Enantioselective Borohydride Reduction Catalyzed by Optically Active Cobalt Complexes

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Abstract: The highly enantioselective borohydride reduction of aromatic ketones or imines to the corresponding alcohols was developed in the presence of a catalytic amount of an optically active cobalt(II) complex catalyst. This enantioselective reduction is carried out using a precisely premodified borohydride with alcohols such as tetrahydrofurfuryl alcohol, ethanol and methanol. High optical yields are obtained by choosing the appropriate alcohol as modifiers and a suitable β-ketoiminato ligand of the catalyst. The enantioselective borohydride reduction has been successfully applied to the preparation of optically active 1,3-diols, the stereoselective reduction of diacylferrocenes, and dynamic and/or kinetic resolution of 1,3-dicarbonyl compounds.

Keywords: asymmetric catalysis · diastereoselectivity · enantioselectivity · kinetic resolution · reduction

Introduction

The enantioselective reduction of prochiral ketones is one of the most reliable and efficient methods to obtain the corresponding optically active secondary alcohols,[1] which are themselves found in various natural or medicinal compounds and are readily converted to other useful functionalized compounds. Various methods involving chemical and biological procedures have been developed for the enantioselective reduction of ketones. High enantioselectivities were achieved in the asymmetric hydrogenation of functionalized ketones such as α-amino ketones and β-ketoesters by using the diphosphine complexes of rhodium[2] and ruthenium.[3] Recently, simple ketones were enantioselectively hydrogenated using iridium[4] or ruthenium[5] complex catalysts. In particular, the combined system of BINAP–ruthenium(II), optically active diamine and KOH acted as a highly efficient catalyst for the enantioselective hydrogenation of aromatic ketones.[1a, 6] For the same purposes, metal hydride reagents modified with various optically active ligands have been alternatively proposed, such as lithium aluminum hydride,[7] sodium borohydride,[8] and borane with camphor, proline, and binaphthol derivatives.[9] It is remarkable that in the presence of a catalytic amount of chiral oxazaborolidines,[1b, 10] the asymmetric reduction of ketones was effectively achieved to obtain various optically active secondary alcohols. Many successful applications have been reported; for example, a prostaglandin precursor,[11] potassium channel blockers[12] and trichloromethyl alcohol used for the preparation of unnatural amino acids.[13] Borohydrides including lithium borohydride and sodium borohydride are some of the most conventional reducing reagents in organic synthesis due to their stability, high selectivity, and ease of handling, therefore, the enantioselective reduction of ketones was proposed[14] with the combined use of stoichiometric amounts of optically active *N*-benzoylcystine[15] as a ligand; for example, it was reported that butyrophenone was converted to the corresponding

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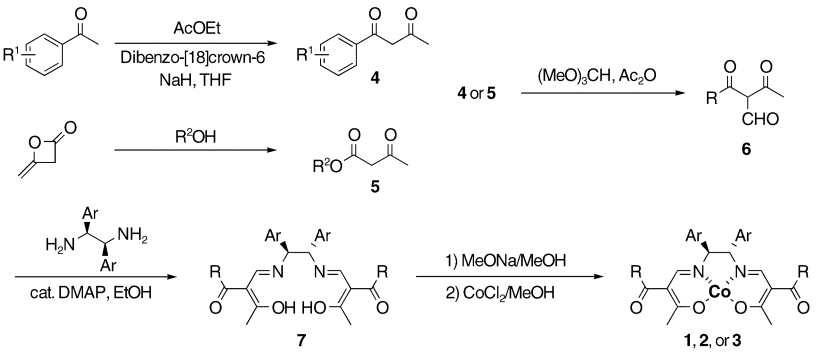
optically active alcohol with 90% *ee* at −40 °C. Although the lanthanoid complexes as a stoichiometric Lewis acid catalysts for the enantioselective reduction with sodium borohydride was reported,[16] there are few reports of the enantioselective reduction of ketones with borohydrides and a catalytic amount of an optically active metal complex. The optically active semicorrin–cobalt(II) complexes were proposed for the enantioselective 1,4-reduction with sodium borohydride but no application to the 1,2-reduction version was found.[17] Whereas the optically active β-ketoiminato cobalt(II) complexes proved to be efficient catalysts for the enantioselective borohydride reduction of aryl ketones and imines to obtain the corresponding optically active alcohols and amines in high yields with high *ee* values. In this article, we would like to fully disclose the highly enantioselective reduction of ketones and imines catalyzed by the optically active β-ketoiminatocobalt(II) complexes and its application to the highly stereoselective preparation of useful compounds.



Scheme 1. Preparation of β-ketoiminato cobalt(II) complexes.

Results and Discussion

Preparation of the optically active β-ketoiminato cobalt(II) complexes: It has been already reported from our laboratory that manganese(III)–chloride complexes with optically active β-ketoiminato-type ligands function as a catalyst during the enantioselective aerobic epoxidation of simple olefins[18] and the asymmetric oxidation of sulfides to optically active sulfoxides.[19] The corresponding cobalt(II) complexes were found to catalyze the enantioselective reduction of ketones with sodium borohydride.[20] Various optically active β-ketoiminato cobalt(II) complexes **1**–**3** (Figure 1) were synthesized as follows (Scheme 1). The benzoyl acetone derivatives **4** were prepared from the corresponding acetophenone using the Claisen condensation. The acetoacetic ester derivatives **5** were prepared from diketene and the corresponding alcohol. The treatment of these 1,3-dicarbonyl compounds (**4** or **5**) with trimethyl orthoformate and acetic anhydride provided 2-formyl-1,3-dicarbonyl compounds **6**. The optically active β-ketoiminato ligand **7** was obtained by imine formation with the optically active 1,2-diaryl-1,2-ethanediamines. The ligand **7** was then treated with two equivalents of sodium methoxide and subsequently treated with one equivalent amount of cobalt(II) chloride under a nitrogen atmosphere to afford the cobalt(II) complex **1**–**3** as an orange-colored powder. A X-ray analysis of the molecular structure of the optically active β-ketoiminato cobalt complex was performed for the cobalt(III)-iodide (Figure 2) and bromide complexes derived from the corresponding cobalt(II) complex **1a**[21] and **3b**,[22] respectively.

Activation of borohydride with appropriate alcohols: Preliminary investigations suggested that the addition of an alcohol was indispensable for achieving a high enantioselectivity. As shown in Table 1, the enantioselective reduction of 6-methoxy-1-tetralone (**8a**) with or without ethanol indicated a significant improvement in both the chemical yield and enantioselectivity. Without ethanol, the alcohol **9a** was obtained in less than 10% yield and its enantiomeric excess was only 5%, whereas in the presence of ethanol, an 83% *ee* in 38% yield in 24 h (entries 1 and 2). A higher enantiomeric excess of 87% as well as a faster reaction rate were realized in the presence of tetrahydrofurfuryl alcohol (THFA) to afford the alcohol **9a** in 82% yield (entry 3). The combined use of ethanol and THFA allowed further improvement in the enantiomeric excess of the alcohol **9a** with 91% (entry 4). In the presence of structurally similar

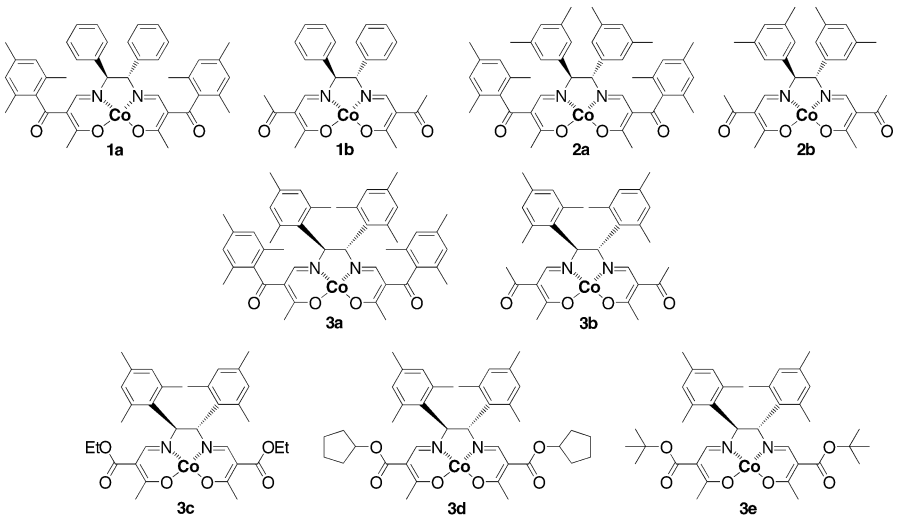


Figure 1. Various cobalt complex catalysts for enantioselective borohydride reduction.

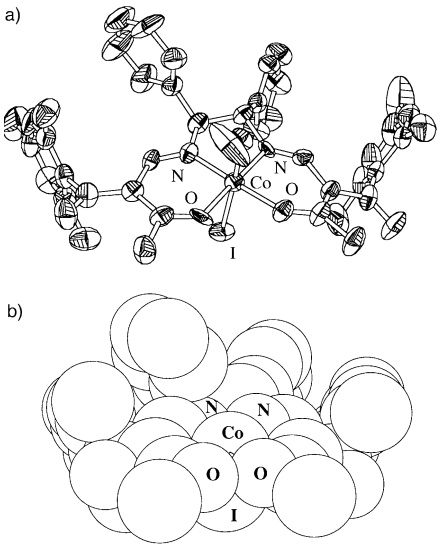
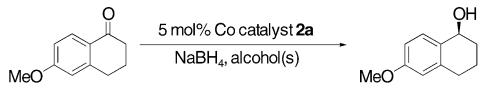
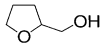
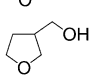
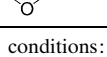


Figure 2. Crystal structure of [*N*,*N*′-bis{2,4,6-trimethylbenzoyl)-3-oxobutylidene}-(1*S*,2*S*)-1,2-diphenylethylenediaminato]cobalt(III) iodide **1a-I**. a) ORTEP drawing. b) Space filling model based on the X-ray structure (MeOH was omitted).

Table 1. Effects of the various alcohol(s) on the enantioselective borohydride reduction catalyzed by cobalt(II) catalyst.[a]



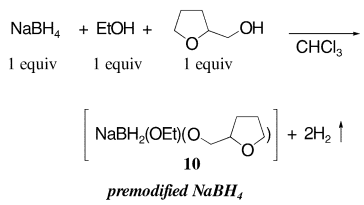
8a **9a**

Entry	Alcohols (equiv vs $NaBH_4$)	Yield [%]	*ee* [%][b]
1	none	< 10	5
2	EtOH (6)	38	83
3	 (THFA) (6)	82	87
4	THFA (6)+EtOH (6)	87	91
5	THFA (1)+EtOH (1)	82	93
6	THFA (14)+EtOH (3)	> 98	93
7	 (6)+EtOH (6)	65	75
8	 (6) + EtOH(6)	27	70

[a] Reaction conditions: 0.50 mmol substrate **8a**, 0.025 mmol Co catalyst **2a**, 0.75 mmol $NaBH_4$, in $CHCl_3$ (10 mL), at −20 °C, 24 h. [b] Determined by HPLC analysis.

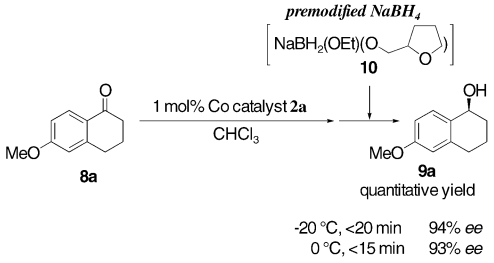
alcohols such as methoxymethanol and tetrahydro-3-furanmethanol, the enantioselectivities were lower (75 and 70 % *ee*, entries 7 and 8, respectively). The molar ratios of THFA versus ethanol was systematically examined for the catalytic and enantioselective reduction of the ketone **8a**, and these surveys indicated that a 1 molar equivalent of both alcohols to $NaBH_4$ were at least required for achieving a high *ee* (91 % *ee*, entry 5). The best result was observed by adding 14 molar equivalents of THFA and 3 molar equivalent of ethanol (entry 6). In the optimized reaction conditions, 1 mol % of the cobalt(II) complex **2a** catalyzed the reaction to quantitatively afford the corresponding alcohol **9a** in 6 h with 93 % *ee*. The non-catalyzed reduction path was also examined by subjecting the modified borohydride to the ketone **8a** in the absence of the cobalt(II) complex catalyst for 48 h, and the starting substrate was nearly quantitatively recovered (> 95 %), thus the observation indicated a very small contribution of the non-catalyzed path in the present enantioselective reduction. The addition of THFA to this reaction system presented two interesting features; 1) THFA made the reaction mixture homogenous, and an appropriately activated borohydride was specifically formed in situ. 2) A modification protocol of the borohydride influenced the reactivity and enantioselectivity during the catalytic reduction of the ketones.

Although $NaBH_4$ is usually employed for the reduction of ketones in alcoholic solvents, the resulting activated borohydride has never been completely characterized.[23] The premodification procedure for the formation of an active borohydride was then examined. The monitoring of the H_2 evolution during the treatment of the borohydride with alcohols revealed that nearly 2 molar equivalents of H_2 versus $NaBH_4$ was gradually liberated as the modification reaction proceeded. This implied that $NaBH_4$ consumed 2 molar equivalents of alcohols. Based on the multiplier effect of ethanol and tetrahydrofurfuryl alcohol mentioned in Table 1, the premodified borohydride in the present reaction is tentatively illustrated as formula **10** (Scheme 2).[24] The



Scheme 2. Preparation of premodified activated borohydride.

borohydride thus modified with THFA/ethanol was subjected to the reduction of 6-methoxy-1-tetralone (**8a**) in the presence of a catalyst **2a**, and drastic acceleration of the enantioselective reduction was observed. When the premodified borohydride **10** solution was used at −20 °C (Scheme 3),



Scheme 3. Efficient borohydride reductant.

the reaction was completed within 20 min even in the presence of 1 mol % of catalyst to afford in quantitative yield the corresponding alcohol **9a** with 94 % *ee*. The modification of the borohydride and the reduction were carried out at 0 °C, and the reaction was completed within 15 min while maintaining the enantioselectivity (93 % *ee*).

The tentative structure of the modified borohydride **10** was supported by the experiments of the asymmetric reduction of

6-methoxy-1-tetralone with 5 mol% of a cobalt(II) catalyst **2a** by using the three kinds of premodified borohydrides treated with one, two, and three equivalent(s) of THFA, respectively (Figure 3). During the reaction of the borohydride with

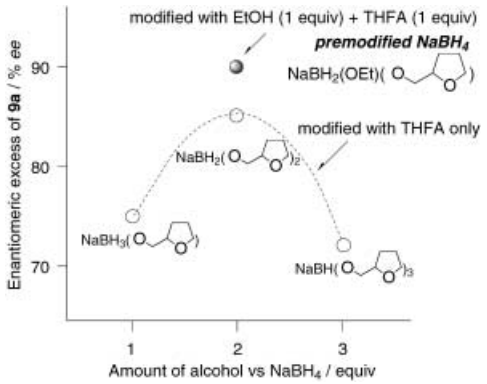


Figure 3. Relationship between the amount of alcohol vs $NaBH_4$ and enantiomeric excess.

THFA at room temperature, the corresponding amount of hydrogen gas was observed versus the amount of THFA employed. The premodified borohydride using one equivalent of THFA afforded the corresponding alcohol in 36% yield with 75% *ee* for 18 h at $-20\,^{\circ}C$. For the premodified borohydride with two equivalents of THFA, the reduction slowly proceeded, but a better enantioselection was observed, that is, the optically active alcohol was obtained in 17% yield with 85% *ee* for 24 h. Both the reactivity and enantioselectivity were lower in the reaction system using the modified borohydride made from sodium borohydride and three equivalents of THFA; the ketone was converted to the corresponding alcohol in 10% yield with 72% *ee* for 24 h. Furthermore, by using one equivalent each of THFA and ethanol, the reactivity as well as the enanitoselectivity were significantly improved; the reaction gave the alcohol in 65% yield with 90% *ee* for 20 h. This was consistent with the above-mentioned result using the in-situ-modified borohydride with one equivalent each of THFA and ethanol (entry 5 in Table 1).

The ^{13}C NMR analysis of the resulting borohydride also supported the tentative structure mentioned above. The sodium borohydride was treated with one equivalent of ethanol and four equivalents of THFA in $CHCl_3$ at $0\,^{\circ}C$. During the treatment, it was observed that almost two equivalents of hydrogen gas were released. Although the peaks for EtOH were not changed after borohydride treatment, a new set of peaks for THFA (peaks **a**, **b**, and **c** in Figure 4) was observed next to the original set of peaks (peaks **A**, **B**, and **C** in Figure 4). The intensity ratio of the unshifted peaks (**A**, **B**, and **C**) for the remaining THFA versus the shifted peaks (**a**, **b**, and **c**) after borohydride treatment was about 3:1. It is reasonable to assume that the borohydride reacted with one molar of EtOH and THFA each to afford $NaBH_2(OEt)(OTHFA)$. It was reported that the borohydrides substituted by two or three alcohols, such as MeOH and EtOH, were not stable and were readily disproportionated to the starting borohydride BH_4^- and the borate

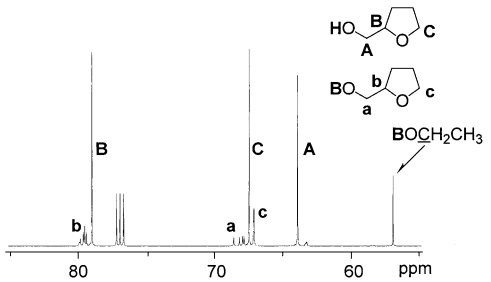
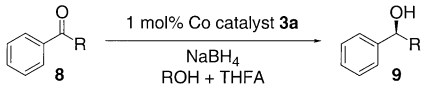


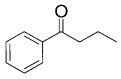
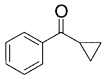
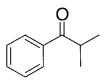
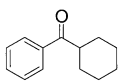
Figure 4. ^{13}C NMR spectra of modified $NaBH_4$ in $CDCl_3$.

$[B(OR)_4]^-$.[23] On the contrary, the oxygen atom on tetrahydrofuran could partially coordinate to borate to form a five-membered chelate structure and stabilize the di-alkoxy-substituted borohydride. The interpretation is quite consistent with the ^{13}C NMR observation that the peak for the 5th position on tetrahydrofuran was significantly shifted after borohydride treatment.

