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Cascade Reaction by Chemo- and Biocatalytic Approaches to Obtain Chiral Hydroxy Ketones and *anti* 1,3-Diols

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A chemo- and biocatalytic cascade approach was applied for the stereoselective synthesis of hydroxy ketones and the corresponding 1,3-diols. A new class of tridentate N,N,O ligands was used with copper(II) complexes for the asymmetric β-borylation of α,β-unsaturated compounds. The complex containing ligand **L5** emerged as the best performer, and it gave the organoborane derivatives with good *ee* values. The corresponding keto–alcohol compounds were then bioreduced by yeasts. The biotransformation set up with *Rhodotorula rubra* allowed (*R*)-keto–alcohols and (*S*,*S*)-diols to be obtained with up to 99% *ee* and up to 99% *de* in favor of the *anti* enantiomers.

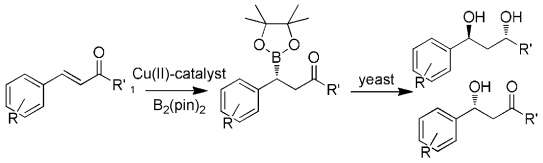
1. Introduction

Asymmetric transition-metal catalysts and enzymes have emerged as the most effective synthetic tools for the stereoselective preparation of many chiral compounds. The possibility to exploit different catalytic approaches for enantio- and diastereoselective catalysis is a challenging topic in chemical synthesis, especially if control of multiple stereogenic centers is involved.[1] Furthermore, the development of improved procedures by means of using less expensive, easy-to-handle, and more sustainable catalyst systems still remains an elusive goal.

Herein, we report a simple, inexpensive, and efficient catalyst system for simultaneous 1,4-conjugate addition and reduction steps on α,β-unsaturated carbonyl compounds through base-controlled transition-metal catalysis or/and by using yeasts under mild conditions at room temperature. In our case, a cascade reaction allowed the asymmetric synthesis of differently substituted diols through the formation of the corresponding chiral keto–alcohols and diols by bioreduction. The first step is based on enriched keto–alcohol formation through Cu^{II}-catalyzed asymmetric boron conjugate addition to α,β-unsaturated carbonyl compounds.[2] In contrast to popular protocols involving the use of chiral Cu^{I} for the enantioselective β-borylation of α,β-unsaturated acceptors, those involving the use of chiral Cu^{II} catalysts have been investigated only recently.

In particular, the complexation of Schiff base bidentate ligands with copper has been shown to result in compounds with interesting catalytic properties. On the other hand, organoboranes are known as extremely useful and versatile synthetic intermediates for organic synthesis[3] that can also display biological activities. Here, for 1,4-conjugate addition to carbon–carbon double bonds, we used bis(pinacolato)diboron [$B_2(pin)_2$], which is one of the most practical tools for the establishment of new C–B bonds through transition-metal catalysis.[4]

To enhance the catalytic performance of asymmetric catalytic boron conjugate addition, tripodal ligands,[5] based on the tetrahydroquinoline or quinolone scaffold, were incorporated into the Cu^{II} complexes. This successful combination led to keto–alcohol derivatives in an enantiomerically enriched form. A subsequent bioreduction step involving the use of different whole cells allowed the reduction of the keto–alcohol substrates to the corresponding enriched chiral diols,[1a,6] leaving the other isomer unreacted (Scheme 1). The obtained substrates are important building blocks in the synthesis of diverse organic molecules that are versatile elements in the pharmaceutical field.[7]



Scheme 1. Combining transition-metal catalysis with a biocatalytic approach to obtain diols.

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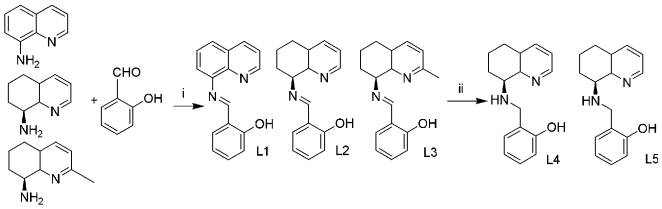
2. Results and Discussion

Considering the use of Schiff bases and their corresponding reduced amines as ligands in copper complexes for the asymmetric β-borylation of α,β-unsaturated carbonyl compounds, the tridentate ligands were easily synthesized starting from 8-aminoquinoline and its chiral derivatives by condensation with salicylaldehyde in EtOH at room temperature for 5 h. Then, the corresponding amines were obtained by reduction with $NaBH_4$ in a mixture of THF/MeOH at 0 °C for 1 h (Scheme 2). Chiral 8-aminotetrahydroquinolines were previously synthesized and studied in our research group as ligands in metal complexes and were used as catalysts in the asymmetric transfer hydrogenation (ATH) of different ketones with good results.[8]



Scheme 2. Synthesis of ligands. Reagents and conditions: i) EtOH, RT, 5 h; ii) $NaBH_4$, THF/CH_2Cl_2, 0 °C, 1 h.

In the case of ligand **L1**, reduction to the corresponding amine did not proceed in the presence of different amounts of $NaBH_4$ or by using Pd/C (1, 5, or 10% molar equivalents) under a H_2 atmosphere pressure, probably because of the extensive double-bond conjugation of the substrate.

The copper(II)/**L** complexes, obtained by treating the ligand with $Cu(OAc)_2$ in EtOH for 3 h at room temperature, were completely characterized. Crystals of the copper complex bearing ligand **L1** suitable for X-ray structure analysis were obtained by slow evaporation of a 33% water/acetone solution at room temperature. The complex crystallized in the centrosymmetric $P\bar{1}$ space group, with five molecules of water and one molecule of acetone, depicted as an ORTEP[9] view in Figure 1. The complex is monomeric, and the central Cu^{II} atom is coordinated by two nitrogen donor atoms, one hydroxy oxygen atom, and one oxygen atom from acetone in a square-planar arrangement. The bond lengths and angles are within the expected ranges. Ligand **L1** is nearly planar with a maximum deviation of 0.026(3) Å for the O1 atom. The crystal structure is consolidated by an extensive network of water contacts, and this leads to the formation of supramolecular chains running along the *a* axis perpendicular to the ligands. In addition, weak $C\pi$–$H\cdots O_{water}$ intermolecular interactions contribute to stabilize the crystal packing.

Catalytic asymmetric β-borylation was conducted starting from different α,β-unsaturated carbonyl compounds. Different reaction solvents (Et_2O, MeOH, EtOH, toluene, water, dichloromethane, acetonitrile, and THF) were evaluated in the presence of variable amounts of MeOH as a hydrogen donor (20–150 equiv.). With all catalysts, good yields were observed within 18 h by using 1,3-diphenyl-2-propenone as a standard substrate. Catalytic experiments showed that the best results were obtained by using Et_2O with 50 equivalents of MeOH at room temperature (Table 1).

