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DEVELOPMENT OF A NOVEL METHOD FOR WARFARIN SYNTHESIS VIA LIPASE-CATALYZED STEREOSELECTIVE MICHAEL REACTION

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Abstract – Stereoselective synthesis of warfarin by promiscuous lipase-catalyzed Michael reaction of 4-hydroxycoumarin to benzylideneacetone has been developed. The best result was obtained using lipase AS as a catalyst in anhydrous DMSO with 1:3 molar ratio of 4-hydroxycoumarin to benzylideneacetone at 20 ºC for 7 days. The yield and enantiomeric excess were 85% and 45% ee (*R*-form), respectively.

INTRODUCTION

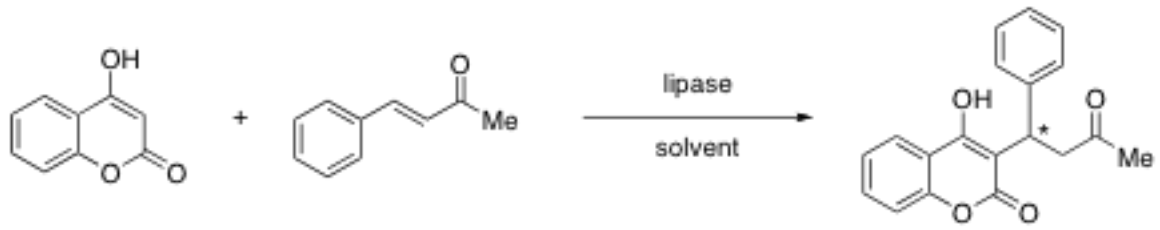
Enzymatic catalytic promiscuity is an enzyme's ability to catalyze an unexpected reaction. A catalytically promiscuous enzyme will catalyze more than one type of chemical reaction—the natural reaction as well as one or more unexpected reactions. Promiscuous reactions may be non-natural reactions that are useful for synthesis. Many type of enzymatic promiscuous reactions have been reported, especially in the last decade. For example, hydrolases, such as lipases and acylases catalyze the construction of carbon–carbon, carbon–nitrogen, carbon–oxygen, and carbon–sulfur bonds *via* Michael reaction and Markovnikov additions,[1] and racemases[2] and arylmalonate decarboxylase[3] catalyze the aldol reaction, etc. Among these reactions, conjugate addition of nucleophiles to α,β-unsaturated carbonyl compounds, *i.e.*, the Michael

reaction, is one of the most attractive. Since the first report by Kitazume *et al*., [1a] several groups has reported enzymatic promiscuous Michael reactions. Serine hydrolases are the most commonly used enzymes for biocatalysis. However, only a few of these enzymes afford enantioselectivity. [1i,j]

A wide range of 4-hydroxycoumarins are used as pharmaceuticals such as anticoagulants and substances that inhibit HIV or malaria.[4,5] Among the most prominent chiral 4-hydroxycoumarins is warfarin, which works as a vitamin K antagonist and is one of the most effective anticoagulants. Although both enantiomers of warfarin show anticoagulant activity, and warfarin has been in clinical use as a racemate for more than 50 years, the enantiomers have different metabolic pathways, and the activity of the *S*-form is three to five times stronger than that of the *R*-form.[6] Furthermore, the enantiomers are metabolized by different drug metabolizing enzymes,[7] administering optically pure warfarin is the possibility of eliminating genetic problems and/or drug-drug interactions. Especially, patients expressing certain allelic variants of CYP2C9 which metabolize (*S*)- but not (*R*)-warfarin can avoid the risk of bleeding complications if they administer pure (*R*)-warfarin.[8] Previously reported enantioselective syntheses of warfarin were mainly accomplished by transition–metal catalysis[9] or organocatalysis,[10] or with the use of a chiral auxiliary;[11] however, enantioselectivity of biocatalytic preparation of warfarin has been unsatisfied.[1j] In this paper, we present a stereoselective synthesis of warfarin using a lipase–catalyzed Michael reaction.