It should be noted that the appropriate choice of alcohol in the combination with THFA was also significantly effective for tuning the enantioselectivity (Table 2). For example, when the borohydride was modified with the combined use of methanol and THFA, the aryl primary alkyl ketone **8b** was converted to the corresponding alcohol **9b** with 90% *ee*. The use of ethanol in place of methanol in this reaction improved the enantioselection to 97% *ee*. A similar effect was observed during the enantioselective reduction of the cyclopropyl phenyl ketone **8c** (76% *ee* with methanol versus 90% *ee* with ethanol). On the contrary, methanol was alternatively effective for the reduction of the aryl secondary alkyl ketones **8d** and **8e** (98 and 95% *ee*, respectively). The following notes for choosing the suitable additive alcohols to achieve a high enantioselection are described; 1) The use of the ethanol-THFA combination for the modification of borohydride is preferable when using sterically less demanding ketones

Table 2. Combination of additive alcohols with various aromatic ketones.[a]



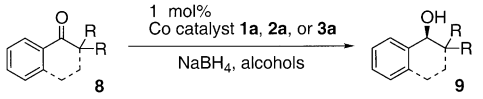
Entry	Ketone		*ee* [%][b] Activator ROH MeOH	EtOH
1		**8b**	90	97
2		**8c**	76	90
3		**8d**	98	77
4		**8e**	95	78

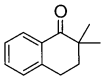
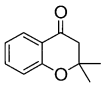
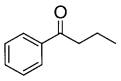
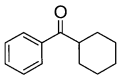
[a] Reaction conditions: 0.50 mmol substrate, 0.005 mmol Co catalyst **3a**, 0.75 mmol $NaBH_4$, 2.25 mmol ROH, 10.3 mmol THFA, in $CHCl_3$ (10 mL), at $-20\,^{\circ}C$, 12 h, quantitative yield. [b] Determined by HPLC analysis.

(primary alkyl or cyclopropyl ketone). 2) For the ketones with a more steric demand (secondary alkyl ketone), methanol is preferable for the combined use with THFA.[25]

Combination of cobalt(II) complexes with various substituted ketones: The preliminary investigations of the asymmetric borohydride reduction of various ketones using the cobalt(II) complex catalysts **1a**, **2a**, or **3a** suggested that the suitable matching of catalyst and substrates is significant in order to achieve a high enantioselection (Table 3). For example, the

Table 3. Combination of cobalt(II) complex catalysts with various substituted ketones.[a]



Entry	Ketone		*ee* [%][b] Co catalyst		
			1a	**2a**	**3a**
1		**8f**	91[c] (81)[a]	75	n.r.[d]
2		**8g**	65	90	60
3		**8h**	88	92	74
4		**8b**	63	87	97
5		**8e**	62	65	95[c]

[a] Reaction conditions: 0.50 mmol substrate, 0.005 mmol Co catalyst, 0.75 mmol $NaBH_4$, 2.25 mmol EtOH, 10.3 mmol THFA, in $CHCl_3$ (10 mL), at $-20\,^{\circ}C$, 12 h, quantitative yield. [b] Determined by HPLC analysis. [c] Using MeOH intead of EtOH. [d] No reaction.

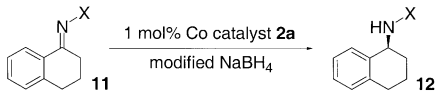
reduction of 2,2-dimethyl-1-tetralone (**8f**) with the combined use of MeOH/THFA or EtOH/THFA was catalyzed by the complex **1a** to afford the corresponding optically active alcohol in 91 or 81 % *ee*, respectively, whereas that it was 75 % *ee* when the complex **2a** was employed. On the contrary, the enantioselectivity during the reduction of 1-tetralone (**8g**) was observed to be higher when using complex **2a** (90 % *ee*) than that for the complex **1a** or **3a** (65 or 60 % *ee*, respectively). Similarly, 2,2-dimethyl-4-chromanone (**8h**) was converted to the corresponding alcohol by the enantioselective borohydride reduction catalyzed by complex **2a** (with 92 % *ee*) than by using complex **1a** (with 88 % *ee*) or **3a** (with 74 % *ee*). For the acyclic ketones such as butyrophenone (**8b**) and cyclohexyl phenyl ketone (**8e**), complex **3a** was the most matched catalyst to achieve a high enantioselectivity and afford the optically active alcohols with 95 and 97 % *ee*, respectively. Enantioselection ranging between 62–87 % *ee* in the same reaction was observed by using complex **1a** and **2a**.[26]

A general rule to choose a matched catalyst was extracted as follows; 1) the complex **1a** having the chiral ligand derived from prototypical 1,2-diphenylethylenediamine was effective for the reduction of aryl ketones which are sterically hindered at the α-position of the carbonyl groups (entry 1). 2) The complex **2a** having the chiral ligand derived from 1,2-bis(3,5-dimethylphenyl)ethylenediamine was the most matched to the cyclic aryl ketones with less steric demand (entries 2 and 3). 3) The complex **3a** having the chiral ligand derived from the bulky 1,2-bis(2,4,6-trimethylphenyl)ethylenediamine was effectively employed during the enantioselective borohydride reduction of acyclic alkyl aryl ketones (entries 4 and 5). The present study indicated that highly enantioselective borohydride reductions of various aryl ketones are achieved by the appropriate choice of the optically active cobalt(II) catalysts and the matched combination of two alcohols used for modifying the borohydride. Various aromatic ketones were smoothly converted to the corresponding optically active alcohols in quantitative yield using 1 mol % of the cobalt(II) complex catalysts.

Catalytic enantioselective reduction of imine: In order to prepare the optically active alcohols with high efficiency, the catalytic enantioselective reduction of prochiral ketones had been extensively investigated. Likewise, analogous catalytic enantioselective reductions of imines to afford optically active amines have been reported in the literature, however, few examples are known for the syntheses of the optically active amines with satisfactory *ee* values. For examples, the recent achievements of the metal catalyzed enantioselective hydrogenations,[27] transfer hydrogenation,[28] hydrosilylations,[29] and oxazaborolidine[30] catalyzed enantioselective borane reduction of imines are not enough in terms of enantioselectivity or applicability. The development of a highly efficient enantioselective reduction of imines still remains as challenging topics in synthetic organic chemistry. The above-mentioned enantioselective borohydride reduction was applied to compounds with a C=N functionality, and it was found that the reduction of *N*-substituted ketimines were effectively catalyzed by the cobalt(II) complexes to form the corresponding optically active amines with high enantiomeric purity.

Preliminary experiments on the synthesis of the optically active primary amines from each aryl ketoximes and *N*-substituted ketimines by the enantioselective borohydride reductions using 1 mol % of the cobalt(II) complex **2a** were tried at 0 °C for 4 h (Table 4). The treatments of oxime **11a** or oxime methyl ether **11b** by the borohydride reductions using the cobalt(II) complex did not afford the optically active primary amines under the above conditions, and the starting substrates were completely recovered. On the contrary, when the reduction of the protected imines such as *N*-toluenesulfonyl imine **11c** (*N*-tosyl imine) or *N*-diphenylphosphinyl imine **11d** was tried, the reactions smoothly took place and the corresponding optically active amines were obtained in 95 and 85 % yields with 71 and 98 % *ee*, respectively. The observed differences in *ee* values of the resulting amines could be attributed to the competitive direct reduction of imines with borohydrides by a non-catalytic reduction pathway. When the *N*-tosyl imine **11c** was subjected to the reduction in

Table 4. Effects of the various substituents of imines.[a]



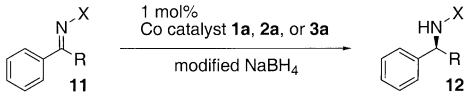
Entry	−X		Yield [%]	*ee* [%][b]
1	−OH	**11a**	n.r.[c]	
2	−OMe	**11b**	n.r.[c]	
3	−Ts	**11c**	95	78
4	$-P(O)Ph_2$	**11d**	85	98

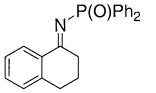
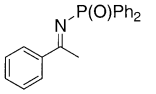
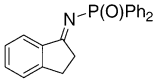
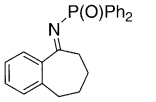
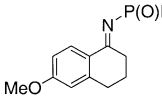
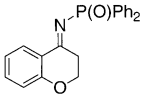
[a] Reaction conditions: 0.50 mmol substrate, 0.005 mmol Co catalyst **2a**, 0.75 mmol modified $NaBH_4$ (0.75 mmol $NaBH_4$, 0.75 mmol EtOH, 10.3 mmol THFA), in $CHCl_3$, at 0 °C, 4 h. [b] Determined by HPLC analysis. [c] No reaction.

the absence of a catalyst, the corresponding racemic amine was obtained in 30% yield. On the other hand, *N*-phosphinyl imine **11d** was inert toward the premodified borohydride alone; this suggested that *N*-phosphinyl imines are suitable substrates for the present reductions. The enantioselective borohydride reduction using an optically active cobalt(II) complex catalyst (**1a**, **2a**, or **3a**) was then examined using various *N*-diphenylphosphinyl imines, and the results are summarized in Table 5.

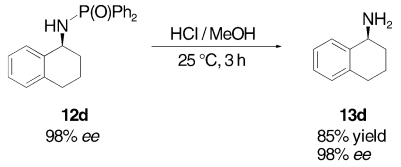
In the presence of 1 mol% of the above-mentioned catalyst **1a**, **2a**, or **3a**, various aryl *N*-phosphinyl imines were smoothly converted to the corresponding optically active amines in good yields at 0 °C within 4 h. As shown in the enantioselective borohydride reduction of aryl ketones, a suitable combination of the cobalt(II) catalyst and aryl imine was one of the important factors in achieving high enantioselectivity (Table 5). When the cyclic aryl imine **11d** was subjected to the reductions, the cobalt(II) complex **2a** was the best choice, and the corresponding amine was obtained in 98% *ee* whereas complex **1a** gave 92% *ee* (entries 1 and 2). It should be noted that when complex **3a** was used, no reaction took place (entry 3). It may be attributed to the high degree of steric congestion for *N*-diphenylphosphinyl imines with cobalt(II) complexes. Complex **3a** gave the corresponding amine with the best enantiomeric excess (90% *ee*, entry 6) for the acyclic aryl imine **11e**. Complexes **1a** and **2a** gave lower yields as 77 and 80% *ee*, respectively (entries 4 and 5). The observed combinations of the catalyst and imine are similar to the suitable pairs found for the aryl ketone reduction, and thus the cyclic aryl substrates with complex **2a** and acyclic aryl substrates with complex **3a** are preferable. Accordingly, various cyclic *N*-phosphinyl imines **11f–i** were applied to the reductions using 1 mol% of complex **2a**, and the corresponding optically active amines were obtained in 91–99% *ee* (entries 7–10).[31] The resulting *N*-phosphinyl amine represents an additional advantage over the *N*-sulfonyl amine, since the conversion to the optically active primary amine by subsequent removal of the diphenylphosphoryl group can be carried out under mild conditions; for example, using HCl/MeOH at 25 °C for 3 h, the optically active primary amine was obtained in good yield without racemization (Scheme 4).

Table 5. Enantioselective borohydride reduction of *N*-diphenylphosphinyl imines.[a]



Entry	Imine		Catalyst	Yield [%]	*ee* [%][b]
1		**11d**	**1a**	88	92
2			**2a**	85	98
3			**3a**	n.r.[c]	
4		**11e**	**1a**	96	77
5			**2a**	95	80
6			**3a**	97	90
7		**11f**	**2a**	86	91
8		**11g**	**2a**	81	94
9		**11h**	**2a**	97	99
10		**11i**	**2a**	81	92

[a] Reaction conditions: 0.50 mmol substrate, 0.005 mmol Co catalyst **2a**, 0.75 mmol modified $NaBH_4$ (0.75 mmol $NaBH_4$, 0.75 mmol EtOH, 10.3 mmol THFA), in $CHCl_3$, at 0 °C, 4 h. [b] Determined by HPLC analysis. [c] No reaction.



Scheme 4. Removal of diphenylphosphoryl group.

Preparation of optically active C_2-symmetrical diol compounds: Enantiomeric pure C_2-symmetrical 1,3-diaryl-1,3-propanediol could be employed as the essential component of chiral ligands in asymmetric syntheses;[32] however, few reports have been published on the successful preparation of the optically active 1,3-diaryl-1,3-propanediols.[33] The optically active ferrocene derivatives have been extensively employed as the powerful chiral ligands of transition-metal complexes for various enantioselective catalyses.[34] The C_2-symmetrical chiral ferrocenyldiol is one of the most accessible precursors for the optically active ligands.[35] Among several preparations,[36] the enantioselective reduction with borane/THF catalyzed by the chiral oxazaborolidine (CBS reduc-

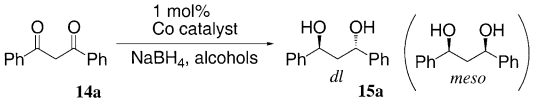
tion)[9a, 10a, 11] of the corresponding diketones is the most reliable method.[37] Though the protocol was effective for various 1,1′-diacylferrocenes, the loading of a large amount (60–200 mol%) of the oxazaborolidine catalyst was required for the high enantioselectivity. In this section, it was described that the efficient and highly asymmetric synthesis of C_2-symmetrical diol compounds from the corresponding diketones was achieved by the enantioselective borohydride reduction catalyzed by the optically active cobalt(II) complexes.

The enantioselective borohydride reduction of 1,3-diaryl-1,3-diketones was first examined using various optically active β-ketoiminato cobalt complex catalysts adopting 1,3-diphenyl-1,3-diketone (**14a**) as the model substrate (Table 6). It was found that the enantioselectivities in this reaction were sensitively affected by the steric demand of the chiral diamine part of the cobalt catalyst ligand. When complex **1a**, **1b** or **2a**, prepared from the optically active 1,2-diphenylethylenediamine or 1,2-bis(3,5-dimethylphenyl)ethylenediamine, was employed as a catalyst, the *ee* values of the product were moderate (entries 1–3). However, catalyst **3**, having the optically active 1,3-bis(2,4,6-trimethylphenyl)ethylenediamine unit, realized an excellent enantioselectivity and a good-to-high *dl* selectivity in each case (entries 4–7). Especially, catalyst **3b**, with attached acyl groups as the side chains, indicated a high *dl* selectivity (81%) and excellent *ee* value (98%) for the enantioselective reduction of 1,3-diphenyl-1,3-propanedione (**14a**).[38] After optimizing the reaction conditions, it was found that the concentration of the reaction mixture depended on the stereoselectivity. In the 8.3×10^{-3} M solution (0.25 mmol substrate versus 30 mL chloroform), the *dl* selectivity was enhanced up to 84% with 98% *ee* (entry 8).

The optimized procedure was successfully applied to the preparation of various 1,3-diaryl-1,3-propanediols from the corresponding 1,3-diketones (Table 7). Diketones with alkyl, electron-donating, and -withdrawing groups were all smoothly reduced in high enantioselectivity with high *dl* selectivity. As examples, the 1,3-diaryl-1,3-diols with *p*-methyl- (**15b**), *p*-methoxy- (**15d**), *p*-fluoro (**15e**), and *o*-fluoro- (**15f**) substituents were obtained in 97, 98, 99, and 97% *ee*, with 85, 84, 76, and 90% *dl* selectivity, respectively (entries 2, and 4–6). For the reduction of 1,3-bis(4-*tert*-butylphenyl)-1,3-propanedione (**14c**), the addition of methanol instead of ethanol was effective in the reduction system (entry 3) for modification of the borohydride. Also, dinaphthyldione with a larger aromatic ring **14g** was smoothly reduced to the 1,3-diol **15g** with 81% *dl* selectivity and 99% *ee* (entry 7).[39]

The present procedure could be readily used for the multigram preparation because one recrystallization of the crude products afforded the enantiomeric pure 1,3-diols. For example, dibenzoylmethane (10.0 g) was treated with the modified borohydride in the presence of a catalytic amount of the cobalt complex **3a** produced a quantitative yield of 1,3-diphenyl-1,3-propanediol. After rinsing the *dl*/*meso* mixture with ethyl acetate/hexane and simple recrystallization from ethyl acetate, optically pure 1,3-diphenyl-1,3-propanediol (6.15 g) was obtained in 60% overall yield (Scheme 5). It should be noted that the obtained pure 1,3-propanediol was quantitatively converted to the optically pure 1,3-diphenyl-1,3-propanediamine by the conventional method.[40]

Table 6. Various cobalt(II) catalysts for enantioselective borohydride reduction of dibenzoylmethane.[a]

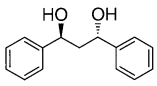
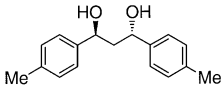
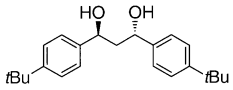
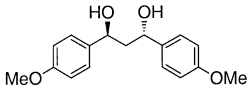
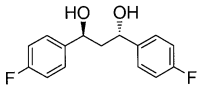
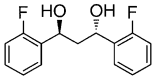
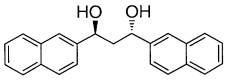


14a 15a

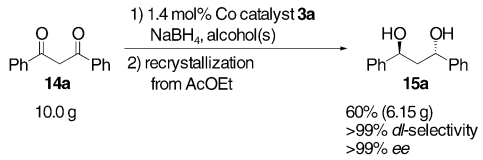
Entry	Catalyst	Yield [%]	*dl*:*meso*[b]	*ee* [%][c]
1	**1a**	93	53:47	41
2	**1b**	93	29:71	61
3	**2a**	quant	56:44	64
4	**3a**	96	85:15	90
5	**3b**	93	81:19	98
6	**3c**	97	66:34	89
7	**3d**	90	72:28	94
8[d]	**3b**	quant	84:16	98

[a] Reaction conditions: 0.50 mmol substrate **14a**, 0.005 mol% Co catalyst, 1.5 mmol $NaBH_4$, 4.5 mmol EtOH, 63 mmol THFA, in $CHCl_3$ (20 mL), at $-20\,^{\circ}C$, 24–48 h. [b] Determined by ^1H NMR analysis of diacylated 1,3-diols after the treatment with Ac_2O/pyridine. [c] Determined by HPLC analysis. [d] Using 30 mL $CHCl_3$ for 0.25 mmol substrate.

Table 7. Enantioselective preparation of various 1,3-diaryl-1,3-propanediols.[a]

Entry	1,3-Diaryl-1,3-propandione		Yield [%]	*dl*:*meso*[b]	*ee* [%][c]
1[d]		**15a**	quant	84:16	98
2		**15b**	94	85:15	97
3[e]		**15c**	94	80:20	96
		15d			
4			99	84:16	98
5		**15e**	98	76:24	99
6		**15f**	99	90:10	97
7		**15g**	93	81:19	99

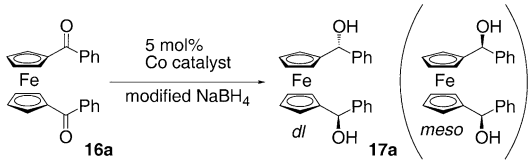
[a] Reaction conditions: 0.25 mmol substrate, 0.0125 mmol Co catalyst, **3b**, 0.75 mmol $NaBH_4$, 2.25 mmol EtOH, 10.5 mmol THFA, in $CHCl_3$ (30 mL), at $-20\,^{\circ}C$, 40–60 h. [b] Determined by ^1H NMR analysis of diacylated 1,3-diols after the treatment with Ac_2O/pyridine. [c] Determined by HPLC analysis. [d] Using 0.005 mmol Co catalyst **3b**. [e] Using MeOH instead of EtOH.