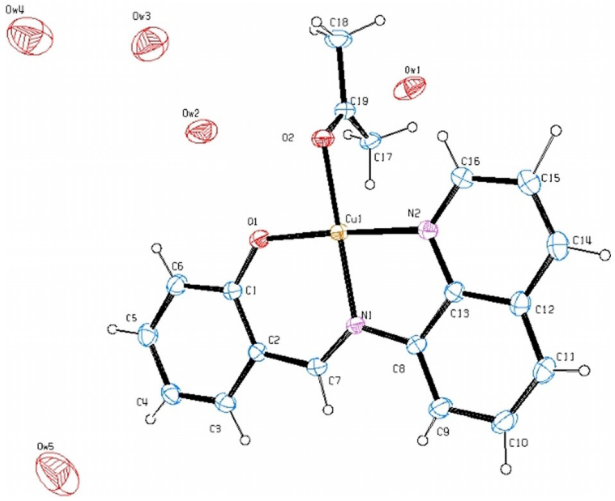
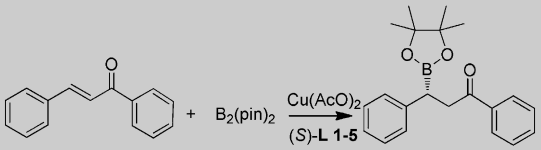


Figure 1. ORTEP[9] view of the asymmetric unit with an arbitrary atom-numbering scheme (ellipsoids are drawn at 40% probability). H atoms are shown as spheres of arbitrary radii.

Table 1. Screening of the copper-catalyzed β-borylation of the standard substrate.[a]



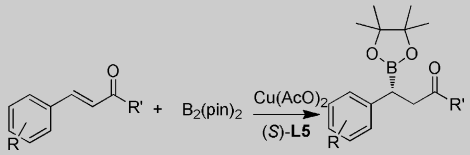
Entry	Ligand	Conversion[b] [%]	*ee* [%][c] (*R*)
1	**L1**	99.9	–
2	**L2**	99.9	*rac*
3	**L3**	99.9	12
4	**L4**	99.9	21
5	**L5**	99.9	45

[a] All reactions were performed for 18 h by using the Cu complex (5 mol%) in diethyl ether; $c(substrate)_{final} = 28$ mM, $c(catalyst)_{final} = 1.4$ mM. [b] Conversion was determined by ^1H NMR spectroscopy. [c] Data were compared by taking the average of three independent experiments. Enantiomeric excess was determined by HPLC with a chiral column (see the Experimental Section).

The enantiomeric excess was evaluated directly on the organoborane compounds by HPLC analysis. Assignment of the configuration was achieved by comparison with the corresponding β-hydroxy keto derivatives reported in the literature after deprotecting the organoborane compounds with $NaBO_3{\cdot}H_2O$ in THF/water for 1 h. Considering that the best results were obtained upon using **L5** as the ligand (Table 1, entry 5), the β-borylation reaction was extended under the same reaction conditions to other α,β-unsaturated carbonyl compounds (Table 2).

For all the chalcone derivatives (Table 1, entries 5–12), the β-borylation reaction products gave very appreciable outcomes

Table 2. Asymmetric β-borylation with a copper catalyst bearing ligand (*S*)-**L5**.[a]

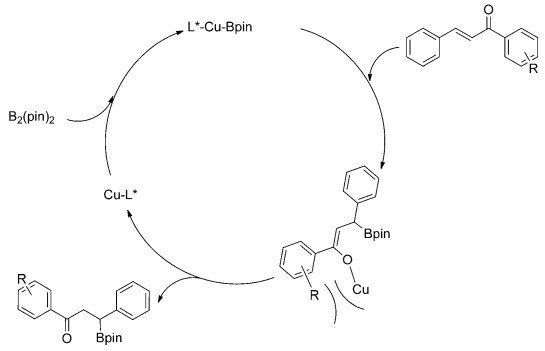


Entry	R	R′	Conversion[b] [%]	*ee*[c] [%] (*R*)
1	H	CH_3	99.9	12
2	3-Cl	CH_3	94	15
3	4-Cl	CH_3	63	21
4	4-NO_2	CH_3	–	–
5	H	C_6H_5	99.9	45
6	H	4-NCC_6H_4	99.9	4
7	H	4-$F_3CC_6H_4$	99.9	13
8	H	4-ClC_6H_4	99.9	11
9	H	3-ClC_6H_4	99.9	37
10	H	4-$CH_3OC_6H_4$	99.9	7
11	H	3-$CH_3OC_6H_4$	99.9	30
12	H	2-$CH_3OC_6H_4$	99.9	50
13	H	4-$CH_3C_6H_4$	99.9	51
14	H	3-$CH_3C_6H_5$	99.9	21
15	H	2-$CH_3C_6H_5$	59	15

[a] All reactions were performed for 18 h by using the Cu complex (5 mol%) in diethyl ether; $c(\text{substrate})_{final} = 28$ mM, $c(\text{catalyst})_{final} = 1.4$ mM. [b] Conversion was determined by ^{1}H NMR spectroscopy. [b] Data were compared by taking the average of three independent experiments. Enantiomeric excess was determined by HPLC with a chiral column (see the Experimental Section).

in terms of enantioselectivity, with the exception of 4-(4-nitrophenyl)but-3-en-2-one, for which the reaction did not proceed. Full conversion was instead generally observed upon using chalcone derivatives as starting materials; it was observed that if the substituent on the benzylic moiety was in the *para* position, the enantioselectivity decreased and was close to a racemate, apart from the methyl group (51% *ee*; Table 2, entry 13). Therefore, different substituents in the *ortho* and *meta* positions were evaluated, and the enantioselectivity increased for the –Cl and $-OCH_3$ groups going from the *para* position to the *ortho* position (Table 2, entries 8–12); on the other hand, the enantiomeric excess decreased in the case of the $-CH_3$ substituent (Table 2, entries 13–15). These data agree with the proposed reaction mechanism, in that the substituent on the benzylic moiety plays a pivotal role in the nucleophilic addition step to form an O-enolate in terms of steric hindrance or electronic properties (Scheme 3).[4a, 10]

With the aim to combine asymmetric chemocatalysis with biocatalytic reactions, the ability of yeasts to reduce the carbonyl group of the resulting β-hydroxy keto derivatives selectively by biotransformation was then evaluated. Racemic 3-hydroxy-1,3-diphenylpropan-1-one was synthesized through β-borylation and deprotection by using a copper(II) complex containing **L1** as the ligand, and it was used as a standard substrate for the screening of different biocatalysts.[11] All reactions were performed in the presence of glucose (50 g L^{-1}) as a co-substrate with a substrate concentration of 2 g L^{-1} in phosphate buffer, and the biotransformation results were evaluated after 48 h.