RESULTS AND DISCUSSION

The synthesis of warfarin was performed by the Michael reaction of 4-hydroxycoumarin to benzylideneacetone (Scheme 1).



Scheme 1. Synthesis of warfarin *via* Michael reaction of 4-hydroxycoumarin to benzylideneacetone

First, a series of commercially available lipases were screened as catalysts in MeOH; the results are summarized in Table 1.

As can be seen from Table 1, lipase AS is the best catalyst among the lipases tested for the Michael reaction (20% yield and 5% ee, Table 1, entry 4). Immobilized lipase had moderate activity (7% yield and 4% ee, Table 1, entry 7), whereas the other lipases tested gave low to medium conversions with no stereoselectivity. To confirm whether the reaction was lipase catalyzed, the reaction was conducted with no enzyme; the product was not observed.

Table 1. Enzyme screening for Michael reaction of 4-hydroxycoumarin to benzylideneacetone in MeOH.

Entry	Enzyme	Yield (%)	ee (%)
1	Lipase PL (Meito)	25	-
2	Lipase AK (Amano)	9	-
3	Lipase OF (Meito)	9	-
4	Lipase AS (Amano)	20	5 (*R*)
5	Lipase QLM (Meito)	28	-
6	Lipase-F-AP-15 (Wako)	9	-
7	immobilized lipase (Toyobo)	7	4 (*R*)
8	Lipase TL (Meito)	7	-
9	Lipase AYS (Amano)	3	-
10	Lipase MY-30 (Meito)	2	-
11	Lipase SL (Meito)	16	-
12	Lipase PS (Amano)	1	-
13	porcine pancreas lipase	25	-
14	no enzyme	n.d.	-

Experimental conditions: benzylideneacetone (0.14 mmol), 4-hydroxycoumarin (0.14 mmol) and lipase (28.4 mg) in MeOH (0.7 mL) were stirred under N_2 at 30 ^oC for 72 h. *n.d.: not detected

The nature of the reaction medium is an important parameter in enzyme-catalyzed reactions, because of its effects on enzyme stability and substrate solubility. Some conventional organic solvents were therefore surveyed. The results indicated that different solvents had significant effects on the activity and enantioselectivity of the lipase AS–catalyzed Michael reaction (Table 2). The best results were obtained

Table 2. Solvent screening for Michael reaction of 4-hydroxycoumarin to benzylideneacetone catalyzed by lipase AS.

Entry	Solvent	Yield (%)	ee (%)
1	DMSO	39	29
2	DMF	21	19
3	acetone	3	-
4	$CHCl_3$	3	-
5	EtOAc	5	-
6	THF	9	-
7	1,4-dioxane	5	-
8	Et_2O	3	-
9	toluene	2	-
10	*n*-Hexane	n.d.	-
11	Cyclohexane	n.d.	-
12	H_2O	n.d.	-
13	ethylene glycol	17	-
14	MeOH	28	5
15	EtOH	3	7
16	*n*-PrOH	3	-

Experimental conditions: benzylideneacetone (0.14 mmol), 4-hydroxycoumarin (0.14 mmol) and lipase AS (28.4 mg) in solvent (0.7 mL) were stirred under N_2 at 30 ^oC for 72 h.

in DMSO and DMF with product yields of 39% and 21%, and enantioselectivities of 29% and 19% ee, respectively (Table 2, entries 1 and 2), after 72 h. In contrast, no enantioselectivity was observed in some of the solvents tested, namely acetone, $CHCl_3$, EtOAc, THF, 1,4-dioxane, Et_2O, toluene, *n*-PrOH (Table 2, entries 3-9, and 16). Moreover, lipase AS did not show any obvious activity in cyclohexane, *n*-hexane, and H_2O (Table 2, entries 10–12). The reason for this seemed to be poor solubilities of the substrates in these solvents.

Since the reaction seemed to give better chemical yields and enantioselectivities in aprotic polar solvents as shown in Table 2, we performed the reaction in various aprotic polar solvents. As expected, the products showed optical activities, but the enantioselectivities were low: 3-17% ee in acetylacetone, acrylonitrile, nitromethane, trichloroacetone, MeCN, DMAC, and NMP (Table 3). DMSO and DMF were therefore used in the following process.