Scheme 5. Preparation of enantiopure 1,3-diphenyl-1,3-propanediol.

The enantioselective reduction of 1,1′-dibenzoylferrocenes (**16a**) into optically active 1,1′-ferrocenyldiols was adopted as a model reaction for screening the various optically active β-ketoiminato cobalt complexes for the catalytic borohydride reduction (Table 8). When complex **1** or **2** was employed as a catalyst, the *ee* values of the product were very low (entries 1–4), whereas excellent *ee* values (>99% *ee*) were achieved by the bulky complex **3** (entries 5–9).[38] Catalyst **3b** (entry 6), with attached acyl groups as the side chains, indicated the highest *dl* selectivity (88%) with excellent *ee* (>99%) for the enantioselective reduction of 1,1′-dibenzoylferrocene (**16a**). The solvent effect was subsequently surveyed and found that the reaction time significantly depended on the reaction solvent. In chloroform, a suitable solvent for the enantioselective borohydride reduction, and other typical solvents, the reduction was completed in 12–72 hours,[41] whereas in diethyl ether, the enantioselective reduction was completed in 0.5 h at −20 °C. In diethyl ether at 0 °C, the reduction to afford 1,1′-bis(α-hydroxypropyl)ferrocene (**17a**) was finished within 15 min while maintaining high enantio- and *dl* selectivities.

Table 8. Various cobalt(II) catalysts for enantioselective borohydride reduction of 1,1′-dibenzoylferrocene.[a]

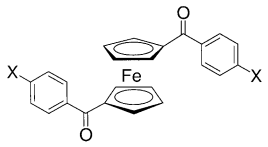
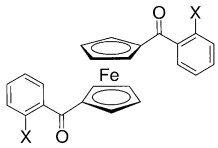
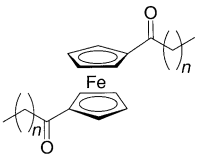


Entry	Catalyst	*dl*:*meso*[b]	*ee* [%][c]
1	**1a**	21:79	31
2	**1b**	22:78	21
3	**2a**	23:77	20
4	**2b**	25:75	32
5	**3a**	86:14	>99
6	**3b**	88:12	>99
7	**3c**	80:20	>99
8	**3d**	72:28	>99
9	**3e**	75:25	>99

[a] Reaction conditions: 0.125 mmol substrate **16a**, 0.00625 mmol Co catalyst, 0.50 mmol modified $NaBH_4$ (0.50 mmol $NaBH_4$, 0.50 mmol EtOH, 7.0 mmol THFA), in $CHCl_3$, at −20 °C, 12 h, quantitative yield. [b] Determined by ^{13}C NMR analysis. [c] Determined by HPLC analysis.

The enantioselective borohydride reduction was successfully applied to the preparation of various optically active 1,1′-ferrocenyldiols using 5 mol% of a cobalt catalyst **3b** in diethyl ether at 0 °C (Table 9). Various 1,1′-dibenzoylferrocene derivatives, possessing *p*-fluorophenyl (**16b**), *p*-chlorophenyl (**16c**), *p*-bromophenyl (**16d**), *p*-methylphenyl (**16e**), *o*-fluorophenyl (**16f**), and *o*-chlorophenyl (**16g**) were converted to the corresponding C_2-symmetrical ferrocenyldiols **17** with excellent *ee* values and high *dl* selectivity (entries 2–7). The reaction of 1,1′-di(*o*-bromobenzoyl)ferrocene (**16h**) was very slow at 0 °C due to steric hindrance. Therefore, the enantioselective reduction was carried out at the diethyl ether reflux temperature to afford the corresponding diols in 96% yield for 0.5 h with 87% *dl* selectivity and 97% *ee* (entry 8). The present enantioselective reduction could be applied to the 1,1′-dialkanoylferrocenes. Although the *dl* selectivity from 1,1′-dihexanoylferrocene (**16k**) was not sufficient at 0 °C, the reduction was tried at −40 °C to afford the corresponding diol with 87% *dl* selectivity and >99% enantioselectivity (entry 11). Also, the 1,1′-dipropanoyl- (**16i**), dibutanoyl- (**16j**), and dioctanoyl- (**16l**) ferrocenes were stereoselectively reduced to the corresponding ferrocenyldiols with high *dl* selectivity and excellent enantioselectivity (entries 9, 10, and 12).[42] It is noted that the efficient and highly stereoselective preparation of the C_2-symmetrical chiral diol compounds was provided by the enantioselective borohydride reduction of the 1,3-diaryl-1,3-propanedione, 1,1′-dialkanoyl-, and 1,1′-dibenzoyl-ferrocenes catalyzed by the optically active β-ketoiminato cobalt(II) complex.

Table 9. Enantioselective borohydride reduction of various 1,1′-diacylferrocenes.[a]

Entry	1,1′-Diacylferrocene		Yield [%]	*ee* [%][b]	*dl*:*meso*[c]
1		X = H **16a**	92	>99	89:11
2		F **16b**	90	>99	87:13
3		Cl **16c**	89	99	87:13
4		Br **16d**	88	>99	89:11
5		CH_3 **16e**	90	>99	88:12
6		X = F **16f**	94	>99	99:1
7		Cl **16g**	87	>99	93:7
8[d]		Br **16h**	96	97	88:12
9[e]		*n* = 1 **16i**	84	>99	82:18
10[e]		2 **16j**	80	>99	80:20
11[e]		4 **16k**	90	>99	87:13
12[e]		6 **16l**	69	>99	85:15

[a] Reaction conditions: 0.125 mmol substrate, 0.00625 mmol Co catalyst **3b**, 0.5 mmol modified $NaBH_4$, in Et_2O, at 0 °C within 3 h. [b] Determined by HPLC analysis. [c] Determined by ^1H NMR analysis and/or ^{13}C NMR analysis. [d] Et_2O reflux temperature, 0.5 h. [e] Using 0.0125 mmol Co catalyst **3b**, 1.25 mmol modified $NaBH_4$, at −40 °C, 48 h.

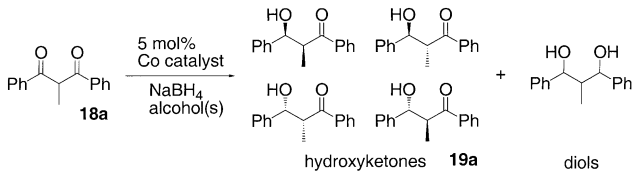
Synthesis of optically active *anti*-aldol compounds: The aldol reaction is one of the most useful and reliable methods in organic synthesis for new carbon–carbon bond formation accompanied by the preparation of 2-substituted-3-hydroxycarbonyl units.[43] Optically active 2-substituted-3-hydroxy-

carbonyl units are often observed in natural products and their hydroxy or carbonyl groups could be converted into various functionalities. Therefore, highly diastereoselective and/or enantioselective versions of the aldol reaction[44] are indispensable for organic synthesis. A wide variety of enantioselective aldol reactions, especially the catalytic enantioselective version by optically active transition-metal complexes, have been dynamically studied for a decade.[45] In almost all catalytic enantioselective aldol reactions, however, the preparation of silyl or metal enolates is required in advance along with a relatively large amount of loading of the catalyst for high enantio- and/or diastereoselectivity. These disadvantages have made the catalytic and enantioselective aldol reactions difficult to use for multigram scale laboratory and manufacturing processes. Alternatively, optically active 2-substituted-3-hydroxycarbonyl compounds could also be prepared from the corresponding 2-substituted-1,3-dicarbonyl compounds with catalytic and enantioselective reductions.

The symmetrical 2-substituted-1,3-diketones was first adopted as a model substrate for the demonstration of the reductive synthesis of optically active aldol compounds using the enantioselective borohydride reduction catalyzed by the optically active β-ketoiminato cobalt complexes. Because the four isomers of the hydroxyketones and diol compounds could be produced in this reaction, the stereoselectivity and reactivity should be controlled at the same time. The enantioselective reduction of 1,3-diphenyl-2-methyl-1,3-propanedione (**18a**) into the optically active 1,3-diphenyl-3-hydroxy-2-methylpropanone (**19a**) was chosen as a model reaction for screening the suitable optically active β-ketoiminato cobalt catalyst (Table 10). Although the *anti*-selectivity of the resulting β-hydroxyketones was excellent in each case, the *ee* values of the *anti*-products widely varied, being sensitive to the structure of the cobalt complex catalysts (entries 1–6). Catalyst **1a** or **2a** afforded a low or moderate *ee* of the *anti*-product (entries 1 and 2), whereas the enantioselectivity was remarkably improved when employing catalysts **3a–c** and **e** derived from the optically active 1,3-bis(2,4,6-trimethylphenyl)ethylenediamine (entries 3–6). Among these catalysts, it was found that catalyst **3b**, having acetyl groups on both side chains, was the most efficient catalyst for the enantioselective reduction of the 1,3-diphenyl-2-methyl-1,3-propanedione (entry 4). After optimization of the reaction temperature ($-20\,^{\circ}C$) and procedure, 99% *ee* of the *anti*-product was isolated in 93% yield with 99% diastereoselectivity (entry 7).

The catalytic and enantioselective reduction was successfully applied in the preparation of various optically active 2-substituted-1,3-diaryl-3-hydroxypropanones **19** from the corresponding 1,3-diketones **18** (Table 11). Various 2-methyl-1,3-diaryl-1,3-diketones, having *p*-methylphenyl- (**18b**), 2-naphthyl- (**18c**), *p*-bromophenyl- (**18d**), and *p*-methoxy-

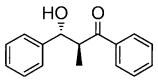
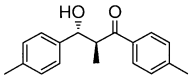
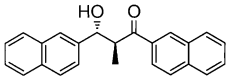
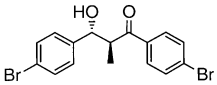
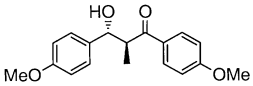
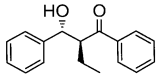
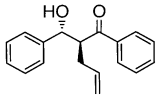
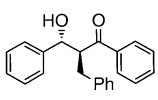
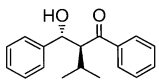
Table 10. Various cobalt(II) catalysts for enantioselective borohydride reduction of 2-methyl-1,3-diphenyl-1,3-propanedione.[a]



Entry	Catalyst	Yield [%]	*anti*-Selectivity [%][b]	*ee* (*anti*) [%][c]	Recovery [%]	Diol Yield [%]
1	**1a**	65	93	33	3	27
2	**2a**	58	99	45	–	39
3	**3a**	65	94	89	24	11
4	**3b**	75	95	92	10	15
5	**3c**	55	98	81	1	41
6	**3e**	71	96	87	1	28
7[d]	**3b**	93	99	99	–	7

[a] Procedure A: A solution of the Co catalyst and the substrate was added to the solution of the modified $NaBH_4$; 0.5 mmol substrate **18a**, 0.025 mmol Co catalyst, 0.5 mmol $NaBH_4$, 1.5 mmol oEtOH, 7 mmol THFA, in $CHCl_3$, at 0 °C, 10 h. [b] Determined by ^1H NMR analysis. [c] Determined by HPLC analysis. [d] Procedure B: To the solution of the Co catalyst and the substrate was added a solution of the modified $NaBH_4$; 0.25 mmol substrate **18a**, 0.0125 mmol Co catalyst **3b**, 0.25 mmol modified $NaBH_4$ (0.25 mmol $NaBH_4$, 0.25 mmol EtOH, 3.5 mmol THFA), in $CHCl_3$, at $-20\,^{\circ}C$, 10 h.

Table 11. Enantioselective borohydride reduction of 2-alkyl-1,3-diaryl-1,3-propanediones.[a]

Entry	Hydroxyketone		Yield [%]	*anti*-selectivity [%][b]	*ee* (*anti*) [%][c]
1		**19a**	93	99	99
2		**19b**	97	99	99
3		**19c**	73	99	99
4		**19d**	68	99	99
5		**19e**	96	99	97
6		**19f**	88	99	99
7		**19g**	88	99	97
8		**19h**	96	99	98
9		**19i**	45	99	91

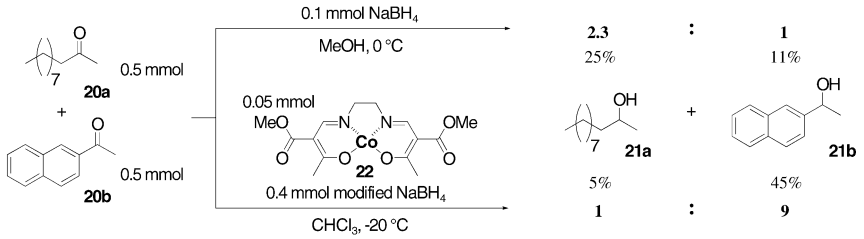
[a] Procedure B (see Table 10). [b] Determined by ^1H NMR. [c] Determined by HPLC analysis.

phenyl- (**18e**) as the aryl group, were converted into the corresponding *anti*-2-methyl-3-hydroxyketones **19b–e** in good-to-high yield with excellent *anti*-selectivity and excellent enantioselectivity (entries 2–5). For the catalytic and enantioselective reduction of various 2-substituted-1,3-diketones, such as 2-ethyl- (**18f**), 2-allyl- (**18g**), 2-benzyl- (**18h**), and 2-isopropyl- (**18i**), the corresponding *anti*-2-alkyl-3-hydroxyketones (**19f–i**) were obtained with excellent *anti*-selectivity and excellent enantioselectivity (entries 6–9).[46]

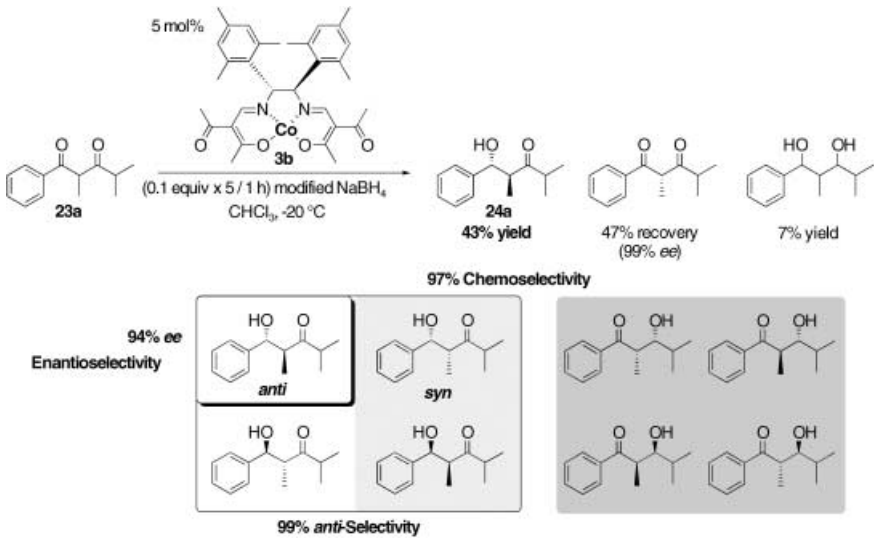
In this reaction system, it is remarkable feature that the *anti*-selectivity is excellent. The highly *anti*-selective aldol reactions of the highly diastereoselective[47] or enantioselective[48] version were very limited. It was expected that the present catalytic reduction could provide an alternative potential for the preparation of optically active *anti*-aldol compounds. Recently, it was revealed in a preliminary examination of the borohydride reduction with a catalytic amount of the β-ketoiminato cobalt complexes that aromatic ketones were preferentially reduced in the presence of aliphatic ketones. As shown in Scheme 6, 0.1 mmol $NaBH_4$ was added to a solution of 0.5 mmol 2-undecanone (**20a**) and 0.5 mmol 2-acetonaphthone (**20b**) in methanol. After 8 h, 2-undecanone (**20a**) (as an alkyl ketone) was reduced to the corresponding alcohol **21a** in 25% yield and 2-acetonaphthone (**20b**) (as an aromatic ketone) in 11% yield. The chemoselectivity for the reduction of the aliphatic ketone was about 70%. In contrast, in the presence of 0.1 mmol of the β-ketoiminato cobalt complex **22**, the chemoselectivity was completely reversed. By treatment of the premodified borohydride, an aromatic ketone, 2-acetonaphthone (**20b**), was selectively reduced to 1-(2-naphthyl)-1-ethanol (**21b**) in 45% yield while the aliphatic ketone **20a** was reduced in only 5% yield. The chemoselectivity for the aromatic ketone was 90%.

These observations encouraged us to apply the cobalt-catalyzed reduction to 1-alkyl-3-aryl-1,3-diketones to prepare the corresponding 1-alkyl-3-aryl-3-hydroxyketones. It was conventionally reported for the chemo- and enantioselective reduction of unsymmetrical 1-alkyl-3-aryl-1,3-diketones that the ketone neighboring alkyl group was selectively reduced because of the reduced bulkiness.[33f] As the unsymmetrical 2-substituted-1,3-diketone model for the chemo-, diastereo- and enantioselective reduction, 2,4-dimethyl-1-phenyl-1,3-pentanedione (**23a**) was adopted. Because the kinetic resolution should be considered for the model substrate, 0.5 equivalent of the premodified borohydride was employed in the presence of 5 mol% of the optically active β-ketoiminato cobalt complex catalyst **3b**. After 24 h, the reaction was quenched to afford the corresponding hydroxyketones **24a** in 44% yield with 88% aromatic versus 12% aliphatic alcohol. Though the diastereoselectivity in the aromatic alcohol was determined to be 93% *anti*, the enantioselectivity of the *anti*-aromatic alcohol **24a** was 67% *ee*.

In the case of using only 0.25 equivalents of the premodified borohydride, it was found that an optically active hydroxyketone was obtained in 21% yield with high chemo- (98%), diastereo- (98%), and enantioselectivities (99% *ee*). These observations suggested that the excess hydride in the catalytic system caused a non-catalytic reduction thus resulting in low selectivities. In order to maintain the initial reaction conditions, therefore, five portions of the 0.1 equivalents premodified borohydride were successively added at one-hour intervals to the reaction to obtain the 3-aryl-3-hydroxyketones **24a** in 43% yield with 97% chemoselectivity, 99% *anti*-selectivity, and with 94% enantiomeric excess (Scheme 7). The *ee* values of the 2-methyl-1,3-diketone **23a** remaining after the kinetic resolution was determined by HPLC. Since racemization of the 2-substituted-1,3-diketones gradually proceeded at room temperature, the reaction mixture was directly injected into the HPLC chiral column (Daicel chiralpak AD, 5.0% propan-2-ol in *n*-hexane) to determine

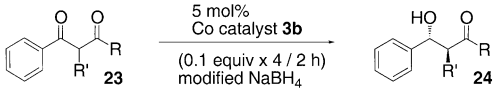


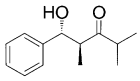
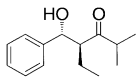
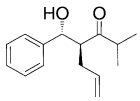
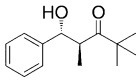
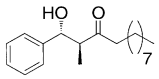
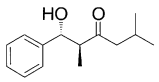
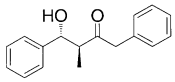
Scheme 6. Chemoselective borohydride reduction of aromatic versus aliphatic ketones.