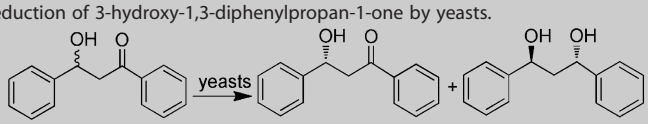
Scheme 3. Proposed reaction mechanism.

The data show that good results were obtained for the biocatalytic reduction upon using whole cells of *Rhodotorula rubra*, *Pichi etchellsii*, *Torulopsis magnoliae*, and *Torulopsis molischiana* (Table 3, entries 1, 5, 11, and 12) as biocatalysts. As good outcomes ensued by employing *Rhodotorula rubra* either in the enantioselective reduction of the carbonyl moiety (97% *ee*, 91% *de*, 23% yield; Table 3, entry 1) or in the bioreduction of the hydroxy ketone substrate (65% *ee*), this yeast seemed to be the best candidate as a biocatalyst in the reduction reaction of different racemic 3-hydroxy ketones, which were eventually obtained by β-borylation and deprotection of the substrates reported in Table 2 by using a copper catalyst containing achiral ligand **L1** (Table 4).

Upon using methyl aryl hydroxy ketones, the results in terms of stereoselectivity were modest both in the formation of the diols and in the resolution of the hydroxy ketone compounds (Table 4, entries 1–4). In the case of biaryl hydroxy ketones, the best results were obtained with *para*-substituted compounds in terms of molar conversion, whereas if the substituent was in the *meta* position, the yield decreased; the product was undetectable for substrates with *ortho* substituents. This behavior could be correlated to a change in steric hindrance of the substrate, as access to the active catalytic site could become challenging if the substituents on the phenyl ring were in a certain unfavorable position. The stereoselective control observed with the yeast seemed to confirm this hypothesis. In fact, the predominance of one configuration of the enantiomers changed between the *para*- and *meta*-substituted substrates: in the first case, the dominant (*S*,*S*)-diol underlined that the yeast followed the Prelog rule, whereas in the presence of *meta*-substituted substrates, (*R*,*R*)-diols were formed (*ante*-Prelog rule) (Table 4, entries 6–8, 10, and 13 vs. entries 9, 11, and 14). Excellent results in terms of stereoselectivity were obtained with 4-H, 4-Cl, and 4-CH_3 substituents for biocatalytic ketone reduction (Table 4, entries 5, 8, and 13).

A cascade reaction was then set up taking into consideration the good results obtained with the biocatalysis approach as regards the molar conversion. Thus, compounds with or without a substituent in the *para* position of the phenyl ring were evaluated. The cascade reaction involved first β-borylation/deprotection and then bioreduction. Although the enantioselectivity of the first step (chemocatalysis) was modest, this was an indispensable condition for bypassing the issue of negligible molar

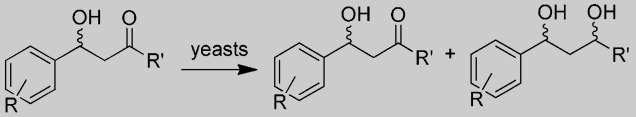
Table 3. Screening results for the bioreduction of 3-hydroxy-1,3-diphenylpropan-1-one by yeasts.



Entry	Yeast	*ee*[a] [%] (*R*)-Hydroxy ketone	Diol conversion[b] [%]	*ee*[a] [%] (*S*,*S*)-diol	*de*[b] [%] Diols
1	*Rhodotorula rubra MIM 147*	65	23	97	91 (*anti*)
2	*Saccharomyces cerevisiae*	2	8	20	92 (*meso*)
3	*Saccharomyces cerevisiae zeus*	4	12	25	42 (*meso*)
4	*Pichia henricii CBS 5765*	*rac*	10	−84	66 (*anti*)
5	*Pichia etchellsii MIM*	55	19	99	85 (*anti*)
6	*Pichia pastoris CBS 2612*	34	8	70	97 (*anti*)
7	*Pichia glucozyma CBS 5766*	8	10	56	74 (*anti*)
8	*Pachysolen tannophylus CBS 4044*	5	89	29	74 (*anti*)
9	*Kluyveromyces marxianus var. lactis CL69*	24	7	87	96 (*anti*)
10	*Kluyveromyces marxianus CBS 1553*	16	10	93	78 (*anti*)
11	*Torulopsis magnoliae MIM 42*	74	28	74	90 (*anti*)
12	*Torulopsis molischiana CBS 837*	67	24	82	91 (*anti*)
13	*Torulopsis castelli MIM 1705*	39	7	36	42 (*meso*)
14	*Torulopsis pinus 207*	8	11	−15	58 (*meso*)
15	*Sporobolomyces salmonicolor MIM*	21	8	67	95 (*anti*)
16	*Lindnera fabiani CBS 5640*	7	9	77	91 (*anti*)

[a] The *ee* value was determined by HPLC with a chiral column (see the Experimental Section). [b] Molar conversion and *de* were calculated by ^{1}H NMR spectroscopy.

Table 4. Biotransformation of different 3-hydroxy ketones with *Rhodotorula rubra*.[a]



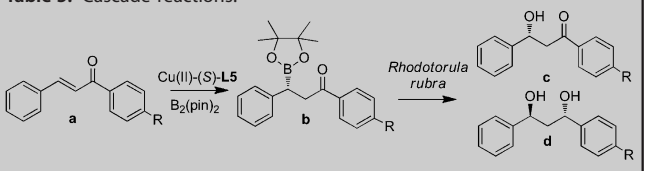
Entry	R	R′	*ee*[b] [%] Hydroxy ketone	*ee*[b] [%] Diol	*de*[c] [%] Diols
1	H	CH_3	*rac*	55 (*R*,*S*)	64 (*anti*)
2	3-Cl	CH_3	70 (*S*)	84 (*R*,*S*)	29 (*anti*)
3	4-Cl	CH_3	47 (*S*)	22 (*R*,*S*)	75 (*anti*)
4	4-NO_2	CH_3	10 (*S*)	43 (*R*,*S*)	46 (*anti*)
5	H	C_6H_5	65 (*R*)	97 (*S*,*S*)	91 (*anti*)
6	H	4-CNC_6H_4	88 (*R*)	*rac*	61 (*anti*)
7	H	4-$CF_3C_6H_4$	85 (*R*)	82 (*S*,*S*)	44 (*anti*)
8	H	4-ClC_6H_4	75 (*R*)	96 (*S*,*S*)	98 (*anti*)
9	H	3-ClC_6H_4	44 (*S*)	37 (*R*,*R*)	89 (*anti*)
10	H	4-$CH_3OC_6H_4$	44 (*R*)	99 (*S*,*S*)	93 (*anti*)
11	H	3-$CH_3OC_6H_4$	53 (*S*)	52 (*R*,*R*)	75 (*anti*)
12	H	2-$CH_3OC_6H_4$	–	–	–
13	H	4-$CH_3C_6H_4$	72 (*R*)	97 (*S*,*S*)	85 (*anti*)
14	H	3-$CH_3C_6H_4$	10 (*S*)	98 (*R*,*R*)	95 (*anti*)
15	H	2-$CH_3C_6H_4$	–	–	–