Table 3. Michael reactions of 4-hydroxycoumarin to benzylideneacetone catalyzed by lipase AS in various aprotic polar solvents.

Entry	Solvent	Yield (%)	ee (%)
1	acetylacetone	2	3
2	acrylonitrile	13	3
3	nitromethane	10	8
4	trichloroacetone	3	4
5	MeCN	5	4
6	DMAC	12	17
7	NMP	14	14
8	HMPA	9	-

Experimental conditions: benzylideneacetone (0.14 mmol), 4-hydroxycoumarin (0.14 mmol) and lipase AS (28.4 mg) in solvent (0.7 mL) were stirred under N_2 at 30 ^{o}C for 72 h.

Some enzymes require specific amount of H_2O bound to them to maintain enzymatic activity; it is therefore important to confirm the optimal H_2O content for the reaction system. The influence of H_2O concentration on the lipase AS-catalyzed Michael reaction was therefore investigated. The mixed solvents tested were 90%, 50% and 10% DMSO/H_2O. Anhydrous DMSO and DMF were also used to evaluate the effect of H_2O (Table 4). The chemical yield and enantioselectivity decreased on addition of H_2O (Table 4, entries 1–3). Moreover, when anhydrous solvents were employed, the model reaction gave better yields with product yields of 60% and 27%, and enantioselectivities of 28% and 18% ee, respectively (Table 4, entries 4 and 5) compared with those achieved using the normal grade of the solvent (Table 2, entries 1 and 2). These results indicated that the best solvent for the lipase AS-catalyzed Michael reaction was anhydrous DMSO. These results contradict the report by Xie *et al.*;[1j] they obtained best result in 90% DMSO/H_2O. Since lipases are very varied in their amino acid sequences and three-dimensional conformational structure (the molecular weight of the lipases tested in this research were 30–130 KDa),

they might have different enzymatic natures, depending on their structures.

Table 4. Influence of water concentration on Michael reaction of 4-hydroxycoumarin to benzylideneacetone catalyzed by lipase AS.

Entry	Solvent	Yield (%)	ee (%)
1	90% DMSO/H_2O	18	14
2	50% DMSO/H_2O	9	3
3	10% DMSO/H_2O	3	-
4	anhydrous DMSO	60	28
5	anhydrous DMF	27	18

Experimental conditions: benzylideneacetone (0.14 mmol), 4-hydroxycoumarin (0.14 mmol) and lipase AS (28.4 mg) in solvent (0.7 mL) were stirred under N_2 at 30 ^oC for 72 h.

To further improve the lipase AS-catalyzed Michael reaction, the effects of the molar ratio of benzylideneacetone to 4-hydroxycoumarin on the reaction were investigated (Table 5). The molar ratio of the substrates had a significant effect on the product yield. An optimal yield of 73% was obtained with a 1:3 molar ratio of 4-hydroxycoumarin to benzylideneacetone at 30 ºC (Table 5, entry 4). Further increasing the number of equivalents of benzylideneacetone gave poorer results than expected (Table 5, entry 5 and 6).

Table 5. Effect of molar ratio of 4-hydroxycoumarin (4-h) to benzylideneacetone (be)

Entry	Molar equivalent (4-h:be)	Yield (%)	ee (%)
1	3:1	40	18
2	1:1	60	28
3	1:2	65	24
4	1:3	73	27
5	1:4	74	28
6	1:5	74	25

Experimental conditions: substrates, in the molar ratios shown in the table (multiples of 0.14 mmol of substrates), and lipase AS (28.4 mg) in anhydrous DMSO (0.7 mL) were stirred under N_2 at 30 ^oC for 72 h.