Scheme 7. Highly chemo-, diastereo-, and enantioselective borohydride reduction of 2-methyl-1,3-diketone.

Table 12. Highly chemo-, diastereo-, and enantioselective reduction of 2-alkyl-1,3-diketones.[a]



Entry	Hydroxyketone		Yield [%]	Conversion [%]	Selectivity		
					Chemo- [%][b]	*anti*- [%][b]	Enantio- [%][c]
1		**24a**	46	48	99	99	96
2		**24b**	41	42	99	99	98
3		**24c**	47	55	95	98	96
4		**24d**	48	49	99	99	97
5		**24e**	47	54	96	98	96
6		**24f**	47	54	99	98	95
7		**24g**	45	52	93	94	98

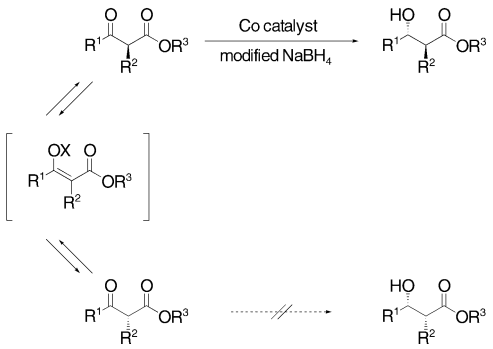
[a] Procedure: Four portions of the 0.1 equiv modified $NaBH_4$ were successively added at 2 h intervals to the solution of the Co catalyst and the substrate; 0.25 mmol substrate, 0.0125 mmol Co catalyst **3b**, 0.1 mmol modified $NaBH_4$ (0.1 mmol $NaBH_4$, 0.1 mmol EtOH, 1.4 mmol THFA), in $CHCl_3$, at $-20\,^{\circ}C$, 10 h. [b] Determined by ^1H NMR analysis. [c] Determined by HPLC analysis.

the *ee* of 2,4-dimethyl-1-phenyl-1,3-pentanedione **23a** which was 99% *ee*.

In order to reduce the excess hydride in the catalytic system and avoid any further non-catalytic reduction, four portions of the 0.1 equivalent premodified borohydride were successively added at two-hour intervals to the reaction mixture to produce a 46% yield, and 99% chemo-, 99% *anti*- and 96% enantioselectivities. These observations indicated that the cobalt-catalyzed reduction selectively afforded only one isomer among the possible eight isomers and that the kinetic resolution was excellent.The present kinetic resolution system was successfully applied to the enantioselective reduction of various 2-substituted-1-alkyl-3-aryl-1,3-diketones **23** to produce optically active 2-substituted-3-hydroxyketones **24** (Table 12). The 1,3-diketones having a 2-methyl- (**23a**), 2-ethyl- (**23b**) or 2-allyl- (**23c**) group were converted into the corresponding 3-aryl-3-hydroxyketones **24a–c** with high chemo-, diastereo- and enantioselectivities (entries 1–3). The kinetic resolution during the enantioselective reduction of the substrate containing a *tert*-butyl ketone **23d** afforded an excellent result such that the corresponding reduced product **24d** obtained in 48% yield indicated 99% chemoselectivity, 99% *anti*-selectivity, and 97% *ee* (entry 4). The present highly selective kinetic resolution could also be applied to the substrates with primary alkyl ketones, such as *n*-nonyl ketone **23e**, isobutyl ketone **23f**, or benzyl ketone **23g** to obtain the corresponding *anti*-hydroxyketones **24e–g** with high selectivities (entries 5–7).[49]

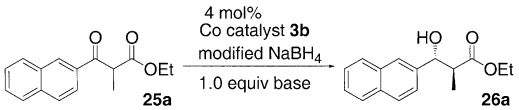
If the racemization equilibrium of the starting material, that is the 2-substituted 3-ketocarbonyl compound, would occur during the kinetic resolution of the enantioselective reaction, it should be a more efficient and promising method for the generation of the chiral centers at the α- and β-positions of the carbonyl compounds in one reaction step ideally in 100% chemical yield.[50] Therefore, the dynamic kinetic resolution with an enantioselective reaction has been applied to the 2-substituted 3-ketoester for the preparation of optically active 2-substituted 3-hydroxyesters, *anti*-aldol-compounds in high yield and with high stereoselectivities (Scheme 8). Several trials of dynamic kinetic resolution during the enantioselective reduction of 2-substituted-3-ketoesters have already been reported; for example, the ruthenium complex catalyzed hydrogenation was successfully applied to 2-substituted 3-ketoesters to obtain aldol products with high stereoselectivities; however, almost all the reactions using enantioselective hydrogenation were *syn*-selective.[51]

For the screening of the reaction conditions for the dynamic kinetic resolution, the 2-methyl-3-(2-naphthyl)-3-oxopropionic acid ethyl ester (**25a**) was adopted as the model substrate and various bases were examined for racemization equilibrium (Table 13). In the presence of 4 mol% of the cobalt catalyst **3b**, the enantioselective borohydride reduction afforded the 3-hydroxy-2-methyl-3-(2-naphthyl)propionic acid ethyl ester (**26a**) with moderate *anti*-selectivity and enantio-



Scheme 8. Dynamic kinetic resolution with borohydride reduction.

Table 13. Various bases for kinetic resolution.[a]



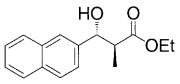
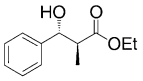
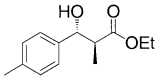
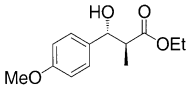
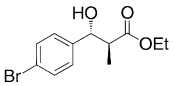
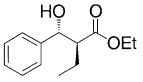
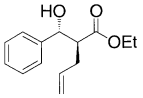
Entry	Base	Yield [%]	*anti*-Selectivity [%][b]	*ee* [%][c]
1	–	99	69	83
2	Na_2CO_3	99	69	81
3	Cs_2CO_3	96	66	82
4	Et_3N	95	79	87
5	HN*i*Pr_2	94	82	87
6	NaOEt	86	88	91
7	NaOMe	66	88	90
8[d]	NaOMe	91	92	95

[a] Reaction conditions: 0.25 mmol substrate **25a**, 0.01 mmol catalyst **3b**, 0.25 mmol base, 0.30 mmol modified $NaBH_4$ (0.30 mmol $NaBH_4$, 0.30 mmol EtOH, 4.2 mmol THFA), in $CHCl_3$ at 0 °C, 24 h. [b] Determined by ^{1}H NMR analysis. [c] Determined by HPLC analysis. [d] At – 10 °C, 15 h.

selectivity (entry 1). These observations indicated that the racemization equilibrium was not sufficient without any base. In order to accelerate the racemization equilibrium via its enolates, several bases were added to the reaction mixture. In the presence of alkalimetal carbonates, the reduction smoothly proceeded though the *anti*-selectivity and enantioselectivity were not improved at all (entries 2 and 3). The addition of amine bases slightly improved the stereoselectivity, but their selectivities did not reach a satisfactory level (entries 4 and 5). The high diastereo- and enantioselectivities were achieved with the addition of an alkalimetal alkoxide, though the isolated yields were low due to the *retro*-aldol reaction from the resulting products. To avoid any side reaction, the reaction was performed at – 10 °C to improve the isolated yield to 91 % while maintaining high diastereo- and enantioselectivities.

Various 2-alkyl-3-aryl-3-ketoesters **25** were successfully subjected to the enantioselective reduction with dynamic kinetic resolution for the preparation of the *anti*-aldol-type compounds (Table 14). The optically active 3-hydroxy-2-methylesters containing 2-naphthyl (**26a**), phenyl (**26b**), *p*-bromophenyl (**26c**), *p*-methylphenyl (**26d**), or *p*-methoxyphenyl (**26e**) as a 3-aryl group could be prepared in the present dynamic kinetic resolution system with high diastereo- and enantioselectivities in high isolated yields (entries 1 – 5). The 3-phenyl-3-ketoesters, having an ethyl **25f** or allyl **25g** group on the active methyne, were also converted into the corresponding 3-aryl-3-hydroxyester **26f**–**g** with good diastereoselectivity and high *ee* values (entries 6 and 7).[52] It was demonstrated that the optically active *anti*-2-substituted-3-hydroxy compounds could be prepared from the corresponding 2-substituted-3-ketocarbonyl compounds using enantioselective borohydride reduction. In contrast, the *syn*-aldol was generally produced in the transition-metal catalyzed reactions; the present enantioselective reduction would provide an alternative approach for the preparation of *anti*-aldol compounds.

Table 14. Dynamic kinetic resolution of enantioselective reduction for *anti*-aldol compounds.[a]

Entry	Hydroxyester		Yield [%]	*anti*-Selectivity [%][b]	*ee* (*anti*) [%][c]
1		**26a**	93	99	99
2		**26b**	97	99	99
3		**26c**	73	99	99
4		**26d**	68	99	99
5		**26e**	96	99	97
6		**26f**	88	99	99[d]
7		**26g**	88	99	97

[a] Reaction conditions: 0.25 mmol substrate, 0.01 mmol Co catalyst **3b**, 0.25 mmol NaOMe, 0.30 mmol modified $NaBH_4$ (0.30 mmol $NaBH_4$, 0.30 mmol EtOH, 4.2 mmol THFA), in $CHCl_3$, at – 10 °C, 10 – 15 h. [b] Determined by ^{1}H NMR analysis. [c] Determined by HPLC analysis. [d] Determined by HPLC analysis after acylation.

Enantiofacial discrimination of asymmetric borohydride reduction: A possible catalytic cycle is explained as follows (Figure 5): When the modified $NaBH_4$ was added to the cobalt(II) complex solution, this reaction mixture was instantly turned from orange, the color of the original catalyst solution, to red. It was implied that new active species, probably cobalt – hydride intermediates were generated from the modified borohydride and cobalt(II) complexes.

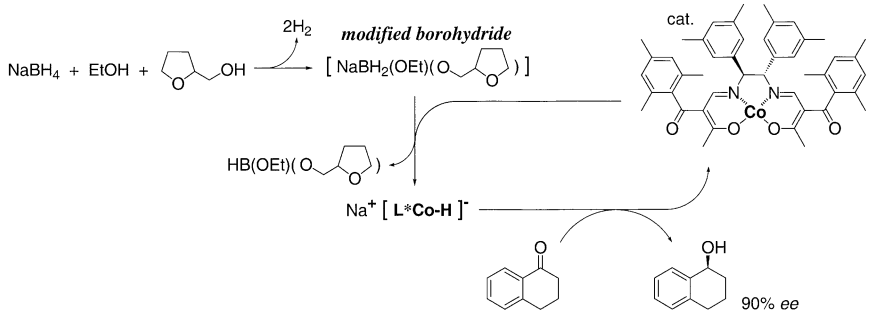


Figure 5. Overall reaction pathway of cobalt catalyzed enantioselective reduction.

The FAB mass analysis of the cobalt complex **1a** treated with borohydride was then examined. A peak at *m*/*z* 697 in the FAB MS spectra was observed under negative mode for the original cobalt complex **1a** (Figure 6a). After treatment of the cobalt complex **1a** with borohydride, the peak at *m*/*z* 697 vanished and a new peak was found at *m*/*z* 698, which can be assigned as a cobalt–hydride complex (Figure 6b).

When borodeuteride was employed in place of borohydride, the original peak at *m*/*z* 697 disappeared and a new peak at *m*/*z* 699 assigned to the cobalt–deuteride complex

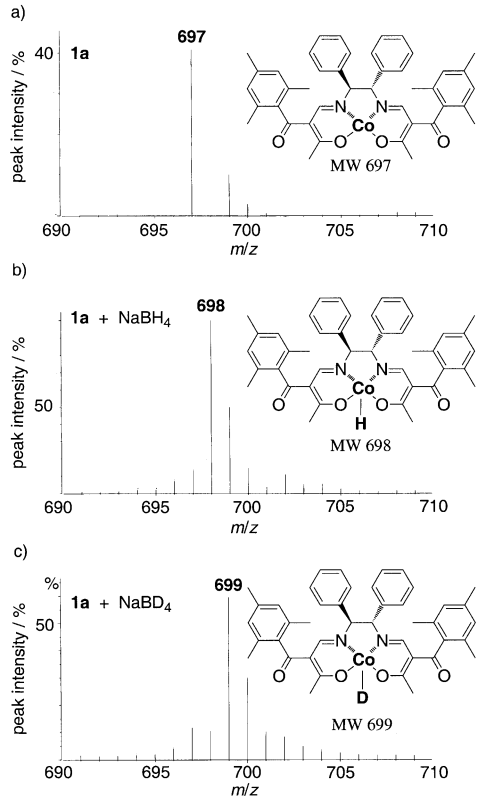
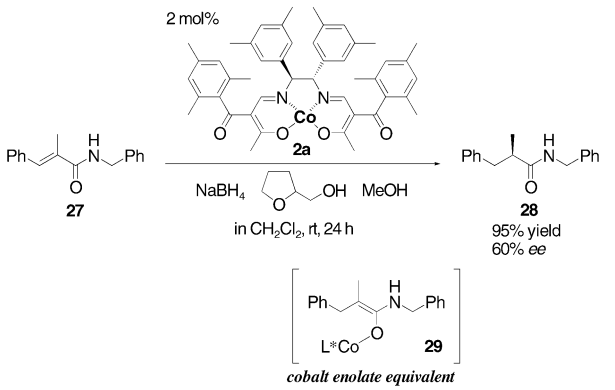


Figure 6. FAB mass spectra of the cobalt complex treated with borohydride.

appeared (Figure 6c). These results clearly indicated that the cobalt–hydride species would mainly exist in the reaction media and could act as the reactive intermediate. Optically active cobalt–hydride species then precisely reacted with the prochiral ketones recognizing the enantioface. As a result, an optically active alcohol was obtained and the cobalt complex was recycled. It was recently found that *N*-benzyl-(*E*)-α-methylcinnamic amide **27** was subjected to the enantioselective reduction system to obtain the optically active 2-methylcarboxamide **28** with 60% *ee* (Scheme 9)[53] This result suggested that the cobalt hydride generated in the reaction system would attack the cinnamic amide in a 1,4-reduction manner to form the cobalt-enolate equivalent **29**, which was then protonated in situ by THFA or methanol to afford the optically active carboxyamide.

As mentioned above, X-ray analysis of the molecular structure of the optically active β-ketoiminato cobalt complex was performed for the cobalt(III)-iodide complex derived from



Scheme 9. Catalytic enantioselective protonation of cobalt enolate equivalent.

the corresponding cobalt(II) complex **1a** and **3b**. It revealed that the centered cobalt was surrounded by the square-planar ligand and that aryl groups in the optically active diamine and a mesitoyl group in the side chain were located nearby. The observed enantiofacial selection of the corresponding (*S*)-alcohols to the (*S*,*S*)-cobalt complexes (*Re* attack) can be explained by considering the favorable transition state illustrated in Figure 7; the substrates, aryl ketones, would

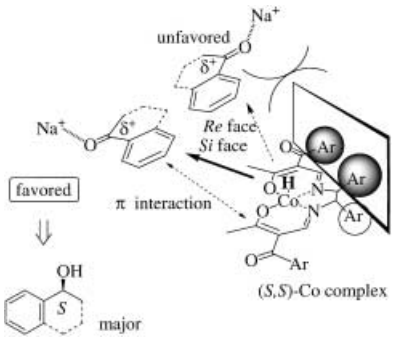


Figure 7. Possible mechanistic explanation for the observed enantioface selection in asymmetric reduction with (*S*,*S*)-cobalt complex.

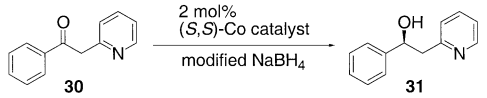
approach the postulated cobalt-hydride through the open site (*Re* attack). The aromatic ring of the aryl ketones was placed parallel to the square delocalized π system plane of the cobalt complex by π interaction. Because $\pi-\pi$ interaction occurred efficiently between the catalyst and aromatic ketone, the reduction of the aryl ketone proceeded faster than the alkyl ketone in the catalytic system (Scheme 6). The approaching carbonyl group of the substrates was oriented away from the cobalt complex to avoid any steric hindrance by the bulky aryl groups. The alternative transition state (*Si* attack) is not rationalized because of the steric repulsion of the bulky aryl groups of the complex with the carbonyl group from the incoming ketones. These closely packed transition states could suggest that the enantiofacial selectivity was fairly dependent on these components as substrates, ligands, and additive alcohols as shown in Tables 1 and 2. Based on these observations, it could be assumed that sodium borohydride was modified in situ with the additive alcohols to form $NaBH_2(OR^1)(OR^2)$ (R^1 = Me or Et, R^2OH = THFA) and

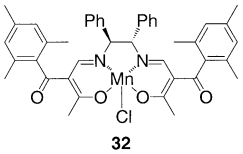
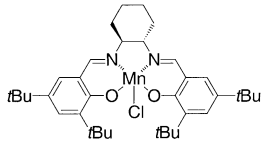
then the modified borohydride was closely located to the cobalt complex and assisted the achieving a high enantioselectivity.

Recently, it was reported that Jacobsen's manganese(III) complexes as well as the β-ketoiminato cobalt(II) complexes could be used as catalysts for the enantioselective borohydride reduction of 2-phenacylpyridine (**30**).[54] It should be pointed out here that (*S*)-1-phenyl-2-(2-pyridyl)ethanol (**31**) was obtained using the (*S*,*S*)-cobalt(II) complexes **1a**, **2a**, **3a**, or **3b**, whereas the (*R*)-*p*roduct was obtained using (*S*,*S*)-β-ketoiminato manganese(III)-chloride complex **32** and Jacobsen's (*S*,*S*)-salen manganese(III)–chloride complex **33** (Table 15).[55] It was proposed that Jacobsen's manganese(III) catalysts could be employed as a chiral Lewis acid to form a stable chelate complex with 2-phenacylpyridine, which was then enantioselectively reduced by the THFA-modified borohydride.[54] On the other hand, the formation of a similar tight chelate with the cobalt(II) complexes could not be expected since the Lewis acidity of the cobalt(II) complex is presumed to be generally weak.[56] Concerning the enantioselective sense, the manganese(III)-chloride complex with the β-ketoiminato ligand afforded the opposite enantiomer against the corresponding β-ketoiminato cobalt(II) complex although both structures of the manganese and cobalt complexes were very similar based on an X-ray analysis.[19] The enantioselective sense in the present reduction of 2-phenacylpyridine was in accord with the cobalt complex catalyzed reductions of carbonyl compounds. These observations should suggest that the enantioselective borohydride reductions with the cobalt(II) and manganese(III) complex catalysts proceeded by different mechanisms. Therefore, it is reasonable to assume that the "cobalt–hydride equivalent" generated from the optically active cobalt catalyst and premodified borohydride could react with carbonyl compounds in a highly enantioselective manner. As mentioned above, all simple ketones **8a–g** were converted to the (*S*)-alcohol **9a–g** in the presence of the (*S*,*S*)-cobalt complexes. Various (*S*)-amines **12d–i** were also obtained corresponding to the (*S*,*S*)-cobalt catalyst. These results indicated that optically active β-ketoiminato cobalt complexes could recognize the prochiral face of imines as well as ketones in the same mechanism.