[a] Substrate concentration was 2 mg mL^{-1}. [b] The *ee* value was determined by HPLC with a chiral column (see the Experimental Section). [c] The *de* was calculated by ^{1}H NMR spectroscopy.

conversion into diols as a consequence of a probable substrate inhibition effect in the biotransformations. Different substrate concentrations were examined to avoid this inhibition effect. Furthermore, the biocatalytic reduction starting from the corresponding diketones did not proceed in terms of product conversion (5% yield) or stereoselectivity. The organoborylation catalyzed by a complex bearing ligand **L5** led to the organoborane compound with the *R* configuration and variable enantiomeric excess values (7–51% *ee*). Subsequently, the solvent was removed in vacuo and $NaBO_3{\cdot}H_2O$ (3 equiv.) in THF/H_2O (1:3, 50 mg substrate/1 mL) was added. After 1 h, phosphate buffer (0.1 M, pH 7, 50 mL), glucose (50 g L^{-1}), and *Rhodotorula rubra* whole cells were added to the previous untreated solution to work with a final substrate concentration of 1 mg mL^{-1} for 48 h (Table 5).

From the data reported in Table 5, it was observed that in the presence of electron-donating groups or hydrogen as a substituent, (*S*,*S*)-diols were provided with high enantiomeric excess values (Table 5, entries 1, 2, and 6). Excellent *ee* values were also obtained for (*R*)-hydroxy ketones, although in the

Table 5. Cascade reactions.



Entry	R	*ee* [%] (*R*)-**b**[a]	*ee* [%] (*R*)-**c**[b]	*ee* [%] (*R*)-**c**[c]	*ee* [%] (*S*,*S*)-**d**	*de* [%] (*anti*)-**d**	Yield [%] Diol
1	H	45	65	96	99 (*S*,*S*)	95 (*anti*)	96
2	CH_3	51	72	99	99 (*S*,*S*)	98 (*anti*)	98
3	CN	4	88	90	7 (*S*,*S*)	63 (*anti*)	78
4	CF_3	13	85	88	83 (*S*,*S*)	46 (*anti*)	75
5	Cl	11	75	85	96 (*S*,*S*)	99 (*anti*)	98
6	OCH_3	7	44	46	99 (*S*,*S*)	94 (*anti*)	95

[a] After catalytic β-borylation/deprotection. [b] After bioreduction by yeast starting from racemic hydroxy ketone. [c] Cascade reaction.

case of the substrate with a *para*-OCH_3 substituent, we believe that the average *ee* value is due to steric hindrance generated by the lone pair of electrons of the methoxy substituent in the pocket of the yeast. Regarding the results obtained with electron-withdrawing substituents, only low enantiomeric excess values were achieved in the reduction of (*S*,*S*)-diols and in the resolution of (*R*)-hydroxy ketones (Table 5, entries 3–5). In this case, it is conceivable that erosion of the biocatalyst performance is a result of the low enantioselectivity of the chemoreaction.

3. Conclusions

In conclusion, a cascade reaction combining transition-metal complexes with biocatalysts was set up for the enantioselective synthesis of keto–alcohols and the corresponding 1,3-diols. A new class of tridentate N,N,O pyridine-based ligands was used for the first time in the β-borylation reaction with copper(II) complexes to afford, in the case of ligand **L5**, keto–alcohols in enriched form with up to 51% *ee*, which was crucial for setting up the subsequent biotransformation. *Rhodotorula rubra*, under optimized condition reactions, gave (*S*,*S*)-diols (up to 99% *ee*), and the *S* enantiomer of the keto–alcohol was consumed completely (up to 99% *ee* for the unreacted *R* enantiomer) with both excellent enantio- and diastereoselectivities.

Experimental Section

Synthetic Procedures

General

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ by using a Bruker DRX Avance (300 and 75 MHz) spectrometer equipped with a nonreverse probe. Chemical shifts [ppm] are referenced to the residual solvent proton/carbon signal. Polarimetry analyses were performed with a PerkinElmer 343 Plus equipped with Na/Hal lamp. MS analyses were performed by using a Thermo Finnigan (MA, USA) LCQ Advantage system MS spectrometer with an electrospray ionization source and an ion-trap mass analyzer. Mass spectra were obtained by direct infusion of a sample solution in MeOH under ionization (ESI+). Catalytic reactions were monitored by HPLC analysis with a Merck-Hitachi L-7100 equipped with Detector UV6000LP and a chiral column (AD, OJ-H Chiralcel, Lux Cellulose-4, Lux Cellulose-2 or Lux Amylose-2).

General Procedure for the Synthesis of Ligands L1–L3

8-Aminoquinoline (1.2 equiv.) was dissolved in EtOH (10 mL), and salicylaldehyde (1 equiv.) was added at room temperature. The mixture was stirred for 5 h and then water (5 mL) was added. The organic layer was extracted with CH_2Cl_2 (3×10 mL). Anhydrous Na_2SO_4 was added, the mixture was filtered, and the solvent was removed in vacuo. The obtained product did not need further purification.

(*E*)-2-[(Quinolin-8-ylimino)methyl]phenol (**L1**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.99 (d, J = 1.5 Hz, 1H), 8.95 (s, 1H) 8,76 (d, J = 1.2 Hz, 1H) 8.17 (d, J = 8.2 Hz, 1H) 8.06 (d, J = 8.2 Hz, 1H) 7.71 (d, J = 8.0 Hz, 2H) 7.23–7.01 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.6, 162.1, 150.5, 145.5, 142.3, 135.9, 133.3, 132.4, 129.1, 126.5, 126.2, 121.3, 119.6, 118.7 118.1, 117.6 ppm; FTIR (NaCl): $\tilde{\nu}$ = 3468, 3368, 3050, 2917, 2894, 1661, 1617, 1372, 1150, 1114, 789 cm^{-1}; MS (ESI): m/z = 249.27 $[M+H]^+$.