Substrate solubility, enzyme stability, and enzymatic activity are strongly associated with the reaction temperature. The effects of temperature on the lipase AS-catalyzed Michael reaction of 4-hydroxycoumarin to benzylideneacetone were investigated at temperatures ranging from 10 ºC to 60 ºC (Figure 1). Although the yield from the enzymatic reaction was significantly increased by raising the temperature, the enantioselectivity of the product decreased with increasing temperature. Additionally, when we performed the reaction with no enzyme at each temperature, no product was detected. Thus, we estimated that the reaction did not proceed spontaneously but catalyzed by the enzyme. The best ee, 45%, with a low yield of 64% was obtained at 20 ºC, and the best yield, 92%, with only 3% ee, was obtained at

60 ºC, after 72 h. Taking both the activity and stereoselectivity of the enzyme into account, we chose 20 ºC for optimizing the reaction conditions.

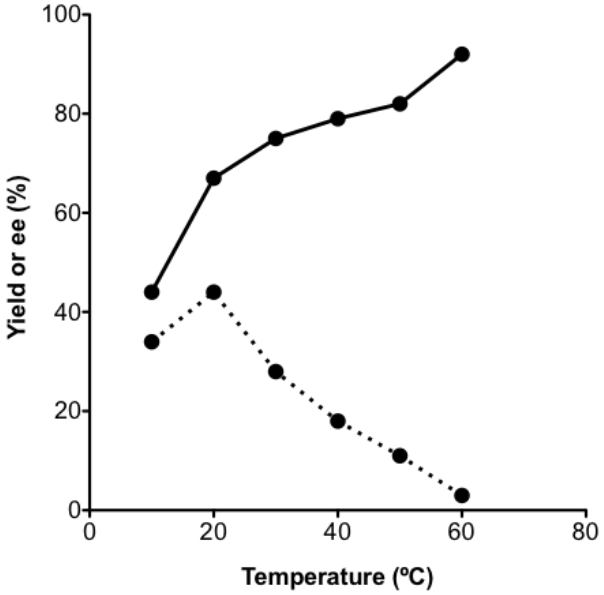


Figure 1. Influence of temperature on lipase AS-catalyzed Michael reaction. Yield, solid line; ee, dotted line. Experimental conditions: benzylideneacetone (0.42 mmol), 4-hydroxycoumarin (0.14 mmol), and lipase AS (28.4 mg) in anhydrous DMSO (0.7 mL) were stirred under N_2 for 72 h.

We then investigated the time course of lipase AS-catalyzed Michael reaction of 4-hydroxycoumarin to benzylideneacetone (Figure 2). The best yield, 85%, was obtained after 7 days but further increasing the reaction time failed to improve the yield. The ee remained constant during the whole reaction period.