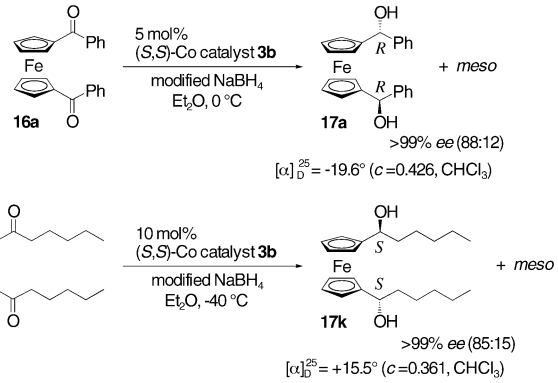
It was revealed that (1*S*,3*S*)-1,3-diphenyl-1,3-propanediol (**15a**) was obtained using to the (*S*,*S*)-cobalt catalyst when compared with the previously reported optical rotation.[39] The enantioselective sense was in accord with the various cobalt-catalyzed reductions of the aryl ketones. The enantioselective sense was also determined for the enantioselective reduction of 1,1′-dibenzoylferrocene (**16a**) in the presence of the (*S*,*S*)-cobalt complex which afforded the (*R*,*R*)-ferrocenyldiol, whereas the (*S*,*S*)-diol was obtained from the 1,1′-dialkanoylferrocene (**16k**) (Scheme 10).[42] The enantioselective sense in the reduction of the 1,1′-dibenzoylferrocene (**16a**) was in accord with that[26] of the acetophenone derivatives. As for the enantioselective reduction of 1,1′-dialkanoylferrocene (**16k**), it is reasonable to consider that the cobalt complex catalyst should recognize the ferrocenyl group as the π system similar to the reduction of phenyl ketone to achieve a high enantioselection. The *anti*-1,3-di(*p*-bromophenyl)-3-hydroxy-2-methyl-1-propanone (**19d**) was converted to (*R*)-α-methoxyphenylacetate for the X-ray analysis. It was found that the (*R*)-alcohol *anti*-form, (2*S*,3*R*)-1,3-di(*p*-bromophenyl)-3-hydroxy-2-methyl-1-propanone (**19d**), was obtained corresponding to the (*R*,*R*)-cobalt complex catalyst (Figure 8).[46] Thus, the excellent stereoselectivity in the present catalytic reduction system can be explained as follows (Figure 9): The hydride equivalent nucleophile should attack one of the carbonyl groups in the 1,3-diaryl-1,3-propanedione according to the Felkin–Anh model to afford the corresponding *anti*-product with high diastereoselectivity. Concerning the excellent enantioselectivity, the optically active β-ketoiminato cobalt complex could

Table 15. Enantioselective reduction of 2-phenacylpyridine with cobalt(II) or manganese(III) catalysts.[a]



Entry	(*S*,*S*)-catalyst	Yield [%]	*ee* [%][b]	Absolute configuration
1	**1a**	89	22	*S*
2	**2a**	93	39	*S*
3	**3a**	93	64	*S*
4	**3b**	92	86	*S*
5	 **32**	90	5	*R*
6	 **33**	82	85	*R*

[a] Reaction conditions: 0.50 mmol substrate, 0.01 mmol Co catalyst, 0.75 mmol $NaBH_4$, 0.75 mmol EtOH, 10.5 mmol THFA, in $CHCl_3$ (10 mL), at 0 °C, 12 h. [c] Determined by HPLC analysis.



Scheme 10. Enantioselective sense for dialkanoylferrocene vs dibenzoylferrocene.

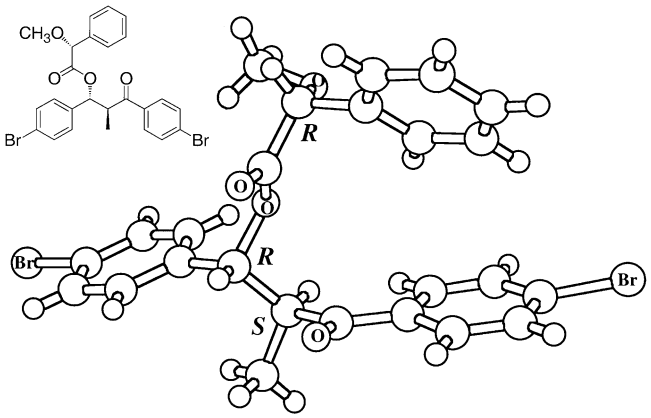


Figure 8. X-ray analysis of (*R*)-α-methoxyphenylacetate of *anti*-1,3-di(*p*-bromophenyl)-3-hydroxy-2-methyl-1-propanone corresponding to the (*R*,*R*)-cobalt catalyst.

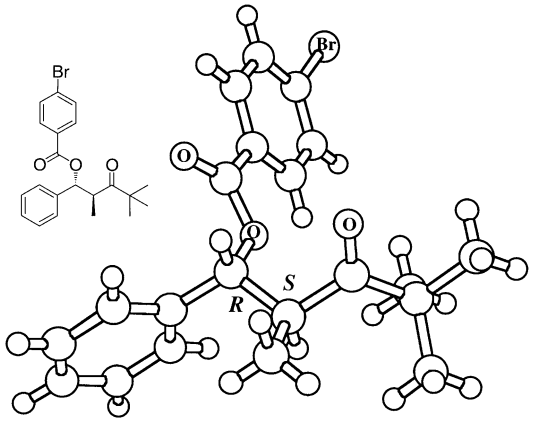


Figure 10. The absolute configuration of *p*-bromobenzoate of *anti*-1-hydroxy-2,4,4-trimethyl-1-phenyl-3-pentanone corresponding to the (*R*,*R*)-cobalt catalyst was determined by X-ray analysis.

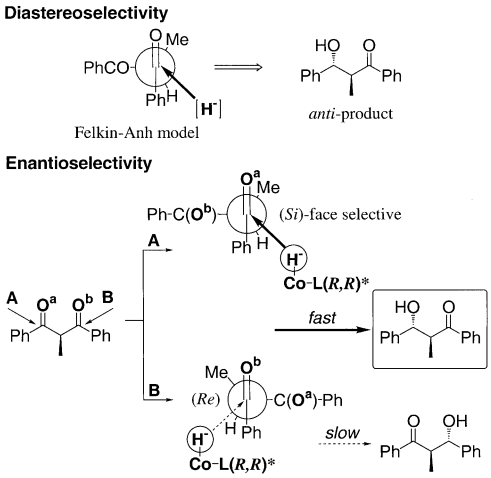


Figure 9. Diastereo- and enantioselectivities in the catalytic reduction system.

distinctly recognize the *Si* face of the carbonyl group using the (*R*,*R*)-cobalt complex catalyst. Therefore, the (*R*)-alcohol *anti*-form was obtained in the presence of the (*R*,*R*)-cobalt catalyst.

The *anti*-1-hydroxy-2,4,4-trimethyl-1-phenyl-3-pentanone (**24d**) was conventionally transformed into the corresponding *p*-bromobenzoate. As a result of the X-ray analysis, it was revealed that the (1*R*,2*S*)-form was obtained corresponding to the (*R*,*R*)-cobalt complex catalyst (Figure 10).[49] The obtained *anti*-3-hydroxy-2-methyl-3-phenylpropionic acid ethyl ester (**26b**) was treated with lithium aluminum hydride for conversion into the corresponding *anti*-1-phenyl-2-methyl-1,3-propanediols. The optical rotation of the resulting 1,3-diol was compared with the previously reported result. It was revealed to be the (2*R*,3*R*)-*anti*-1,3-diol, therefore, the (2*S*,3*R*)-*anti*-3-hydroxyester should be generated and correspond to the (*R*,*R*)-catalyst. The absolute configurations of the obtained products could be fully explained by the above-mentioned surveys, that is, the presentation in Figure 7.

Conclusion

We have developed a novel method of the enantioselective borohydride reduction in which aromatic ketones are smoothly and quantitatively converted into the corresponding alcohols in the presence of a catalytic amount of the optically active cobalt(II) complex catalyst. This enantioselective reduction is carried out using a precisely premodified borohydride with alcohols such as tetrahydrofurfuryl alcohol, ethanol and methanol, and high *ee* values are obtained by choosing the appropriate alcohols as modifiers and a suitable β-ketoiminato ligand of the catalyst. The enantioselective borohydride reduction has been successfully applied to the reduction of imines protected by a phosphinyl group. The optically active amines are obtained with high chemical yields and high *ee* values. The subsequent hydrolysis smoothly gives the corresponding primary amine while maintaining a high enantiomeric excess. In the catalytic system, optically active C_2-symmetrical diols, 1,3-diaryl-1,3-propanediols and 1,1′-ferrocenyldiols were prepared with high stereoselectivities and a high catalytic efficiency. Also, it was demonstrated that the optically active *anti*-2-substituted-3-hydroxycarbonyl compounds could be prepared from the corresponding 2-substituted 3-ketocarbonyl compounds using enantioselective borohydride reduction. In contrast, the *syn*-aldol was generally produced by the transition-metal catalyzed reactions; the present enantioselective reduction could provide an alternative approach for the preparation of the *anti*-aldol-type compounds.

Experimental Section

General: ^{1}H NMR spectra were measured on a JOEL model FX-270 (270 MHz) or GX-400 (400 MHz) spectrometer using $CDCl_3$ as a solvent with tetramethylsilane (0.00 ppm) as an internal standard. ^{13}C NMR spectra (100 MHz) were measured on a JOEL model GX-400 spectrometer using $CDCl_3$ (77.0 ppm) or C_6D_6 (128.0 ppm) as a solvent. Infrared spectra were recorded on a JASCO model IR-700 or FTIR-410 infrared spec-

trometer on 3M IR card (Type 61 and 62) or as KBr pellets. The melting points (m.p.) were measured on a Mettler FP62 apparatus, an Electrothermal IA9100 apparatus, a Seiko Denshi Kogyo Ltd. DSC-100 apparatus (DSC), or Shimadzu DSC-60 apparatus (DSC) and were uncorrected. Elemental analyses were determined with an Elemental Vario EL apparatus. High-resolution mass spectra (HRMS) were obtained with a HITACHI M-80B. FAB mass spectra were obtained with JOEL JMS-700 mass spectrometer using 3-nitrobenzyl alcohol as matrix with 10 kV acceleration voltage. High-performance liquid chromatography (HPLC) analyses were performed with a Shimadzu LC-6A chromatograph using an optically active column (Daicel Chiralcel OB, Chiralcel OD-H, Chiralpak AD, or Chiralpak AD-H); the peak areas were obtained with a Shimadzu Chromatopack CR-4A or Varian Dynamax MacIntegrater. Optical rotations were measured with a JASCO DIP-360 or DIP-370 digital polarimeter.

General procedure for preparation of optically active cobalt complexes: These ligands were prepared by the reported method[18] from 3-oxo-2-(2,4,6-trimethylbenzoyl)butanal and the corresponding (1*S*,2*S*)-1,2-diarylethylenediamines. The optically active cobalt(II) complexes were prepared by the reported method.[21, 57]

[*N*,*N*′-Bis{2-(2,4,6-trimethylbenzoyl)-3-oxobutylidene}-(1*S*,2*S*)-1,2-bis(2,4,6-trimethylphenyl)ethylenediaminato]-iodocobalt(III) (1a-I): Cobalt(III) complex **1a-I** was prepared by adding 0.5 equiv iodine to a dichloromethane solution of the cobalt(II) complex **1a** at room temperature. The crystal appropriate for X-ray analysis was obtained as dark brown plate by recrystallization (dichloromethane/Et_2O/hexane 1:1:4) at room temperature.

X-ray Crystallography of complex 1a-I: Accurate unit cell parameters were obtained on a Rigaku AFC-6R diffractometer with $Cu_{K\alpha}$ radiation (λ = 1.54178 Å). The structure was solved by direct methods and refined by full-matrix least squares calculations.

Crystal data of 1a-I ($C_{48}H_{54}N_2O_4ICo \cdot H_2O$): $F_W = 926.78$, monoclinic, space group $P2_1$, $a = 17.432(2)$, $b = 18.096(2)$, $c = 16.4(10)$ Å, $\beta = 113.725(8)^\circ$, $V = 4744(289)$ Å^3, $Z = 4$, $\rho = 1.298$ Mg m^{-3}, $F(000) = 1912$, crystal size 0.25 × 0.30 × 0.03 mm, $T = 298$ K, $\mu = 8.291$ mm^{-1}, no. of reflections measured 8133 (total) and 7834 (unique), $R = 0.1242$ and $wR = 0.3113$.

X-ray Crystallography of complex 3b-Br: The complex **3b-Br** was prepared from the complex **3b** and bromine similarly to the complex **1a-I**. Accurate unit cell parameters were obtained on a Rigaku AFC-7R diffractometer with $Mo_{K\alpha}$ radiation ($\lambda = 0.7107$ Å). The structure was solved by direct methods and refined by full-matrix least squares calculations.

Crystal data of 3b-Br ($C_{32}H_{38}N_2O_4BrCo \cdot H_2O \cdot C_4H_8O$): $F_W = 743.62$, monoclinic, space group $P2_1$, $a = 13.667(2)$, $b = 15.046(2)$, $c = 17.764(2)$ Å, $\beta = 100.32(1)^\circ$, $V = 3593.8(8)$ Å^3, $Z = 4$, $D = 1.374$ Mg m^{-3}, $F(000) = 1552$, crystal size 0.50 × 0.30 × 0.1 mm, $T = 297$ K, $\mu = 1.64$ mm^{-1}, no. of reflections measured 12278 (total) and 11744 (unique), $R = 0.064$ and $wR = 0.186$.

Preparation of ketones: The chromanone derivative **8h** was prepared according to the literature method.[58] Tetralone derivatives **8a** and **8g** were purchased from Tokyo Kasei Kogyo (TCI), and the ketones **8f**[59] was prepared by reported procedure. Alkyl phenyl ketones **8b**, **8e**, **8c**, and **8d** were purchased from Tokyo Kasei Kogyo (TCI).

General procedure for enantioselective reduction of aromatic ketones using premodified borohydride

Exclusive formation of premodified dialkoxyborohydride 10: Under argon atmosphere, in a precooled vessel at 0 °C, were placed fine grained $NaBH_4$ (29 mg, 0.75 mmol), $CHCl_3$ (5.0 mL), EtOH (0.44 mL, 0.75 mmol) and THFA (1.0 mL, 10.3 mmol), and the mixture was continued to stir for 3 h.

Catalytic enantioselective borohydride reduction: The solution of **10** was added (while maintaining the solution at 0 °C) to the solution of (*S*,*S*)-cobalt(II) catalyst **2b** (3.7 mg, 0.005 mmol, 1 mol %) and 6-methoxy-1-tetralone (**8a**, 88 mg, 0.50 mmol) in $CHCl_3$(5.0 mL), and the mixture was continued to stir for 30 min at 0 °C. The reaction was quenched by the addition of saturated aqueous ammonium chloride, and extracted with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and then the excess solvent were removed under reduced pressure. The purification by column chromatography on silica gel (hexane/ethyl acetate 4:1) gave the corresponding alcohol **9a** as colorless oil (99 %, 88 mg). The enantiomeric excess was determined to be 93 % by HPLC analysis using Daicel Chiralpak AD (2.0 % propan-2-ol in hexane, flow 1.0 mL min^{-1}); $[\alpha]_D^{28} = +29.7^\circ$ ($c = 0.81$, Et_2O).

6-Methoxy-1-tetralol (9a): ^{1}H NMR ($CDCl_3$): $\delta = 1.74 - 1.92$ (m, 5H), 2.65 – 2.87 (m, 2H), 3.78 (s, 3H), 4.73 (br, 1H), 6.62 (d, 1H, $J = 2.6$ Hz), 6.76 (dd, 1H, $J = 2.6$, 8.6 Hz), 7.33 (d, 1H, $J = 8.6$ Hz); IR: $\tilde{\nu} = 3392$, 2930, 1609, 1577, 1501, 1457 cm^{-1}. Enantiomeric excess was determined to be 93 % by HPLC analysis (Chiralpak AD; 2.0 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 44.1 min (major), 47.7 min (minor)); $[\alpha]_D^{28} = +29.7^\circ$ ($c = 0.81$ in Et_2O).

1-Phenyl-1-butanol (9b): ^{1}H NMR ($CDCl_3$): $\delta = 0.88$ (t, 3H, $J = 7.25$ Hz), 1.26 – 1.35 (m, 2H), 1.68 – 1.81 (m, 2H), 1.91 (m, 1H), 4.62 (t, 1H, J = 6.6 Hz), 7.23 – 7.34 (m, 5H); IR: $\tilde{\nu} = 3356$, 2956, 2870, 1492, 1454 cm^{-1}. Enantiomeric excess was determined to be 97 % by HPLC analysis (Chiralcel OB; 1.0 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 14.2 min (major), 16.8 min (minor)); $[\alpha]_D^{28} = -47.9^\circ$ ($c = 0.34$ in benzene). (lit.[60] $[\alpha]_D = +43.4^\circ$ (benzene), 96 % *ee* (*R*)).

Cyclopropylphenylmethanol (9c): ^{1}H NMR ($CDCl_3$): $\delta = 0.32 - 0.68$ (m, 4H), 1.15 – 1.28 (m, 1H), 2.00 (d, 1H, $J = 3.0$ Hz), 4.00 (dd, 1H, $J = 3.0$, 8.3 Hz), 7.25 – 7.44 (m, 5H); IR: $\tilde{\nu} = 3384$, 3080, 3004, 1493, 1452 cm^{-1}. Enantiomeric excess was determined to be 90 % by HPLC analysis (Chiralpak AD; 2.0 % propan-2-ol in hexane, flow 0.7 mL min^{-1}, 36.5 min (minor), 38.2 min (major)); $[\alpha]_D^{25} = +22.6^\circ$ ($c = 0.234$ in $CHCl_3$).