(*E*)-2-{[(5,6,7,8-Tetrahydroquinolin-8-yl)imino]methyl}phenol (**L2**): *S* isomer: $[\alpha]_D^{20} = -42.13$ (c = 1.1 in $CHCl_3$); *R* isomer: $[\alpha]_D^{20} = +42.05$ (c = 0.7 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (s, 1H), 8.39 (d, J = 4.67 Hz, 1H), 7.43 (d, J = 7.69 Hz, 1H), 7.32–7.24 (m, 2H), 7.12–7.08 (m, 1H), 6.97–6.83 (m, 2H), 4.56 (t, J = 3.85 Hz, 1H), 2.94–2.76 (m, 2H), 2.15–2.04 (m, 3H), 1.94–1.89 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.62, 161.32, 155.02, 147.72, 137.58, 132.81, 132.35, 131.92, 122.84, 119.27, 118.77, 117.07, 68.19, 31.30, 28.82, 18.84 ppm; FTIR (NaCl): $\tilde{\nu}$ = 3436, 3046, 2927, 1964, 1629, 1262, 1088, 1031, 803 cm^{-1}; MS (ESI): m/z = 254.0 $[M+H]^+$, 276.3 $[M+Na]^+$.

(*E*)-2-{[(2-Methyl-5,6,7,8-tetrahydroquinolin-8-yl)imino]methyl}phenol (**L3**): *R* isomer: $[\alpha]_D^{20} = -53.4$ (c = 0.4 in $CHCl_3$); *S* isomer: $[\alpha]_D^{20} = +59.9$ (c = 0.5 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 13.60 (s, 1H), 8.60 (s, 1H), 7.33–7.25 (m, 3H), 7.04–6.84 (m, 3H), 4.56 (s, 1H), 2.88–2.63 (m, 2H), 2.24–2.04 (m, 3H), 1.94–1.87 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.48, 161.43, 156.18, 153.95, 137.83, 132.26, 131.81, 129.50, 122.64, 119.37, 118.68, 117.10, 67.62, 31.31, 28.35, 24.34, 18.68 ppm; FTIR (NaCl): $\tilde{\nu}$ = 3056, 2930, 2864, 2733, 2665, 1731, 1627, 1472, 1416, 1081, 757 cm^{-1}; MS (ESI): m/z = 267.21 $[M+H]^+$.

General Procedure for the Synthesis of Ligands L4 and L5

The ligand (1 equiv.) was dissolved in MeOH/THF (1:1, 5 mL), and the mixture was cooled to 0 °C. $NaBH_4$ (0.5 equiv.) was added, and the mixture was stirred at room temperature for 1 h. The solution was quenched with saturated NH_4Cl solution (4 mL) and was extracted with CH_2Cl_2 (3×8 mL). The combined organic layer was dried (Na_2SO_4), and the solvent was evaporated. The obtained product did not need further purification.

2-{[(5,6,7,8-Tetrahydroquinolin-8-yl)amino]methyl}phenol (**L4**): *S* isomer: $[\alpha]_D^{20} = +20$ (c = 0.1 in $CHCl_3$); *R* isomer: $[\alpha]_D^{20} = -24.2$ (c = 0.1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.39 (d, J = 3.96 Hz, 1H), 7.42 (d, J = 7.62 Hz,1H), 7.18–7.03 (m, 3H), 6.84–6.76 (m, 2H), 4.14 (s, 2H), 3.86 (t, J = 6.15 Hz, 1H), 2.89–2.63 (m, 2H), 2.22–2.15 (m, 1H), 2.02–1.73 (m, 3H),1.25 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.01, 155.95, 146.87, 137.24, 132.63, 128.68, 128.33, 123.61, 122.38, 119.05, 116,49, 57.99, 50.79, 28.55, 28.44, 19.74 ppm; FTIR (NaCl): $\tilde{\nu}$ = 3282, 2924, 1924, 1690, 1589, 1456, 1259, 1037, 754 cm^{-1}; MS (ESI): m/z = 256.1 $[M+H]^+$.

2-{[(2-Methyl-5,6,7,8-tetrahydroquinolin-8-yl)amino]methyl}phenol (**L5**): *S* isomer: $[\alpha]_D^{20} = -39.1$ (c = 0.6 in $CHCl_3$); *R* isomer: $[\alpha]_D^{20} = +32.9$ (c = 0.3 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.2 Hz, 1H), 7.13 (m, 1H) 6.96 (d, J = 7.9 Hz, 2H) 6.83 (m, 2H) 4.14 (m, 3H) 2.47 (s, 4H) 1.86 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.7, 155.1, 137.5, 129.1, 128.9, 128.8, 128.0, 123.7, 121.9, 116.2, 57.9, 50.7, 28.7, 28.2, 20.4, 19.8 ppm; FTIR (NaCl) ν = 3281, 2925, 2858, 1597, 1499, 1471, 1258, 1091, 1035, 816 cm^{-1}; MS (ESI): m/z = 269.15 $[M+H]^+$.

Synthesis of α,β-Unsaturated Ketones

An aqueous solution of sodium hydroxide (30%, 25 mL) was slowly added to a methanol solution (30 mL) of the appropriate acetophenone (1 equiv.). The solution was cooled to room temperature, and the appropriate benzaldehyde (1.2 equiv.) was added. The mixture was stirred at room temperature overnight and was then

poured into water (100 mL). The obtained solid was filtered, washed with water until neutral pH, and recrystallized (ethanol). The chemical structure was confirmed on the basis of previously reported data.[12]

General Procedure for Asymmetric Boron Conjugate Addition

A mixture of $Cu(OAc)_2$ (5% mol), chiral ligand **L1–L5** (6% mol), and $B_2(pin)_2$ (1.2 equiv.) in Et_2O (7.5 mL) was stirred at room temperature for 1 h under a nitrogen atmosphere. A mixture of the α,β-unsaturated carbonyl compound (1 equiv.) and MeOH (50 equiv.) in Et_2O (2.5 mL) was added, and the mixture was stirred at room temperature for 15 h. The mixture was concentered in vacuo, the residue was dissolved in THF/H_2O (1.5:1, 4 mL), and $NaBO_3{\cdot}H_2O$ was added. The mixture was stirred for 2 h and then filtered. The aqueous layer was extracted with EtOAc (2×5 mL), and the combined organic layer was dried (Na_2SO_4). The solvent was evaporated, and the enantiomeric excess of the product was checked by HPLC analysis.