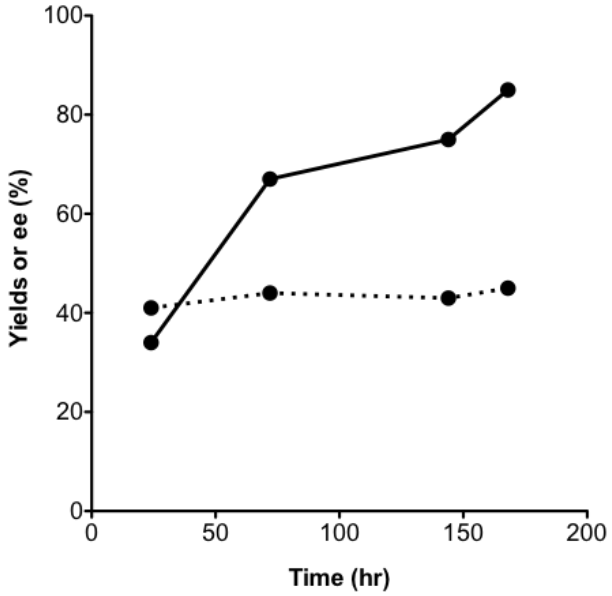
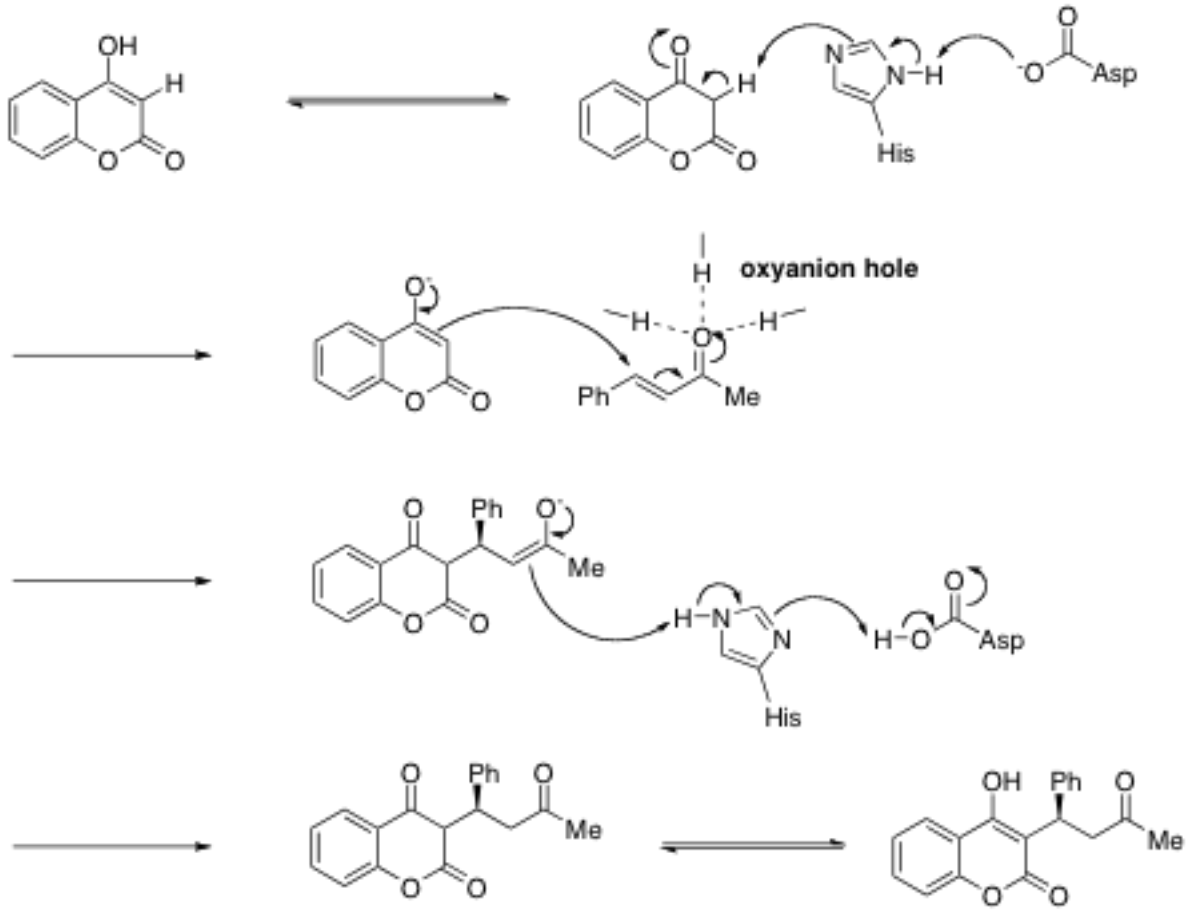


Figure 2. Time course of lipase AS-catalyzed Michael reaction. Yield, solid line; ee, dotted line. Experimental conditions: benzylideneacetone (0.42 mmol), 4-hydroxycoumarin (0.14 mmol), and lipase AS (28.4 mg) in anhydrous DMSO (0.7 mL) were stirred under N_2 at 20 ºC.

Generically, hydrolases present histidine, aspartic acid and serine in their active site for hydrolysis. Although the amino acid sequence of lipase AS has still not been clarified, we suppose that histidine, aspartic acid and oxyanion hole contribute to the mechanism of this lipase-catalyzed Michael reaction. As shown in Scheme 2, 4-hydroxycoumarin possesses carbonyl-enol tautomers. Negatively charged carboxylate anion of aspartic acid abstract the imidazolic proton of histidine. Then, the imidazolic anion of histidine play as a base to abstract the carbonyl α-proton of 4-hydroxycoumarin. Meanwhile, carbonyl oxygen of benzylideneacetone may be trapped by oxyanion hole and α,β-unsaturated ketone is activated. Then, 4-hydroxycoumarin attacked as a Michael donor to benzylideneacetone, and finally, carbanion abstract a proton of histidine to give warfarin. Stereoselectivity might be introduced by the conformation of lipase which block the *Si*-face of benzylideneacetone slightly more than *Re*-face, however, the detailed conformation of lipase AS is still not clear.