2-Methyl-1-phenyl-1-propanol (9d): ^{1}H NMR ($CDCl_3$): $\delta = 0.80$ (d, 3H, $J = 6.93$ Hz), 1.00 (d, 3H, $J = 6.9$ Hz), 1.83 (br, 1H), 1.92 – 2.02 (m, 1H), 4.36 (dd, 1H, $J = 3.3$, 6.9 Hz), 7.26 – 7.37 (m, 5H); IR: $\tilde{\nu} = 3422$, 2958, 2872, 1492, 1453 cm^{-1}. Enantiomeric excess was determined to be 98 % by HPLC analysis (Chiralcel OB; 0.5 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 18.0 min (major), 19.1 min (minor)); $[\alpha]_D^{34} = -48.6^\circ$ ($c = 0.288$, Et_2O). (lit.[61] $[\alpha]_D^{20} = -47.7^\circ$ ($c = 5.80$ in Et_2O), (*S*)).

Cyclohexylphenylmethanol (9e): ^{1}H NMR ($CDCl_3$): $\delta = 0.89 - 1.84$ (m, 11H), 1.97 (br, 1H), 4.35 (dd, 1H, $J = 3.0$, 7.3 Hz), 7.22 – 7.35 (m, 5H); IR: $\tilde{\nu} = 3362$, 3070, 3006, 1492, 1452 cm^{-1}. Enantiomeric excess was determined to be 95 % by HPLC analysis (Chiralcel OD-H; 10.0 % propan-2-ol in hexane, flow 0.5 mL min^{-1}, 11.8 min (major), 13.3 min (minor)); $[\alpha]_D^{31} = -21.8^\circ$ ($c = 0.461$ in EtOH). (lit.[61] $[\alpha]_D^{20} = +22.5^\circ$ ($c = 5.13$ in EtOH), (*R*)).

2,2-Dimethyl-1-tetralol (9f): ^{1}H NMR ($CDCl_3$): $\delta = 0.98$ (s, 3H), 1.00 (s, 3H), 1.50 – 1.58 (m, 1H), 1.62 (br, 1H), 1.76 – 1.86 (m, 1H), 2.75 – 2.83 (m, 2H), 4.26 (s, 1H), 7.08 – 7.15 (m, 1H), 7.17 – 7.24 (m, 2H), 7.41 – 7.46 (m, 1H); IR: $\tilde{\nu} = 3388$, 3020, 2918, 1453 cm^{-1}. Enantiomeric excess was determined to be 94 % by HPLC analysis (Chiralcel OD-H; 1.0 % propan-2-ol in hexane, flow 0.5 mL min^{-1}, 30.2 min (minor), 33.7 min (major)); $[\alpha]_D^{31} = +21.6^\circ$ ($c = 0.817$ in $CHCl_3$). (lit.[62] $[\alpha]_D^{25} = +23.5^\circ$ (c = 3.37 in $CHCl_3$), (*S*)).

1-Tetralol (9g): ^{1}H NMR ($CDCl_3$): $\delta = 1.71 - 2.00$ (m, 4H), 2.01 – 2.10 (br, 1H), 2.69 – 2.85 (m, 2H), 4.74 (t, 1H, $J = 4.6$ Hz), 7.05 – 7.14 (m, 1H), 7.16 – 7.21 (m, 2H), 7.36 – 7.41 (m, 1H); IR: $\tilde{\nu} = 3348$, 2930, 2860, 1489, 1453 cm^{-1}. Enantiomeric excess was determined to be 90 % by HPLC analysis (Chiralpak AD; 2.5 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 18.4 min (major), 20.1 min (minor)); $[\alpha]_D^{24} = +28.8^\circ$ ($c = 0.55$ in $CHCl_3$). (lit.[63] $[\alpha]_D^{17} = +32.7^\circ$ ($c = 10.7$ in $CHCl_3$), >99 % *ee* (*S*)).

2,2-Dimethyl-4-hydroxychroman (9h): ^{1}H NMR ($CDCl_3$): $\delta = 1.32$ (s, 3H), 1.43 (s, 3H), 1.58 – 1.77 (br, 1H), 1.87 (dd, 1H, $J = 8.4$, 14.3 Hz), 2.18 (dd, 1H, $J = 8.4$, 14.3 Hz), 4.87 (d, 1H, $J = 8.4$ Hz), 6.77 – 6.83 (m, 1H), 6.90 – 6.97 (m, 1H), 7.14 – 7.21 (m, 1H), 7.42 – 7.48 (m, 1H); IR: $\tilde{\nu} = 3230$, 2976, 1608, 1580, 1484, 1456 cm^{-1}. Enantiomeric excess was determined to be 92 % by HPLC analysis (Chiralpak AD; 2.5 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 20.5 min (major), 21.7 min (minor)); $[\alpha]_D^{28} = +49.0^\circ$ ($c = 1.00$ in $CHCl_3$). (lit.[64] $[\alpha]_D = +51.5^\circ$ ($c = 1.12$ in $CHCl_3$),(*S*)).

Preparation of aryl *N*-diphenylphosphinyl imines: Aryl *N*-diphenylphosphinyl imines **1d – i** were prepared from the corresponding oxime and chlorodiphenylphosphine according to the literature method.[65]

***N*-(1,2,3,4-Tetrahydro-1-naphthylidene)-*P*,*P*-diphenylphosphinamide (11d)**: ^{1}H NMR ($CDCl_3$): $\delta = 2.07 - 2.13$ (m, 2H), 2.67 (t, 2H, $J = 7.8$ Hz), 4.76 (d, 1H, $J = 7.8$ Hz), 5.91 (d, 1H, $J = 4.9$ Hz), 7.13 – 7.28 (m, 3H), 7.38 – 7.52 (m, 7H), 7.89 – 7.94 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 22.0$, 27.8, 113.2 (d, $J_{C\text{-}P} = 5.0$ Hz), 120.2, 126.4, 127.5, 127.8, 128.6 (d, $J_{C\text{-}P} = 13.3$ Hz), 131.7 (d, $J_{C\text{-}P} = 10.0$ Hz), 131.9 (d, $J_{C\text{-}P} = 2.5$ Hz), 132.0 (d, $J_{C\text{-}P} = 130.2$ Hz), 132.2 (d, $J_{C\text{-}P} = 8.3$ Hz), 133.0 (d, $J_{C\text{-}P} = 1.7$ Hz), 137.4; IR (KBr): $\tilde{\nu} = 3051$, 2871, 1462,

1438, 1201, 1123, 1109, 694 cm^{-1}; m.p. 156.3–156.6 °C; HRMS: *m/z*: calcd for $C_{22}H_{20}NOP$: 345.1283; found: 345.1276 [M^+].

***N*-(1-Phenylethylidene)-*P,P*-diphenylphosphinamide (11e)**:[66] ^1H NMR ($CDCl_3$): $\delta = 2.96$ (s, 3H), 7.39–7.54 (m, 9H), 7.97–8.09 (m, 6H); ^{13}C NMR ($CDCl_3$): $\delta = 23.0$ (d, $J_{C\text{-}P} = 12.4$ Hz), 127.7, 128.2 (d, $J_{C\text{-}P} = 12.4$ Hz), 128.3, 131.2 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.4 (d, $J_{C\text{-}P} = 9.1$ Hz), 132.2, 133.5 (d, $J_{C\text{-}P} = 131.0$ Hz), 139.1 (d, $J_{C\text{-}P} = 24.0$ Hz), 181.2 (d, $J_{C\text{-}P} = 7.5$ Hz); IR (KBr): $\tilde{\nu} = 3060$, 1642, 1438, 1200, 1125, 1109, 727, 715, 694, 550 cm^{-1}; m.p. 139.6–140.4 °C.

***N*-(1-Indanylidene)-*P,P*-diphenylphosphinamide (11f)**:[67] ^1H NMR ($CDCl_3$): $\delta = 3.08$ (t, 2H, $J = 5.6$ Hz), 3.24–3.27 (m, 2H), 7.33–7.52 (m, 9H), 7.97–8.03 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 28.5$, 34.9 (d, $J_{C\text{-}P} = 11.6$ Hz), 123.7, 125.8 (d, $J_{C\text{-}P} = 1.7$ Hz), 127.0, 128.1 (d, $J_{C\text{-}P} = 12.4$ Hz), 131.1 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.3 (d, $J_{C\text{-}P} = 9.1$ Hz), 133.9, 134.6 (d, $J_{C\text{-}P} = 127.7$ Hz), 140.0 (d, $J_{C\text{-}P} = 23.2$ Hz), 153.1, 190.5 (d, $J_{C\text{-}P} = 7.5$ Hz); IR (KBr): $\tilde{\nu} = 1637$, 1436, 1199, 1122, 870, 762, 519 cm^{-1}; m.p. 165.3–166.6 °C.

***N*-(6,7,8,9-Tetrahydro-5*H*-benzocyclohepten-5-ylidene)-*P,P*-diphenylphosphinamide (11g)**: ^1H NMR ($CDCl_3$): $\delta = 1.63$ (q, 2H, $J = 7.6$ Hz), 1.99 (quintet, 2H, $J = 7.6$ Hz), 2.57 (t, 2H, $J = 7.6$ Hz), 4.70 (d, 1H, $J = 7.6$ Hz), 5.88 (t, 1H, $J = 7.6$ Hz), 7.18–7.33 (m, 3H), 7.42–7.61 (m, 7H), 7.92–7.97 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 23.3$, 32.2, 35.1, 112.4 (d, $J_{C\text{-}P} = 5.0$ Hz), 125.5, 126.2, 127.9, 128.5 (d, $J_{C\text{-}P} = 12.4$ Hz), 129.1, 131.7 (d, $J_{C\text{-}P} = 10.0$ Hz), 131.8 (d, $J_{C\text{-}P} = 3.3$ Hz), 131.9 (d, $J_{C\text{-}P} = 129.4$ Hz), 135.6 (d, $J_{C\text{-}P} = 1.6$ Hz), 138.3 (d, $J_{C\text{-}P} = 8.3$ Hz), 142.0; IR (KBr): $\tilde{\nu} = 3054$, 2873, 1438, 1206, 1190, 692, 526 cm^{-1}; m.p. 165.5–166.7 °C; HRMS: *m/z*: calcd for $C_{23}H_{22}NOP$: 359.1439; found: 359.1458 [M^+].

***N*-(6-Methoxy-1,2,3,4-tetrahydro-1-naphthylidene)-*P,P*-diphenylphosphinamide (11h)**: ^1H NMR ($CDCl_3$): $\delta = 1.96$ (quin, 2H, $J = 6.2$ Hz), 2.84 (t, 2H, $J = 6.2$ Hz), 3.23–3.27 (m, 2H), 3.85 (s, 3H), 6.67 (d, 1H, $J = 2.7$ Hz), 6.87 (dd, 1H, $J = 2.7$, 8.8 Hz), 7.38–7.45 (m, 6H), 7.95–8.00 (m, 4H), 8.40 (d, 1H, $J = 8.8$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 23.0$, 30.1, 35.4 (d, $J_{C\text{-}P} = 12.4$ Hz), 55.4, 112.4, 113.4, 127.3 (d, $J_{C\text{-}P} = 24.1$ Hz), 128.2 (d, $J_{C\text{-}P} = 12.4$ Hz), 129.7, 131.0 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.3 (d, $J_{C\text{-}P} = 9.1$ Hz), 135.3 (d, $J_{C\text{-}P} = 130.2$ Hz), 145.9 (d, $J_{C\text{-}P} = 1.7$ Hz), 163.1, 181.2 (d, $J_{C\text{-}P} = 6.6$ Hz); IR (KBr): $\tilde{\nu} = 1627$, 1587, 1569, 1252, 1205, 813, 726, 550, 517 cm^{-1}; m.p. 172.4–174.7 °C; HRMS: *m/z*: calcd for $C_{23}H_{22}NO_2P$: 375.1388; found: 375.1366 [M^+].

***N*-(Chroman-4-ylidene)-*P,P*-diphenylphosphinamide (11i)**: ^1H NMR ($CDCl_3$): $\delta = 3.50–3.54$ (m, 2H), 4.35 (t, 2H, $J = 6.3$ Hz), 6.92 (d, 1H, $J = 7.9$ Hz), 7.04 (t, 1H, $J = 7.9$ Hz), 7.41–7.48 (m, 7H), 7.95–8.01 (m, 4H), 8.26 (dd, 1H, $J = 1.7$, 7.9 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 33.8$ (d, $J_{C\text{-}P} = 12.4$ Hz), 66.0, 117.9, 121.1, 121.9, 122.2, 127.1, 128.3 (d, $J_{C\text{-}P} = 12.4$ Hz), 131.3 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.3 (d, $J_{C\text{-}P} = 9.2$ Hz), 134.5 (d, $J_{C\text{-}P} = 131.0$ Hz), 160.5 (d, $J_{C\text{-}P} = 1.7$ Hz), 175.1 (d, $J_{C\text{-}P} = 6.6$ Hz); IR (KBr): $\tilde{\nu} = 1629$, 1604, 1481, 1457, 1438, 1190, 1126, 1108, 896, 760, 728, 703, 551 cm^{-1}; m.p. 161.3–163.0 °C; HRMS: *m/z*: calcd for $C_{21}H_{18}NO_2P$: 347.1075; found: 347.1057 [M^+].

Typical procedure for enantioselective reduction of aryl *N*-diphenylphosphinyl imines

Formation of premodified borohydride: Under argon atmosphere, in a precooled vessel at 0 °C were placed fine grained $NaBH_4$ (29 mg, 0.75 mmol), $CHCl_3$ (5.0 mL), EtOH (0.044 mL, 0.75 mmol) and THFA (1.0 mL, 10.3 mmol), and the mixture was continued to stir for 3 h.

Catalytic enantioselective borohydride reduction: While maintaining solution of premodified borohydride at 0 °C, its solution was slowly added to the solution of (*S,S*)-cobalt(II) catalyst **2a** (3.7 mg, 0.005 mmol, 1 mol %) and *N*-diphenylphosphinyl imine (**11d**, 172.6 mg, 0.50 mmol) in $CHCl_3$ (5.0 mL), and the mixture was continued to stir for 4 h at 0 °C. The reaction was quenched by the addition of saturated aqueous ammonium chloride, and extracted with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and then the excess solvents were removed under reduced pressure. The purification by column chromatography on silica gel (hexane/ethyl acetate/dichloromethane 1:2:1) gave the corresponding amine **12d** as white solid (148.0 mg, 85 %). Enantiomeric excess was determined to be 98 % by HPLC analysis using Daicel Chiralpak AD (20.0 % propan-2-ol in hexane, flow 1.0 mL min^{-1}); $[\alpha]_D^{28} = -65.2°$ ($c = 0.43$ in MeOH).

Removal of diphenylphosphinyl group: Aryl *N*-diphenylphosphinyl amine (−)-**12d** (191.6 mg, 0.55 mmol) was mixed with 5 % HCl/methanol solution (15 mL). The solution was stirred for 3 h at ambient temperature. It was evaporated, and treated with aqueous NaOH, extracted with Et_2O, dried with anhydrous sodium sulfate, to quantitatively provide the free amine (*S*)-(+)-**13d** as a white solid, $[\alpha]_D^{26} = +47.8°$ ($c = 0.68$ in benzene) (lit.[68] $[\alpha]_D^{21} = -47.6°$ ($c = 0.47$ in benzene), (*R*)).

***N*-(Diphenylphosphinyl)-1,2,3,4-tetrahydro-1-naphthylamine (12d)**: ^1H NMR ($CDCl_3$): $\delta = 1.63–1.98$ (m, 3H), 2.04–2.18 (m, 1H), 2.60–2.85 (m, 2H), 3.15–3.26 (m, 1H), 4.24–4.38 (m, 1H), 7.04 (d, 1H, $J = 7.3$ Hz), 7.12–7.26 (m, 2H), 7.38–7.56 (m, 6H), 7.71 (d, 1H, $J = 7.6$ Hz), 7.93–8.02 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 19.9$, 29.2, 33.4 (d, $J_{C\text{-}P} = 2.5$ Hz), 49.8 (d, $J_{C\text{-}P} = 1.7$ Hz), 126.2, 127.0, 128.4 (d, $J_{C\text{-}P} = 12.4$ Hz), 128.5 (d, $J_{C\text{-}P} = 12.4$ Hz), 128.9 (d, $J_{C\text{-}P} = 1.7$ Hz), 131.8 (d, $J_{C\text{-}P} = 1.7$ Hz), 132.1 (d, $J_{C\text{-}P} = 10.0$ Hz), 132.1 (d, $J_{C\text{-}P} = 9.1$ Hz), 132.4 (d, $J_{C\text{-}P} = 126.1$ Hz), 132.9 (d, $J_{C\text{-}P} = 128.5$ Hz), 137.3, 138.5, 138.6; IR (KBr): $\tilde{\nu} = 3120$, 2925, 2860, 1438, 1196, 1182, 1118, 750, 736, 694, 531 cm^{-1}; m.p. 132.1–136.7 °C; HRMS: *m/z*: calcd for $C_{22}H_{22}NOP$: 347.1439; found: 347.1411 [M^+]. Enantiomeric excess was determined to be 98 % by HPLC analysis (Chiralpak AD; 20.0 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 12.9 min (major), 16.3 min (minor)); $[\alpha]_D^{28} = -65.2°$ ($c = 0.43$ in MeOH). The corresponding free amine was assigned as (*S*) configuration as mentioned above.

***N*-(Diphenylphosphinyl)-1-phenylethylamine (12e)**: ^1H NMR ($CDCl_3$): $\delta = 1.57$ (d, 3H, $J = 6.6$ Hz), 3.14–3.23 (m, 1H), 4.31–4.47 (m, 1H), 7.20–7.52 (m, 11H), 7.77–7.96 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 26.0$, 51.0, 125.8, 127.0, 128.2 (d, $J_{C\text{-}P} = 12.4$ Hz), 128.3 (d, $J_{C\text{-}P} = 12.4$ Hz), 128.4, 131.6 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.7 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.8 (d, $J_{C\text{-}P} = 9.1$ Hz),131.9 (d, $J_{C\text{-}P} = 130.2$ Hz), 132.3 (d, $J_{C\text{-}P} = 9.1$ Hz), 133.0 (d, $J_{C\text{-}P} = 127.7$ Hz), 144.9 (d, $J_{C\text{-}P} = 6.6$ Hz); IR (KBr): $\tilde{\nu} = 3431$, 3165, 2974, 2869, 1437, 1181, 1126, 1109, 727, 692, 545 cm^{-1}; m.p. 182.7–194.3 °C; HRMS: *m/z*: calcd for $C_{20}H_{20}NOP$: 321.1283; found: 321.1263 [M^+]. Enantiomeric excess was determined to be 90 % by HPLC analysis (Chiralpak AD; 10.0 % propan-2-ol in hexane, flow 0.5 mL min^{-1}, 47.7 min (minor), 50.0 min (major)). The corresponding free amine was assigned as (*S*) configuration, $[\alpha]_D^{28} = -20.0°$ ($c = 0.13$ in EtOH) (lit.[69] $[\alpha]_D^{20} = -31.0°$ ($c = 2.1$ in EtOH), (*S*)).

