000**, *56*, 1387.
29. Schmid, A.; Dordick, J. S.; Hauer, B.; Kieners, A.; Wubbolts, M.; Witholt, B. *Nature* **2001**, *409*, 258.
30. Irimescu, R.; Katu, K. *Tetrahedron Lett.* **2004**, *45*, 523.
31. van Rantwijk, F.; Hacking, M. A. P. J.; Sheldon, R. A. *Monatsh. Chem.* **2000**, *131*, 549.