The ^{1}H NMR and ^{13}C NMR spectra of 4-hydroxy-4-phenylbutan-2-one, 4-(3-chlorophenyl)-4-hydroxybutan-2-one, 4-(4-chlorophenyl)-4-hydroxybutan-2-one, 4-(4-nitrophenyl)-4-hydroxybutan-2-one, 3-hydroxy-1,3-diphenylpropan-1-one, 3-hydroxy-3-phenyl-1-(*p*-tolyl)-propan-1-one, 3-(4-chlorophenyl)-3-hydroxy-1-phenylpropan-1-one, 3-(3-chlorophenyl)-3-hydroxy-1-phenylpropan-1-one, 3-hydroxy-1-(4-methoxyphenyl)-3-phenylpropan-1-one, 4-(3-hydroxy-3-phenylpropanoyl)benzonitrile, 3-hydroxy-1-(4- trifluoromethyl phenyl)-3-phenylpropan-1-one, 3-hydroxy-1-(2-methoxyphenyl)-3-phenylpropan-1-one, 3-hydroxy-1-(3-methylphenyl)-3-phenylpropan-1-one, and 3-hydroxy-1-(2-methylphenyl)-3-phenylpropan-1-one correspond to those reported in the literature.[4d, 13]

3-Hydroxy-1-(3-methoxyphenyl)-3-phenylpropan-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.25 (m, 8H), 7.12 (d, J = 8.2 Hz, 1H), 5.35–5.31 (m, 1H), 3.87 (s, 3H), 3.37–3.34 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8, 144.8, 143.0, 137.9, 129.7, 128.5, 127.6, 125.7, 120.8, 120.1, 112.3, 55.4, 47.5, 24.5 ppm; MS (ESI): m/z = 279.1 $[M+Na]^+$.

General Procedure for the Biotransformation

The biotransformation screening was performed in 10 mL screw-capped test tubes by resuspending the yeast cells in 0.1 M phosphate buffer (pH 7, 5 mL) containing glucose (50 g L^{-1}) and adding substrate (2 g L^{-1}) dissolved in DMSO (1%). The mixtures were magnetically stirred at 28 °C for 48 h. The mixtures were extracted with diethyl ether (2×5 mL), dried (Na_2SO_4), and concentrated in vacuo.

The ^{1}H NMR and ^{13}C NMR spectra of 1-phenylbutane-1,3-diol, 1-(3-chlorophenyl)butane-1,3-diol, 1-(4-chlorophenyl)butane-1,3-diol, 1-(4-nitrophenyl)butane-1,3-diol, 1,3-diphenyl-1,3-propanediol, benzoyl(4′-methylbenzoyl)methane, and benzoyl(4′-chlorobenzoyl)methane correspond to those reported in the literature.[1a, b, 14]

4-(1,3-Dihydroxy-3-phenylpropyl)benzonitrile: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65–7.61 (m, 2H), 7.48 (d, J = 7.4 Hz, 2H), 7.46–7.28 (m, 5H), 5.12–5.03 (m, 2H, *syn*), 4.98–4.94 (m, 2H, *anti*), 2.20–2.05 (m, 2H, *anti*), 1.97–1.91 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.5, 143.6, 132.3, 128.7, 128.6, 128.1, 127.8, 126.3, 126.3, 126.0, 125.6, 125.4, 118.8, 111.2, 75.4 (*anti*), 74.0 (*anti*), 71.8 (*syn*), 70.9 (*syn*), 47.5 (*anti*), 46.3 (*syn*), 29.6, 25.3 ppm; MS (ESI): m/z = 276.4 $[M+Na]^+$.

1-Phenyl-3-[4-(trifluoromethyl)phenyl]propane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61–7.57 (m, 2H), 7.52–7.46 (m, 2H), 7.39–7.25 (m, 5H), 5.29–5.05 (m, 2H, *syn*), 4.99–4.50 (m, 2H, *anti*), 2.22–2.15 (m, 2H, *anti*), 2.05–1.88 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 143.8, 128.9, 128.6, 128.5, 127.9, 127.7, 125.9, 125.8, 125.6, 125.5, 125.3, 75.2 (*anti*), 74.2 (*anti*), 71.7 (*syn*), 71.1 (*syn*), 47.6 (*anti*), 46.4 (*syn*), 28.3 ppm; MS (ESI): m/z = 319.0 $[M+Na]^+$.

1-(3-Chlorophenyl)-3-phenylpropane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 9H), 5.06–5.00 (m, 2H, *syn*), 4.99–4.95 (m, 2H, *anti*), 2.23–2.11 (m, 2H, *anti*), 1.99–1.92 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.3, 143.8, 134.4, 129.7, 128.6, 128.5, 127.9, 127.7, 127.5, 125.9, 125.8, 125.6, 125.5, 123.7, 123.7, 75.1 (*anti*), 74.2 (*anti*), 71.7 (*syn*), 71.1 (*syn*), 47.7 (*anti*), 46.3 (*syn*), 22.8 ppm; MS (ESI): m/z = 285.8 $[M+Na]^+$.

1-(4-Methoxyphenyl)-3-phenylpropane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.23 (m, 7H), 6.86 (dd, J = 8.72 Hz, 2H), 5.02–4.96 (m, 2H, *syn*), 4.93–4.90 (m, 2H, *anti*), 3.80 (s, 3H), 2.22–2.13 (m, 2H, *anti*), 1.97–1.91 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.2, 136.4, 136.3, 128.6, 128.5, 127.6, 127.4, 126.9, 126.8, 125.7, 125.6, 114.0, 113.9, 74.9 (*anti*), 74.6 (*anti*), 71.7 (*syn*), 71.3 (*syn*), 55.3, 47.7 (*anti*), 46.5 (*syn*), 29.6 ppm; MS (ESI): m/z = 282.0 $[M+Na]^+$.

1-(3-Methoxyphenyl)-3-phenylpropane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.18 (m, 5H), 7.0–6.79 (m, 2H), 5.30–4.68 (m, 2H), 3.81 (s, 3H), 2.21–2.15 (m, 2H, *anti*), 2.05–1.89 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8, 145.9, 144.1, 129.6, 128.3, 127.7, 127.4, 125.7, 125.6, 117.8, 113.2, 112.8, 111.1, 75.0 (*syn*), 74.9 (*syn*), 71.7 (*anti*), 71.6 (*anti*), 55.2, 47.7 (*syn*), 46.4 ppm (*anti*); MS (ESI): m/z = 282.0 $[M+Na]^+$.

1-(2-Methoxyphenyl)-3-phenylpropane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.17 (m, 5H), 6.90 (d, J = 7.5 Hz, 2H), 5.01–4.95(m, 2H, *syn* + *anti*), 3.80 (s, 3H), 3.51 (br s, 1H), 2.22–2.12(m, 2H, *anti*), 1.98–1.89 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 144.2, 136.4, 128.5, 128.4, 127.7, 127.6, 126.6, 126.5, 125.2, 125.1, 113.8, 74.9 (*syn*), 74.6 (*syn*), 71.7 (*anti*), 71.3 (*anti*), 55.3, 47.7 (*syn*), 46.5 ppm (*anti*); MS (ESI): m/z = 259.0 $[M+H]^+$.