***N*-(Diphenylphosphinyl)-1-indanamine (12f)**: ^1H NMR ($CDCl_3$): $\delta = 1.87–1.99$ (m, 1H), 2.49–2.97 (m, 3H), 3.24 (dd, 1H, $J = 6.3$, 11.2 Hz), 4.54–4.69 (m, 1H), 7.14–7.27 (m, 3H), 7.40–7.55 (m, 6H), 7.67 (d, 1H, $J = 7.3$ Hz), 7.91–8.03 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 30.0$, 37.2 (d, $J_{C\text{-}P} = 4.1$ Hz), 56.8 (d, $J_{C\text{-}P} = 1.7$ Hz), 124.4, 126.6, 127.6, 128.4 (d, $J_{C\text{-}P} = 13.3$ Hz), 128.4 (d, $J_{C\text{-}P} = 12.4$ Hz), 131.68 (d, $J_{C\text{-}P} = 1.7$ Hz), 131.70 (d, $J_{C\text{-}P} = 2.5$ Hz), 132.0 (d, $J_{C\text{-}P} = 9.1$ Hz), 132.1 (d, $J_{C\text{-}P} = 9.1$ Hz), 132.4 (d, $J_{C\text{-}P} = 129.4$ Hz), 132.6 (d, $J_{C\text{-}P} = 125.2$ Hz), 142.6, 144.6 (d, $J_{C\text{-}P} = 6.6$ Hz); IR (KBr): $\tilde{\nu} = 3434$, 3175, 1438, 1182, 1126, 1108, 1165, 744, 727 cm^{-1}; m.p. 119.1–122.4 °C; HRMS: *m/z*: calcd for $C_{21}H_{20}NOP$: 333.1283; found: 333.1284 [M^+]. Enantiomeric excess was determined to be 91 % by HPLC analysis (Chiralpak AD; 20.0 % propan-2-ol in hexane, flow 1.0 mL min^{-1}, 12.3 min (minor), 14.9 min (major); $[\alpha]_D^{30} = +36.5°$ ($c = 0.663$ in MeOH). The corresponding free amine was assigned as *S* configuration, $[\alpha]_D^{30} = +9.9°$ ($c = 0.19$ in MeOH) (lit.[70] $[\alpha]_D^{20} = +15°$ ($c = 1.7$ in MeOH), (*S*)).

***N*-(Diphenylphosphinyl)-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-ylamine (12g)**: ^1H NMR ($CDCl_3$): $\delta = 1.45–2.19$ (m, 6H), 2.57–2.86 (m, 2H), 3.43 (dd, 1H, $J = 5.4$, 10.7 Hz), 4.37–4.52 (m, 1H), 7.01–7.20 (m, 3H), 7.22–7.56 (m, 7H), 7.75–7.98 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 27.3$, 27.7, 36.1, 37.4, 55.5, 126.1, 126.9, 128.3 (d, $J_{C\text{-}P} = 11.6$ Hz), 128.4 (d, $J_{C\text{-}P} = 12.4$ Hz), 129.8, 131.6 (d, $J_{C\text{-}P} = 3.3$ Hz), 131.7 (d, $J_{C\text{-}P} = 9.1$ Hz), 131.7 (d, $J_{C\text{-}P} = 2.5$ Hz), 131.9 (d, $J_{C\text{-}P} = 140.1$ Hz), 133.2 (d, $J_{C\text{-}P} = 136.0$ Hz), 140.8, 143.0 (d, $J_{C\text{-}P} = 6.6$ Hz); IR (KBr): $\tilde{\nu} =$ 3432, 2098, 2923, 2858, 1438, 1198, 1182, 1112, 749, 720, 695, 537 cm^{-1}; m.p. 214.7–215.0 °C; HRMS: *m/z*: calcd for $C_{23}H_{24}NOP$: 361.1596; found: 361.1582 [M^+]. Enantiomeric excess was determined to be 94 % by HPLC analysis (Chiralcel OD-H; 30.0 % propan-2-ol in hexane, flow 0.5 mL min^{-1}, 9.9 min (major), 13.5 min (minor)); $[\alpha]_D^{30} = -40.8°$ ($c = 0.556$ in MeOH).

***N*-(Diphenylphosphinyl)-6-methoxy-1,2,3,4-tetrahydro-1-naphthylamine (12h)**: ^1H NMR ($CDCl_3$): $\delta = 1.60–2.13$ (m, 4H), 2.57–2.88 (m, 2H), 3.12–3.25 (m, 1H), 3.76 (s, 3H), 4.20–4.34 (m, 1H), 6.56 (d, 1H, $J = 2.6$ Hz), 6.78 (dd, 1H, $J = 2.6$, 8.6 Hz), 7.37–7.53 (m, 6H), 7.62 (d, 1H, $J = 8.6$ Hz), 7.89–8.00 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 19.8$, 29.5, 33.4 (d, $J_{C\text{-}P} = 2.5$ Hz), 49.2 (d, $J_{C\text{-}P} = 1.7$ Hz), 55.1, 112.5, 113.0, 128.3 (d, $J_{C\text{-}P} = 12.4$ Hz), 128.4 (d, $J_{C\text{-}P} = 12.4$ Hz), 130.3, 130.7 (d, $J_{C\text{-}P} = 7.5$ Hz), 131.6 (d, $J_{C\text{-}P} = 1.7$ Hz), 131.6 (d, $J_{C\text{-}P} = 2.5$ Hz), 132.0 (d, $J_{C\text{-}P} = 9.1$ Hz), 132.5 (d, $J_{C\text{-}P} = 127.8$ Hz), 132.9 (d, $J_{C\text{-}P} = 129.4$ Hz), 138.5, 158.2; IR (KBr): $\tilde{\nu} =$ 3210, 1607, 1500, 1436, 1255, 1181, 1107, 703, 529 cm^{-1}; m.p. 156.1–157.3 °C;

HRMS: *m*/*z*: calcd for $C_{23}H_{24}NO_2P$: 377.1545; found: 377.1521 [M^+]. Enantiomeric excess was determined to be 99% by HPLC analysis (Chiralpak AD; 20.0% propan-2-ol in hexane, flow 1.0 mL min^{-1}, 15.2 min (minor), 18.5 min (major)); $[\alpha]_D^{28} = -50.8^\circ$ ($c = 1.560$ in MeOH).

***N*-(Diphenylphosphinyl)-chroman-4-ylamine (12i)**: ^{1}H NMR ($CDCl_3$): $\delta =$ 2.13–2.30 (m, 2H), 3.31 (dd, 1H, $J = 6.9$, 10.2 Hz), 4.10–4.41 (m, 3H), 6.74–6.79 (m, 1H), 6.89–6.97 (m, 1H), 7.10–7.18 (m, 1H), 7.39–7.58 (m, 7H), 7.89–8.04 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 32.1$ (d, $J_{C\text{-}P} = 2.5$ Hz), 45.5, 63.2, 116.9, 120.6, 123.9, 124.0, 128.5, (d, $J_{C\text{-}P} = 13.3$ Hz), 128.6, (d, $J_{C\text{-}P} = 13.3$ Hz), 129.4, 131.8 (d, $J_{C\text{-}P} = 9.1$ Hz), 131.9 (d, $J_{C\text{-}P} = 3.3$ Hz), 131.9 (d, $J_{C\text{-}P} = 128.5$ Hz), 132.1 (d, $J_{C\text{-}P} = 10.0$ Hz), 132.6 (d, $J_{C\text{-}P} = 128.5$ Hz), 154.6; IR (KBr): $\tilde{\nu} = 3432$, 3196, 1438, 1177, 1126, 1077, 747, 701, 694, 533 cm^{-1}; m.p. 239.1–241.2 °C; HRMS: *m*/*z*: calcd for $C_{21}H_{20}NO_2P$: 349.1232; found: 349.1223 [M^+]. Enantiomeric excess was determined to be 92% by HPLC analysis (Chiralpak AD; 20.0% propan-2-ol in hexane, flow 1.0 mL min^{-1}, 9.8 min (minor), 11.4 min (major)); $[\alpha]_D^{28} = -64.3^\circ$ ($c = 1.130$ in $CHCl_3$).

Preparation of 1,3-diaryl-1,3-propanedione: 1,3-Diaryl-1,3-propanediones **14a** and **14d** are commercially available. 1,3-Diaryl-1,3-propanediones **14b**, **14c**, **14e**, **14f**, and **14g** were prepared by the conventional Claisen condensation reaction.

1,3-Bis(*p*-methylphenyl)-1,3-propanedione (14b): ^{1}H NMR ($CDCl_3$): $\delta =$ 2.43 (s, 6H), 6.82 (s, 1H), 7.29 (d, 4H, $J = 8.3$ Hz), 7.89 (d, 4H, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 21.8$, 92.4, 127.0, 129.3, 132.8, 143.0, 185.3; IR (KBr): $\tilde{\nu} = 1608$, 1527, 1481, 1184, 1120, 1014, 773 cm^{-1}; m.p. 127.0–127.4 °C; elemental analysis calcd (%) for $C_{17}H_{16}O_2$: C 80.93, H 6.39; found: C 80.76, H 6.32.

1,3-Bis(*p*-*tert*-butylphenyl)-1,3-propanedione (14c): ^{1}H NMR ($CDCl_3$): $\delta = 1.36$ (s, 18H), 6.82 (s, 1H), 7.50 (d, 2H, $J = 8.2$ Hz), 7.92 (d, 2H, $J =$ 8.2 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 31.2$, 35.2, 92.6, 125.5, 126.9, 132.8, 155.9, 185.3; IR (KBr): $\tilde{\nu} = 2960$, 1606, 1495, 1362, 1296, 1109, 796, 546 cm^{-1}; m.p. 107.3–107.7 °C; elemental analysis calcd (%) for $C_{23}H_{28}O_2$: C 82.10, H 8.39; found: C 82.00, H 8.37.

1,3-Bis(*p*-fluorophenyl)-1,3-propanedione (14e): ^{1}H NMR ($CDCl_3$): $\delta =$ 6.75 (s, 1H), 7.11–7.24 (m, 4H), 7.93–8.12 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 92.5$, 115.8 (d, $J_{C\text{-}F} = 21.6$ Hz), 129.5 (d, $J_{C\text{-}F} = 9.1$ Hz), 131.5 (d, $J_{C\text{-}F} =$ 3.3 Hz), 165.3 (d, $J_{C\text{-}F} = 253.7$Hz), 184.3; IR (KBr): $\tilde{\nu} = 1599$, 1481, 1223, 1157, 850, 785, 567, 488 cm^{-1}; m.p. 171.8–172.0 °C; HRMS: *m*/*z*: calcd for $C_{15}H_{10}O_2F_2$: 260.0649; found: 260.0675 [M^+].

1,3-Bis(*o*-fluorophenyl)-1,3-propanedione (14f): ^{1}H NMR ($CDCl_3$): $\delta =$ 7.07 (s, 1H), 7.10–7.21 (m, 2H), 7.22–7.33 (m, 2H), 7.44–7.56 (m, 2H), 7.94–8.04 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 102.4$, 116.6 (d, $J_{C\text{-}F} = 23.2$ Hz), 123.7 (d, $J_{C\text{-}F} = 9.7$ Hz), 124.4 (d, $J_{C\text{-}F} = 4.1$ Hz), 130.1 (d, $J_{C\text{-}F} = 1.6$ Hz), 133.7 (d, $J_{C\text{-}F} = 9.1$ Hz), 161.1 (d, $J_{C\text{-}F} = 256.3$ Hz), 182.1; IR (KBr): $\tilde{\nu} = 1612$, 1487, 1219, 1153, 820, 762, 602 cm^{-1}; m.p. 101.6–102.6 °C; HRMS: *m*/*z*: alcd for $C_{15}H_{10}O_2F_2$: 260.0649; found: 260.0618 [M^+].

1,3-Bis(2-naphthyl)-1,3-propanedione (14g): ^{1}H NMR ($CDCl_3$): $\delta = 7.17$ (s, 1H), 7.53–7.66 (m, 4H), 7.87–8.12 (m, 8H), 8.60 (s, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 93.8$, 123.2, 126.7, 127.7, 128.1, 128.3, 128.4, 129.3, 132.66, 132.73, 135.2, 185.3; IR (KBr): $\tilde{\nu} = 1599$, 1523, 1496, 1429, 1190, 951, 789, 478 cm^{-1}; m.p. 171.8–172.0 °C; HRMS: *m*/*z*: calcd for $C_{23}H_{16}O_2$: 324.1150; found: 324.1156 [M^+].

Typical procedure for enantioselective reduction of 1,3-diaryl-1,3-propanedione: Under a dry nitrogen atmosphere in a vessel at −20 °C, ethanol (0.13 mL, 2.25 mmol) and tetrahydrofurfuryl alcohol (THFA, 1.0 mL, 10.5 mmol) were added to the suspension of $NaBH_4$ (28 mg, 0.75 mmol) in $CHCl_3$ (22 mL). After 15 min, to the solution was added a $CHCl_3$ solution (4 mL) of a cobalt catalyst (complex (*S*,*S*)-**3b**, 1.4 mg, 0.0025 mmol) and then dibenzoylmethane (56 mg, 0.25 mmol) in $CHCl_3$ (4 mL) was added and stirred for 40 h at −20 °C. The reaction was quenched by pH 7 buffer solution and the crude products were extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to give (1*S*,3*S*)-1,3-diphenyl-1,3-propanediol in quantitative yield. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD, Hexane/EtOH) to be 98%. The ratio of *dl*/*meso* was determined by ^{1}H NMR analysis of the corresponding diacetate after treatment with Ac_2O/pyridine to be 84:16.

***dl*-1,3-Diphenyl-1,3-propanediol (15a)**:[33c] HPLC: Daicel Chiralpak AD (5% ethanol in hexane, flow 1.0 mL min^{-1}), 25.9 min (*meso*), 29.4 min (minor), 46.6 min (major).

***dl*-1,3-Bis(*p*-methylphenyl)-1,3-propanediol (15b)**: ^{1}H NMR ($CDCl_3$): $\delta =$ 2.16 (t, 2H, $J = 5.2$ Hz), 2.35 (s, 6H), 2.72 (d, 2H, $J = 5.2$ Hz), 4.94 (q, 2H, $J = 5.2$ Hz), 7.15–7.17 (m, 4H), 7.24–7.26 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta =$ 21.2, 46.4, 71.6, 125.5, 129.1, 137.0, 141.1; IR (KBr): $\tilde{\nu} = 3562$, 2939, 1512, 1063, 812, 517 cm^{-1}; m.p. 108.9–109.4 °C; HRMS: *m*/*z*: calcd for $C_{17}H_{20}O_2$: 256.1463; found: 256.1444 [M^+]; HPLC: Daicel chiralpak AD (1 mL min^{-1}, 5% propan-2-ol in hexane), 25.9 min (*meso*), 29.4 min (minor), 46.6 min (major); $[\alpha]_D^{23} = -27.6^\circ$ ($c = 0.56$ in $CHCl_3$).

***dl*-1,3-Bis(*p*-*tert*-butylphenyl)-1,3-propanediol (15c)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.32$ (s, 18H), 2.19 (t, 2H, $J = 5.1$ Hz), 2.66 (d, 2H, $J = 5.1$ Hz), 4.98 (q, 2H, $J = 5.1$ Hz), 7.29–7.31 (m, 4H), 7.37–7.39 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 31.4$, 34.6, 46.3, 71.5, 125.3, 141.1, 150.3; IR (KBr): $\tilde{\nu} = 3450$, 2962, 1363, 1269, 1049, 823, 588 cm^{-1}; m.p. 174.1–176.3 °C; HRMS: *m*/*z*: calcd for $C_{23}H_{32}O_2$: 340.2402; found: 340.2411 [M^+]. HPLC: Daicel chiralpak AD (1 mL min^{-1}, 2% ethanol in hexane), 31.0 min (*meso*), 49.4 min (minor), 55.9 min (major); $[\alpha]_D^{23} = -16.9^\circ$ ($c = 1.01$ in $CHCl_3$).

***dl*-1,3-Bis(*p*-methoxylphenyl)-1,3-propanediol (15d)**: ^{1}H NMR ($CDCl_3$): $\delta = 2.14$ (t, 2H, $J = 4.9$ Hz), 2.72 (d, 2H, $J = 4.9$ Hz), 3.81 (s, 6H), 4.91 (q, 2H, $J = 4.9$ Hz), 6.88 (d, 4H, $J = 8.5$ Hz), 7.28 (d, 4H, $J = 8.5$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 46.4$, 55.3, 71.3, 113.7, 126.8, 136.2, 158.8; IR (KBr): $\tilde{\nu} = 3357$, 2949, 1612, 1512, 1250, 1039, 822 cm^{-1}; m.p. 79.7–81.3 °C; HRMS: *m*/*z*: calcd for $C_{17}H_{20}O_4$: 288.1361; found: 288.1405 [M^+]. HPLC: Daicel chiralpak AD (1 mL min^{-1}, 4% 2-propanpl in hexane), 90.0 min (*meso*), 98.1 min (minor), 118.5 min (major); $[\alpha]_D^{23} = -20.7^\circ$ ($c = 0.86$ in $CHCl_3$).

***dl*-1,3-Bis(*p*-fluorophenyl)-1,3-propanediol (15e)**: ^{1}H NMR ($CDCl_3$): $\delta =$ 2.12 (t, 2H, $J = 5.0$ Hz), 2.76 (d, 2H, $J = 5.0$ Hz), 4.97 (q, 2H, $J = 5.0$ Hz), 6.99–7.09 (m, 4H), 7.29–7.38 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 46.6$, 71.1, 115.3 (d, $J_{C\text{-}F} = 21.6$ Hz), 127.1 (d, $J_{C\text{-}F} = 7.5$ Hz), 139.7 (d, $J_{C\text{-}F} = 3.3$ Hz), 162.0 (d, $J_{C\text{-}F} = 245.5$ Hz); IR (KBr): $\tilde{\nu} = 3421$, 3301, 2943, 1604, 1152, 1221, 831, 553 cm^{-1}; m.p. 122.0–123.5 °C; HRMS: *m*/*z*: calcd for $C_{15}H_{14}F_2O_2$: 264.0962; found: 264.0951 [M^+]. HPLC after acetylation: Daicel chiralpak AD (1 mL min^{-1}, 2% ethanol in hexane), 11.4 min (major), 15.1 min (*meso*), 22.2 min (minor); $[\alpha]_D^{23} = -52.3^\circ$ ($c = 0.61$ in $CHCl_3$).