Scheme 2. Proposed mechanism of lipase AS-catalyzed Michael reaction of 4-hydroxycoumarin to benzylideneacetone

CONCLUSION

In summary, we describe the lipase-catalyzed Michael reaction of 4-hydroxycoumarin to benzylideneacetone in anhydrous DMSO. The reaction conditions, including type of lipase, organic

solvent, H_2O content, molar ratio, temperature, and reaction period, were investigated. Warfarin, one of the most effective anticoagulants, was prepared in one step in good yield (85%) with 45%ee (*R*-form), using lipase AS as the catalyst, in anhydrous DMSO with a 1:3 molar ratio of 4-hydroxycoumarin to benzylideneacetone, at 20 ºC for 7 days. Although the enantioselectivity was still low, it is still the best result obtained in the enantioselective synthesis of warfarin using a biocatalyst (maximal reported ee: 22%).[1i] Among the many reported enzyme-catalyzed Michael reactions, only a few have shown enantioselectivity. The asymmetric Michael reaction activity of lipase AS is therefore an important example of enantioselective lipase catalytic promiscuity. Further studies focusing on improvement of the enentioselectivity of the lipase AS-catalyzed transformation are currently under investigation.

EXPERIMENTAL

Materials

Lipase AS (from *Aspergillus niger*), lipase AYS (from *Candida rugosa*), lipase PS (from *Burkholderia cepacia*), and lipase AK (from *Pseudomonas fluorescens*) were kindly provided by Amano Enzyme Inc (Nagoya, Japan). Lipase PL (from *Alcaligenes sp.*), lipase QLM (from *Alcaligenes sp.*), lipase OF (from *Candida cylindracea*), lipase SL (from *Burkholderia cepacia*), lipase TL (from *Pseudomonas stutzeri*), and lipase MY-30 (from *Candida cylindracea*) were kindly provided by Meito Sangyo Co (Nagoya, Japan). Lipase F-AP15 (from *Rhizopus oryzae*) was purchased from Wako Pure Chemical Industries Ltd (Osaka, Japan). Immobilized lipase (from *Pseudomonas sp.*) was purchased from TOYOBO Co (Osaka, Japan). PPL (from porcine pancreas) was purchased from Nacalai Tesque Inc (Kyoto, Japan). 4-Hydroxycoumarin was purchased from Tokyo Chemical Ind. Co. (Tokyo, Japan) and benzylideneacetone was purchased from Kanto Kagaku Reagent Division (Tokyo, Japan). All reactions were monitored by thin-layer chromatography (TLC) using 60-F_{254} silica gel plates (Merck, Darmstadt, Germany). Column chromatography was carried out using silica gel PSQ 60 (Fuji Silysia Chemical Ltd., Kasugai, Japan). ^{1}H NMR spectra and ^{13}C NMR spectra were recorded at 500 MHz and 125 MHz on a JEOL JNM-ECA (JEOL, Tokyo, Japan) in $CDCl_3$ using tetramethylsilane as an internal standard. ESI-MS analysis of the samples was performed using an LCQ Advantage mass spectrometer (AB SCIEX (MA, USA) API 2000) equipped with an ESI ion source, in positive ionization mode, with data acquisition using Analyst version 1.4.2 software. HPLC analyses were performed using PU-2080 Plus Intelligent HPLC Pump (JASCO, Tokyo, Japan) equipped with a CHIRALPAK AD-H (Daicel Chemical Industries Ltd., Tokyo, Japan) column, and the eluent was monitored using a PU-2075 Plus Intelligent UV/Vis Detector (JASCO, Tokyo, Japan). Chromatographs were recorded using Chromato-Pro PC integrator (Run Time Co, Sagamihara, Japan).