1-Phenyl-3-(*m*-tolyl)propane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.05 (m, 7H), 4.96–4.90 (m, 2H), 2.35 (s, 3H), 2.16–2.11 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.5, 144.3, 138.0, 128.4, 128.3, 127.5, 127.2, 126.2, 126.3, 125.6, 122.6, 74.8, 71.4, 46.6, 24.8 ppm; MS (ESI): m/z = 243.9 $[M+Na]^+$.

1-Phenyl-3-(*o*-tolyl)propane-1,3-diol: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, J = 7.2 Hz, 2H), 7.40–7.21 (m, 5H), 5.23–5.16 (m, 2H, *syn*), 5.08–5.03 (m, 2H, *anti*), 2.31 (s, 3H), 2.17–2.07 (m, 2H, *anti*), 1.98–1.91 ppm (m, 2H, *syn*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.2, 142.1, 133.9, 130.4, 128.4, 127.7, 127.4, 127.3, 126.4, 125.3, 125.5, 125.1, 75.2 (*anti*), 71.9 (*syn*), 71.4 (*anti*), 68.2 (*syn*), 46.5 (*anti*), 45.1 (*syn*), 18.9 (*anti*), 18.6 ppm (*syn*); MS (ESI): m/z = 243.8 $[M+H]^+$.

Analytical Conditions

The products were analyzed by ^{1}H NMR spectroscopy to determinate the molar conversion, whereas the diastereomeric and enantiomeric excess values were evaluated by HPLC analysis.

4-Hydroxy-4-phenylbutan-2-one: *S* isomer: t_R = 21 min, *R* isomer: t_R = 18.7 min; 1-phenylbutane-1,3-diol: (*anti* form) *S*,*R* isomer: t_R = 16 min, *R*,*S* isomer: t_R = 17 min, (*syn* form) *R*,*R* isomer: t_R = 19.7 min, *S*,*S* isomer: t_R = 21 min; column: Lux cellulose-4, eluent: 2-propa-

nol/hexane = 5:95, flow = 0.9 mL min^{-1}, λ = 216 nm; data recorded prior to TLC separation.

4-(3-Chlorophenyl)-4-hydroxybutan-2-one: *S* isomer: t_R = 15 min, *R* isomer: t_R = 19 min; 1-(3-chlorophenyl)butane-1,3-diol: (*anti* form) *S,R* isomer: t_R = 11 min, *R,S* isomer: t_R = 15 min, (*syn* form) *R,R* isomer: t_R = 11.5 min, *S,S* isomer: t_R = 13 min; column: Lux amylose-2, eluent: 2-propanol/hexane = 15:85, flow = 0.5 mL min^{-1}, λ = 216 nm.

4-(4-Chlorophenyl)-4-hydroxybutan-2-one: *S* isomer: t_R = 18 min, *R* isomer: t_R = 20 min; 1-(4-chlorophenyl)butane-1,3-diol: (*anti* form) *S,R* isomer: t_R = 14 min, *R,S* isomer: t_R = 24 min, (*syn* form) *R,R* isomer: t_R = 13.5 min, *S,S* isomer: t_R = 26 min; column: Lux amylose-2, eluent: 2-propanol/hexane = 5:95, flow = 1.0 mL min^{-1}, λ = 216 nm.

4-(4-Nitrophenyl)-4-hydroxybutan-2-one: *S* isomer: t_R = 72 min, *R* isomer: t_R = 65 min; 4-(4-nitrophenyl)butane-1,3-diol: (*anti* form) *S,R* isomer: t_R = 33 min, *R,S* isomer: t_R = 35 min, (*syn* form) *R,R* isomer: t_R = 37 min, *S,S* isomer: t_R = 40 min; column: OJ-H Chiralcel, eluent: ethanol/hexane = 5:95, flow = 1.0 mL min^{-1}, λ = 254 nm.

3-Hydroxy-1,3-diphenylpropan-1-one: *S* isomer: t_R = 24 min, *R* isomer: t_R = 41 min; 1,3-diphenyl-1,3-propanediol: *meso* form: t_R = 13 min, *R,R* isomer: t_R = 15.5 min, *S,S* isomer: t_R = 18 min; column: Lux amylose-2, eluent: ethanol/hexane = 10:90, flow = 1.0 mL min^{-1}, λ = 216 nm.

4-(3-Hydroxy-3-phenylpropanoyl)benzonitrile: *R* isomer: t_R = 36 min, *S* isomer: t_R = 46 min; 4-(1,3-dihydroxy-3-phenylpropyl)benzonitrile: (*anti* form) *S,S* isomer: t_R = 17 min, *R,R* isomer: t_R = 19 min, (*syn* form) *S,R* isomer: t_R = 8.8 min, *R,S* isomer: t_R = 9.6 min; column: Lux cellulose-4, eluent: 2-propanol/hexane = 3:97, flow = 1.0 mL min^{-1}, λ = 216 nm.

3-Hydroxy-1-(4-trifluoromethylphenyl)-3-phenylpropan-1-one: *R* isomer: t_R = 25.4 min, *S* isomer: t_R = 37.5 min; 1-phenyl-3-[4-(trifluoromethyl)phenyl]propane-1,3-diol: (*anti* form) *S,S* isomer: t_R = 30 min, *R,R* isomer: t_R = 34.5 min; (*syn* form) *S,R* isomer: t_R = 49 min, *R,S* isomer: t_R = 51 min; column: Lux cellulose-4, eluent: 2-propanol/hexane = 3:97, flow = 1.0 mL min^{-1}, λ = 216 nm.

3-(4-Chlorophenyl)-3-hydroxy-1-phenylpropan-1-one: *S* isomer: t_R = 37 min, *R* isomer: t_R = 42 min; benzoyl-(4′-chlorobenzoyl)methane: (*anti* form) *S,S* isomer: t_R = 34 min, *R,R* isomer: t_R = 21 min, (*syn* form) *R,S* isomer: t_R = 18 min, *S,R* isomer: t_R = 23.5 min; column: Lux amylose-2, eluent: ethanol/hexane = 5:95, flow = 1.0 mL min^{-1}, λ = 220 nm.

3-(3-Chlorophenyl)-3-hydroxy-1-phenylpropan-1-one: *R* isomer: t_R = 22 min, *S* isomer: t_R = 29 min; 1-(3-chlorophenyl)-3-phenylpropane-1,3-diol: (*anti* form) *S,S* isomer: t_R = 36 min, *R,R* isomer: t_R = 41 min, (*syn* form) *R,S* isomer: t_R = 62 min, *S,R* isomer: t_R = 54 min; column: Lux cellulose-4, eluent: 2-propanol/hexane = 3:97, flow = 1.0 mL min^{-1}, λ = 216 nm.