Typical reaction procedure

A mixture of benzylideneacetone (61.4 mg, 0.42 mmol), 4-hydroxycoumarin (22.7 mg, 0.14 mmol), and lipase AS (28.4 mg) in anhydrous DMSO (0.7 mL) was stirred under N_2 at 20 ºC for 72 h. The progress of the reaction was monitored by TLC. The enzyme was filtrated off on the Celite pad and H_2O was added to the filtrate. The residual solution was extracted with Et_2O and the organic layer was dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Purification of the residual mixture by column chromatography on silica gel using hexane : EtOAc (85:15, then 70:20) gave (*R*)-warfarin (22.7 mg, 64% yield, 45% ee) as colorless needles. mp 160-161 ºC. $[\alpha]^{24}_D$ +5.00 (*c* 0.1, MeCN) (lit.,[10e] $[\alpha]^{25}_D$ -10.7 (*c* 1.0, MeCN) for *S*-form, 99% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.67 (s, 3.00H, CH_3, ketal), 1.71 (s, 2.64H, CH_3, keto), 2.00 (t, *J* = 12.3 Hz, 0.50H, CH_2, ketal), 2.29 (s, 0.50H, CH_2, ketal), 2.39-2.55 (m, 1.23H, CH_2, keto), 3.22-3.47 (m, 1.00 H, CH_2, ketal), 3.85 (dd, *J* = 10.0 Hz, 19.4 Hz, 0.53H, CH_2, keto), 4.16 (dd, *J*=6.9 Hz, 11.5 Hz, 0.50H, CH, ketal), 4.28 (dd, *J* = 3.2 Hz, 6.85 Hz, 0.50H, CH, ketal), 4.70 (d, *J* = 8.3 Hz, 0.88H, CH, keto), 7.19-7.23 (m, 7.00H, ArH, ketal), 7.27-7.36 (m, 6.16H, ArH, keto), 7.49 (dt, *J* = 1.7 Hz, 7.8 Hz, 1.0H, ArH, ketal), 7.56 (dt, *J* = 1.7 Hz, 7.8 Hz, 0.88H, ArH, keto), 7.81 (dd, *J* = 7.8 Hz, 1.0H, ArH, ketal), 7.89 (dd, *J* = 1.5 Hz, 8.0 Hz, 1.0H, ArH, ketal), 7.94 (dd, *J* = 1.4 Hz, 7.6 Hz, 0.9H, ArH, keto). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 27.41, 27.98, 34.79, 35.43, 40.42, 42.83, 50.76, 99.30, 100.78, 101.42, 104.09, 116.08, 116.47, 116.67, 122.89, 123.17, 123.76, 124.06, 126.52, 127.16, 128.41, 128.64, 129.10, 131.63, 132.09, 143.47, 152.87, 159.30, 161.83, 162.45. ESI-MS: $C_{19}H_{16}O_4H^+$: [M+H] found 309.4. The enantiomeric excess was determined by HPLC, using CHIRALPAK AD-H column, and eluted with hexane:2-propanol (4:1 v/v) at 1.0 mL/min [t_R=5.0 min for (*R*)-warfarin and t_R=11.0 min for (*S*)-warfarin] monitored at 254 nm.

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REFERENCES

1. a) T. Kitazume, T. Ikeya, and K. Murata, *J. Chem. Soc., Chem. Commun.*, 1986, 1331; b) O. Torre, I. Alfonso, and V. Gotor, *Chem. Commun.*, 2004, 1724; c) M. Svedendahl, K. Hult, and P. Berglund, *J. Am. Chem. Soc.*, 2005, **127**, 17988; d) P. Carlqvist, M. Svedendahl, C. Branneby, K. Hult, T. Brinck, and P. Berglund, *ChemBioChem*, 2005, **6**, 331; e) W. B. Wu, N. Wang, J. M. Xu, Q. Wu, and X. F. Lin, *Chem. Commun.*, 2005, **18**, 2348; f) W. B. Wu, J. M. Xu, Q. Wu, D. S. Lv, and X. F. Lin, *Adv. Synth. Catal.*, 2006, **348**, 487; g) J. M. Xu, F. Zhang, B. K. Liu, Q. Wu, and X. F. Lin, *Chem. Commun.*, 2007, **20**, 2078; h) F. W. Lou, B. K. Liu, Q. Wu, D. S. Lv, and X. F. Lin, *Adv. Synth.*

Catal., 2008, **350**, 1959; i) J. F. Cai, Z. Guan, and Y. H. He, *J. Mol. Cat. B. Enzym.*, 2011, **68**, 240; j) B. H. Xie, Z. Guan and Y. H. He, *J. Chem. Tech. Biotech.*, 2012, **87**, 1709.

2. F. P. Seebeck and D. Hilvert, *J. Am. Chem. Soc.*, 2003, **125**, 10158.
3. Y. Terao, K. Miyamoto, and H. Ohta, *Chem. Lett.*, 2007, **36**, 420.
4. L. E. Visser, R. H. N. van Schaik, M. van Vliet, P. H. Trienekens, P. A. G. M. De Smet, A. G. Vulto, A. Hofmann, C. M. van Duijn, and B. H. C. Stricker, *Clin. Pharmacol. Ther.*, 2005, **77**, 479.
5. M. Ufer, *Clin. Pharmacokinet.*, 2005, **44**, 1227.
6. D. Marez, M. Legrand, N. Sabbagh, J. M. Lo Guidice, C. Spire, J. J. Lafitte, U. A. Meyer, and F. Broly, *Pharmacogenetics*, 1997, **7**, 193.
7. A. E. Rettie, K. R. Korzekwa, K. L. Kunze, R. F. Lawrence, A. C. Eddy, T. Aoyama, H. V. Gelboin, F. J. Gonzalez and W. F. Trager, *Chem. Res. Toxicol.*, 1992, **5**, 54.
8. H. J. Bardsley and A. K. Daly, PCT Int. Appl. Patent 2000, WO 0043003.
9. a) A. Robinson, and H. Y. Li, *Tetrahedron Lett.*, 1996, **37**, 8321; b) A. S. Demir, C. Tanyeli, V. Gulbeyaz and H. Akgun, *Turk. J. Chem*., 1996, **20**, 139; c) Y. Tsuchiya, Y. Hamashima, and M. Sodeoka, *Org. Lett.*, 2006, **8**, 4851; d) S. K. Ray, P. K. Singh, N. Molleti and V. K. Singh, *J. Org. Chem.*, 2012, **77**, 8802.
10. a) N. Halland, T. Hansen, and K. A. Jørgensen, *Angew. Chem. Int. Ed.*, 2003, **42**, 4955; b) H. Kim, C. Yen, P. Preston, and J. Chin, *Org. Lett.*, 2006, **8**, 5239; c) J. W. Xie, L. Yue, W. Chen, W. Du, J. Zhu, J. G. Deng, and Y.C. Chen, *Org. Lett.*, 2007, **9**, 413; d) Z. Dong, L. Wang, X. Chen, X. Liu, L. Lin, and X. Feng, *Eur. J. Org. Chem.*, 2009, 5192; e) M. Rogozinska, A. Adamkiewicz, and J. Mlynarski, *Green Chem.*, 2011, **13**, 1155; f) J. Dong and D. M. Du, *Org. Biomol. Chem.*, 2012, **10**, 8125; g) S. Ma, L. Wu, M. Liu, and Y. Wang, *Org. Biomol. Chem.*, 2012, **10**, 3721; h) Y. Liu, X. Liu, M. Wang, P. He, L. Lin, and X. Feng, *J. Org. Chem.*, 2012, **77**, 4136; i) M. Leven, J. M. Neudörfl, and B. Goldfuss, *Beilstein J. Org. Chem.*, 2013, **9**, 155.
11. G. Cravotto, G. M. Nano, G. Palmisano, and S. Tagliapietra, *Tetrahedron: Asymmetry*, 2001, **12**, 707.