3-Hydroxy-1-(4-methoxyphenyl)-3-phenylpropan-1-one: *R* isomer: t_R = 76 min, *S* isomer: t_R = 88 min; 1-(4-methoxyphenyl)-3-phenylpropane-1,3-diol: (*anti* form) *S,S* isomer: t_R = 46 min, *R,R* isomer: t_R = 50 min, (*syn*-form) *S,R* isomer: t_R = 58 min, *R,S* isomer: t_R = 69 min; column: Lux amylose-2, eluent: 2-propanol/hexane = 10:90, flow = 0.8 mL min^{-1}, λ = 220 nm.

3-Hydroxy-1-(3-methoxyphenyl)-3-phenylpropan-1-one: *S* isomer: t_R = 57 min, *R* isomer: t_R = 102 min; 1-(3-methoxyphenyl)-3-phenylpropane-1,3-diol: (*anti* form) *S,S* isomer: t_R = 43 min, *R,R* isomer: t_R = 48 min, (*syn*-form) *S,R* isomer: t_R = 64 min, *R,S* isomer: t_R = 68 min; column: Lux amylose-2, eluent: ethanol/hexane = 5:95, flow = 1.0 mL min^{-1}, λ = 220 nm.

3-Hydroxy-1-(2-methoxyphenyl)-3-phenylpropan-1-one: *S* isomer: t_R = 12 min, *R* isomer: t_R = 19 min; column: AD CHIRALCEL, eluent: 2-propanol/hexane = 10:90, flow = 1.0 mL min^{-1}, λ = 220 nm.

3-Hydroxy-3-phenyl-1-(*p*-tolyl)propan-1-one: *R* isomer: t_R = 13.5 min, *S* isomer: t_R = 20.5 min; benzoyl-(4′-methylbenzoyl)methane: (*anti* form) *S,S* isomer: t_R = 11 min, *R,R* isomer: t_R = 17 min, (*syn* form) *S,R* isomer: t_R = 16 min, *R,S* isomer: t_R = 10 min; column: Lux cellulose-4, eluent: ethanol/hexane = 10:90, flow = 1.0 mL min^{-1}, λ = 216 nm.

3-Hydroxy-1-(3-methylphenyl)-3-phenylpropan-1-one: *S* isomer: t_R = 14 min, *R* isomer: t_R = 11 min; 1-phenyl-3-(m-tolyl)propane-1,3-diol: (*anti* form) *S,S* isomer: t_R = 6 min, *R,R* isomer: t_R = 10 min, (*syn* form) *S,R* isomer: t_R = 21 min, *R,S* isomer: t_R = 24 min; column: Lux cellulose-2, eluent: 2-propanol/hexane = 10:90, flow = 0.8 mL min^{-1}, λ = 220 nm.

3-Hydroxy-1-(2-methylphenyl)-3-phenylpropan-1-one: *S* isomer: t_R = 12 min, *R* isomer: t_R = 13.5 min; column: AD CHIRALCEL, eluent: 2-propanol/hexane = 8:92, flow = 1.0 mL min^{-1}, λ = 220 nm.

Cascade Reaction Procedure

A mixture of $Cu(OAc)_2$ (5% mol), chiral ligand **L5** (6% mol), and $B_2(pin)_2$ (1.2 equiv.) in Et_2O (7.5 mL) was stirred at room temperature for 1 h under a nitrogen atmosphere. A mixture of the α,β-unsaturated ketone (1 equiv.) and MeOH (50 equiv.) in Et_2O (2.5 mL) was added, and the mixtures was stirred at room temperature for 15 h. The mixture was concentrated in vacuo, the residue was dissolved in THF/H_2O (1:3, 50 mg substrate/1 mL), and $NaBO_3{\cdot}H_2O$ (5 equiv.) was added. The mixture was stirred for 1 h. *Rhodotorula rubra* was then added to 0.1 M phosphate buffer (pH 7, 50 mL) containing glucose (50 g L^{-1}) to work at a final substrate concentration of 1 mg mL^{-1}. The mixture was magnetically stirred at 28 °C for 48 h. The mixture was extracted with diethyl ether (2×5 mL), dried (Na_2SO_4), and concentrated in vacuo.

Material and Methods

Microorganisms: Culture Conditions

Strains from official collections or from our collection were routinely maintained on a malt extract (8 g L^{-1} agar 15 g L^{-1}, pH 5.5). To obtain cells for the biocatalytic activity tests, the microorganisms were grown on solid medium at 28 °C for 72 h, and then, they were cultured in 1000 mL Erlenmeyer flasks containing the medium (100 mL, OD_{530nm} mL^{-1} = 0.1 at t_0). The microorganisms were incubated at 28 °C for 48 h on a reciprocal shaker (100 rpm). The yeasts were grown on malt extract with 5 g L^{-1} Difco yeast extract, pH 5.6. Fresh cells from submerged cultures were centrifuged (4000×*g* for 15 min at 4 °C) and washed with tap water before using. The cells used in the screening biotransformations were concentrated in a ratio of 1:2.

Crystallography

Diffraction data for the crystal of complex/**L1**[19] were collected by means of a Enraf–Nonius CAD4 four circle diffractometer working at ambient temperature with graphite-monochromated MoKα X-radiation (λ = 0.7107 Å). X-ray diffraction data in the 2θ range of 4 to 60° and in the (*hkl*) range $\pm h, \pm k, +l$ were collected by using a

profiled ω-scan mode with scan angles of $(1.2+0.35\tan\theta)^\circ$ and prescan speed of $4.12^\circ\,min^{-1}$. Accurate unit-cell parameters were obtained by a least-squares fit of the 2θ values for 25 reflections in the 2θ range of 30 to 40°. Data reductions (including intensity integration, background, Lorentz, and polarization corrections) were performed with the WinGX package.[15] Absorption effects were evaluated with the psi-scan method,[16] and absorption correction was applied to the data (min/max transmission factors were 0.808/0.924). The structure was solved by direct methods (SIR-97)[17] and were completed by iterative cycles of full-matrix least-squares refinement on F_o^2 and ΔF synthesis by using the SHELXL-97[18] program (WinGX suite). All non-hydrogen atoms were refined anisotropically. The positions of the H atoms were detected in a difference Fourier and were refined with isotropic thermal factors or were introduced in calculated positions in their described geometries and allowed to ride on the attached carbon atom with fixed isotropic thermal parameters.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: biocatalysis · borylation · copper · reduction · yeast

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[19] CCDC 1818501 (Cu–**L1** complex) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre

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