***dl*-1,3-Bis(*o*-fluorophenyl)-1,3-propanediol (15f)**: ^{1}H NMR ($CDCl_3$): $\delta =$ 2.27 (t, 2H, $J = 5.4$ Hz), 2.91 (d, 2H, $J = 5.4$ Hz), 5.29 (q, 2H, $J = 5.4$ Hz), 6.97–7.05 (m, 2H), 7.14–7.20 (m, 2H), 7.21–7.30 (m, 2H), 7.52–7.61 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 43.2$, 66.4, 115.2 (d, $J_{C\text{-}F} = 21.6$ Hz), 124.1 (d, $J_{C\text{-}F} = 3.3$ Hz), 127.1 (d, $J_{C\text{-}F} = 4.1$ Hz), 128.8 (d, $J_{C\text{-}F} = 8.3$ Hz), 130.7 (d, $J_{C\text{-}F} = 13.3$ Hz), 159.2 (d, $J_{C\text{-}F} = 244.6$ Hz); IR (KBr): $\tilde{\nu} = 3462$, 3348, 1493, 1219, 1049, 752 cm^{-1}; m.p. 79.6–80.6 °C; HRMS: *m*/*z*: calcd for $C_{15}H_{14}F_2O_2$: 264.0962; found: 264.0995 [M^+]. HPLC: Daicel chiralpak AD (1 mL min^{-1}, 5% ethanol in hexane), 18.4 min (*meso*), 22.3 min (minor), 38.9 min (major); $[\alpha]_D^{23} = -47.2^\circ$ ($c = 0.29$ in $CHCl_3$).

***dl*-1,3-Bis(2-naphthyl)-1,3-propanediol (15g)**: ^{1}H NMR ($CDCl_3$): $\delta = 2.38$ (t, 2H, $J = 4.9$ Hz), 3.00 (d, 2H, $J = 4.9$ Hz), 5.19 (q, 2H, $J = 4.9$ Hz), 7.43–7.50 (m, 6H), 7.79–7.87 (m, 8H); ^{13}C NMR ($CDCl_3$): $\delta = 46.1$, 72.1, 123.8, 124.2, 125.8, 126.2, 127.6, 127.9, 128.3, 132.8, 133.2, 141.4; IR (KBr): $\tilde{\nu} =$ 3390, 3311, 3053, 1398, 1034, 814 cm^{-1}; m.p. 198.5–200.2 °C; HRMS: *m*/*z*: calcd for $C_{23}H_{20}O_2$: 328.1463; found: 328.1450 [M^+]. HPLC after acetylation: Daicel chiralpak AD (1 mL min^{-1}, 10% ethanol in hexane), 13.5 min (major), 15.1 min (*meso*), 44.7 min (minor); $[\alpha]_D^{23} = 47.1^\circ$ ($c = 0.13$ in $CHCl_3$).

Typical procedure for multigram preparation of optically pure 1,3-diaryl-1,3-diols: Ethanol (15.5 mL, 268 mmol) and tetrahydrofurfuryl alcohol (90.7 mL, 936 mmol) were added at −20 °C to the suspension of $NaBH_4$ (5.06 g, 134 mmol) and $CHCl_3$ (350 mL). After stirring for 15 min, to the solution was added a $CHCl_3$ solution (25 mL) of cobalt catalyst (complex (*S*,*S*)-**3a**, 500 mg, 0.64 mmol) and then dibenzoylmethane (10.0 g, 44.6 mmol) in $CHCl_3$ (25 mL). The solution was stirred for 3 d at −20 °C. The reaction mixture was quenched by pH 7 buffer solution and extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. Solvent and tetrahydrofurfuryl alcohol were removed under reduced pressure. The crude products were rinsed with ethyl acetate/hexane and recrystallized from ethyl acetate to obtain the optically pure (1*S*,3*S*)-1,3-diphenyl-1,3-propanediol (6.15 g, 60%). Optically pure 1,3-diaryl-1,3-propanediols were quantitatively converted to the corresponding 1,3-diamines without racemization.[40]

Preparation of 1,1′-diacylferrocenes: 1,1′-Diacylferrocenes were prepared by the conventional Friedel-Crafts reaction from ferrocene and acyl chlorides.[37c]

1,1′-Dibenzoylferrocene (16a):[37c] ^{1}H NMR ($CDCl_3$): $\delta = 4.56-4.62$ (m, 4H), 4.90–4.96 (m, 4H), 7.39–7.46 (m, 4H), 7.51–7.58 (m, 2H), 7.76–7.82 (m, 4H).

1,1′-Bis(*p*-fluorobenzoyl)ferrocene (16b):[37c] ^{1}H NMR ($CDCl_3$): $\delta = 4.57-4.61$ (m, 4H), 4.86–4.90 (m, 4H), 7.06–7.14 (m, 4H), 7.77–7.84 (m, 4H).

1,1′-Bis(*p*-chlorobenzoyl)ferrocene (16c): ^{1}H NMR ($CDCl_3$): $\delta = 4.58-4.61$ (m, 4H), 4.85–4.88 (m, 4H), 7.37–7.42 (m, 4H), 7.67–7.72 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 73.2$, 74.5, 79.4, 128.5, 129.4, 137.1, 138.3, 196.3; IR (KBr): $\tilde{\nu} = 1631$, 1444, 1288, 1087, 836, 763 cm^{-1}; m.p. 187.4–187.7 °C; elemental analysis calcd (%) for $C_{24}H_{16}O_2Cl_2Fe$: C 62.24, H 3.48; found: C 61.99, H 3.26.

1,1′-Bis(*p*-bromobenzoyl)ferrocene (16d): ^{1}H NMR ($CDCl_3$): $\delta = 4.58-4.62$ (m, 4H), 4.84–4.88 (m, 4H), 7.54–7.58 (m, 4H), 7.60–7.64 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 73.2$, 74.5, 79.3, 126.9, 129.5, 131.5, 137.5, 196.4; IR (KBr): $\tilde{\nu} = 1631$, 1442, 1286, 1010, 835, 760, 504 cm^{-1}; m.p. 196.3–197.2 °C; elemental analysis calcd (%) for $C_{24}H_{16}O_2Br_2Fe$: C 52.22, H 2.92; found: C 52.04, H 3.16.

1,1′-Bis(*p*-methylbenzoyl)ferrocene (16e): ^{1}H NMR ($CDCl_3$): $\delta = 2.43$ (s, 6H), 4.54–4.57 (m, 4H), 4.89–4.92 (m, 4H), 7.20–7.24 (m, 4H), 7.69–7.74 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 21.7$, 73.1, 74.5, 79.7, 128.3, 128.9, 136.3, 142.4, 197.3; IR (KBr): $\tilde{\nu} = 1628$, 1446, 1288, 1165, 760, 505 cm^{-1}; m.p. 178.5–178.9 °C; elemental analysis calcd (%) for $C_{26}H_{22}O_2Fe$: C 73.95, H 5.25; found: C 73.82, H 5.06.

1,1′-Bis(*o*-fluorobenzoyl)ferrocene (16f): ^{1}H NMR ($CDCl_3$): $\delta = 4.61-4.64$ (m, 4H), 4.82–4.85 (m, 4H), 7.09–7.16 (m, 2H), 7.18–7.23 (m, 2H), 7.44–7.52 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 72.5$, 75.0, 79.8, 116.3 (d, $J_{C\text{-}F} = 21.6$ Hz), 123.9 (d, $J_{C\text{-}F} = 4.2$ Hz), 128.0 (d, $J_{C\text{-}F} = 15.8$ Hz), 129.1 (d, $J_{C\text{-}F} = 3.3$ Hz), 132.3 (d, $J_{C\text{-}F} = 8.3$ Hz), 159.1 (d, $J_{C\text{-}F} = 251.3$ Hz), 195.1; IR (KBr): $\tilde{\nu} = 1638$, 1455, 1301, 836, 754, 649, 492 cm^{-1}; m.p. 154.3–154.8 °C; HRMS: *m*/*z*: calcd for $C_{24}H_{16}O_2F_2Fe$: 430.0468; found: 430.0438 [M^+].

1,1′-Bis(*o*-chlorobenzoyl)ferrocene (16g): ^{1}H NMR ($CDCl_3$): $\delta = 4.68-4.71$ (m, 4H), 4.80–4.83 (m, 4H), 7.30–7.36 (m, 2H), 7.39–7.42 (m, 4H), 7.44–7.47 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 72.4$, 74.7, 79.7, 126.3, 128.7, 130.3, 130.9, 131.1, 138.5, 197.3; IR (KBr): $\tilde{\nu} = 1638$, 1447, 1297, 1064, 837, 755 cm^{-1}; m.p. 162.2–162.4 °C; elemental analysis calcd (%) for $C_{24}H_{16}O_2Cl_2Fe$: C 62.24, H 3.48; found: C 62.14, H 3.43.

1,1′-Bis(*o*-bromobenzoyl)ferrocene (16h): ^{1}H NMR ($CDCl_3$): $\delta = 4.70-4.73$ (m, 4H), 4.81–4.84 (m, 4H), 7.30–7.41 (m, 4H), 7.44–7.48 (m, 2H), 7.58–7.62 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 72.5$, 74.7, 79.5, 119.4, 126.9, 128.8, 131.2, 133.5, 140.4, 198.2; IR (KBr): $\tilde{\nu} = 1650$, 1444, 1291, 1036, 839, 742 cm^{-1}; m.p. 196.0–196.7 °C; elemental analysis calcd (%) for $C_{24}H_{16}O_2Br_2Fe$: C 52.22, H 2.92; found: C 52.07, H 2.96.

1,1′-Dipropanoylferrocene (16i): ^{1}H NMR ($CDCl_3$): $\delta = 1.19$ (t, 6H, $J = 7.3$ Hz), 2.68 (q, 4H, $J = 7.3$ Hz), 4.44–4.49 (m, 4H), 4.75–4.80 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 8.2$, 33.0, 70.4, 73.2, 80.2, 203.8; IR (KBr): $\tilde{\nu} = 2935$, 1673, 1458, 1243, 1102, 1050, 808 cm^{-1}; m.p. 53.8–55.2 °C; elemental analysis calcd (%) for $C_{16}H_{18}O_2Fe$: C 64.45, H 6.08; found: C 64.53, H 6.12.

1,1′-Dibutanoylferrocene (16j): ^{1}H NMR ($CDCl_3$): $\delta = 1.01$ (t, 6H, $J = 7.3$ Hz), 1.73 (sextet, 4H, $J = 7.3$ Hz), 2.64 (t, 4H, $J = 7.3$ Hz), 4.47–4.50 (m, 4H), 4.76–4.79 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 14.0$, 17.7, 41.8, 70.5, 73.3, 80.4, 203.3; IR (KBr): $\tilde{\nu} = 2968$, 1662, 1456, 1242, 840, 507 cm^{-1}; m.p. 75.7–76.4 °C; elemental analysis calcd (%) for $C_{18}H_{22}O_2Fe$: C 66.27, H 6.80; found: C 66.28, H 6.57.

1,1′-Dihexanoylferrocene (16k):[37c] ^{1}H NMR ($CDCl_3$): $\delta = 0.93$ (t, 6H, $J = 6.6$ Hz), 1.31–1.43 (m, 8H), 1.70 (quintet, 4H, $J = 7.3$ Hz), 2.65 (t, 4H, $J = 7.3$ Hz), 4.45–4.51 (m, 4H), 4.74–4.80 (m, 4H).

1,1′-Dioctanoylferrocene (16l): ^{1}H NMR ($CDCl_3$): $\delta = 0.90$ (t, 6H, $J = 7.1$ Hz), 1.22–1.43 (m, 16H), 1.67 (quintet, 4H, $J = 7.3$ Hz), 2.65 (t, 4H, $J = 7.3$ Hz), 4.46–4.49 (m, 4H), 4.76–4.79 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 14.1$, 22.7, 24.4, 29.2, 29.5, 31.8, 40.0, 70.5, 73.3, 80.4, 203.6; IR (KBr): $\tilde{\nu} = 2925$, 1681, 1464, 1241, 824 cm^{-1}; m.p. 55.8–57.5 °C; elemental analysis calcd (%) for $C_{26}H_{38}O_2Fe$: C 71.23, H 8.74; found: C 71.42, H 8.63.

Typical procedure of the stereoselective reduction of 1,1′-diacylferrocenes

Preparation of the modified borohydride solution: EtOH (0.11 mL, 2 mmol) and tetrahydrofurfuryl alcohol (THFA) (2.71 mL, 28 mmol) were added at 0 °C under a dry nitrogen atmosphere to a suspension of $NaBH_4$ (75.7 mg, 2 mmol) in $CHCl_3$ (13.3 mL). The mixture was stirred for 3 h at 0 °C and then cooled at −20 °C.

Enantio- and diastereoselective reduction of the 1,1′-dibenzoylferrocene (16a): 1,1′-Dibenzoylferrocene (**16a**) (0.125 mmol) and (*S*,*S*)-cobalt complex catalyst **3b** (3.6 mg, 0.00625 mmol, 5.0 mol% against 1,1′-dibenzoylferrocene) were dissolved in Et_2O (10 mL) and cooled to 0 °C under a dry nitrogen atmosphere. The modified borohydride solution (4 mL, 0.5 mmol) was added to the reaction mixture and stirred for 0.5 h at 0 °C. The reaction was quenched by drop-wise addition of ice-cold water (10 mL). The reaction mixture was extracted with AcOEt. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to afford the corresponding 1,1′-ferrocenyldiols **17a** and *meso*-form. The *dl*/*meso* selectivity was determined by ^{13}C NMR analysis and the enantiomeric excess was determined by HPLC analysis (Daicel chiralpak AD-H, propan-2-ol/hexane).

***dl*-1,1′-Bis(α-hydroxyphenylmethyl)ferrocene (17a)**:[37c] HPLC: Daicel Chiralpak AD-H (10% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 9.6 min (minor), 11.2 min (major), 12.6 min (*meso*).

***dl*-1,1′-Bis(α-hydroxy-*p*-fluorophenylmethyl)ferrocene (17b)**:[37c] HPLC: Daicel Chiralpak AD-H (10% propan-2-ol in hexane, flow 0.5 mL min^{-1}), 21.1 min (minor), 25.9 min (*meso*), 31.9 min (major).

***dl*-1,1′-Bis(α-hydroxy-*p*-chlorophenylmethyl)ferrocene (17c)**: ^{1}H NMR ($CDCl_3$): $\delta = 4.12-4.19$ (m, 4H), 4.21–4.30 (m, 4H), 4.34–4.38 (m, 2H), 5.49 (s, 2H), 7.17–7.24 (m, 8H); ^{13}C NMR ($CDCl_3$): $\delta = 66.5$, 66.8, 68.1, 68.4, 72.1, 93.2, 127.4, 128.3, 128.4, 133.2, 142.5; IR (KBr): $\tilde{\nu} = 3267$, 1289, 1012, 811, 517 cm^{-1}; m.p. 130.8–132.1 °C; elemental analysis calcd (%) for $C_{24}H_{20}O_2Cl_2Fe$: C 61.70, H 4.32; found: C 61.99, H 4.39. HPLC: Daicel Chiralcel OD-H (10% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 7.0 min (minor), 7.6 min (major), 9.1 min (*meso*); $[\alpha]_D^{23} = -34.1°$ ($c = 0.73$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxy-*p*-bromophenylmethyl)ferrocene (17d)**: ^{1}H NMR ($CDCl_3$): $\delta = 4.12-4.17$ (m, 4H), 4.21–4.26 (m, 2H), 4.33–4.37 (m, 2H), 4.52–4.58 (m, 2H), 5.44 (s, 2H), 7.08–7.14 (m, 4H), 7.32–7.37 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 66.5$, 66.7, 68.1, 68.4, 72.1, 93.1, 121.3, 127.7, 131.3, 143.0; IR (KBr): $\tilde{\nu} = 3281$, 1486, 1009, 756, 494 cm^{-1}; m.p. 129.6–130.3 °C; elemental analysis calcd (%) for $C_{24}H_{20}O_2Br_2Fe$: C 51.84, H 3.63; found: C 51.65, H 3.64. HPLC: Daicel Chiralcel OD-H (10% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 8.3 min (minor), 10.9 min (major), 15.3 min (*meso*); $[\alpha]_D^{23} = -39.2°$ ($c = 2.08$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxy-*p*-methylphenylmethyl)ferrocene (17e)**: ^{1}H NMR ($CDCl_3$): $\delta = 2.29$ (s, 6H), 3.68 (br, 2H), 4.12–4.15 (m, 2H), 4.16–4.19 (m, 2H), 4.21–4.24 (m, 2H), 4.38–4.42 (m, 2H), 5.55 (s, 2H), 7.06–7.10 (m, 4H), 7.19–7.23 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 21.1$, 66.7, 66.8, 67.9, 68.2, 72.6, 93.7, 126.1, 128.9, 137.0, 141.4; IR (KBr): $\tilde{\nu} = 3253$, 1511, 1015, 806, 529 cm^{-1}; m.p. 129.5–130.5 °C; elemental analysis calcd (%) for $C_{26}H_{16}O_2Fe$: C 73.25, H 6.15; found: C 73.08, H 5.95. HPLC: Daicel Chiralpak AD-H (10% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 11.5 min (major), 15.1 min (*meso*), 16.9 min (minor); $[\alpha]_D^{23} = -13.5°$ ($c = 0.66$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxy-*o*-fluorophenylmethyl)ferrocene (17f)**: ^{1}H NMR ($CDCl_3$): $\delta = 4.10-4.15$ (m, 2H), 4.20–4.27 (m, 4H), 4.32–4.38 (m, 2H), 4.39–4.44 (m, 2H), 5.88 (s, 2H), 6.86–6.96 (m, 2H), 6.99–7.08 (m, 2H), 7.10–7.19 (m, 2H), 7.32–7.41 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 66.0$ (d, $J_{C\text{-}F} = 3.3$ Hz), 66.8 (d, $J_{C\text{-}F} = 11.6$ Hz), 68.1 (d, $J_{C\text{-}F} = 21.6$ Hz), 92.6, 115.1 (d, $J_{C\text{-}F} = 21.6$ Hz), 124.1 (d, $J_{C\text{-}F} = 3.3$ Hz), 127.3 (d, $J_{C\text{-}F} = 4.1$ Hz), 128.8 (d, $J_{C\text{-}F} = 8.3$ Hz), 131.2 (d, $J_{C\text{-}F} = 13.3$ Hz), 159.5 (d, $J_{C\text{-}F} = 245.5$ Hz); IR (KBr): $\tilde{\nu} = 3271$, 1485, 1221, 1044, 756, 494 cm^{-1}; m.p. 132.6–133.3 °C; HRMS: *m*/*z*: calcd for $C_{24}H_{20}O_2F_2Fe$: 434.0781; found: 434.0786 [M^+]. HPLC: Daicel Chiralpak AD-H (10% propan-2-ol in hexane, flow 0.5 mL min^{-1}), 16.7 min (major), 18.8 min (minor), 23.8 min (*meso*); $[\alpha]_D^{23} = -31.2°$ ($c = 1.75$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxy-*o*-chlorophenylmethyl)ferrocene (17g)**: ^{1}H NMR ($CDCl_3$): $\delta = 4.10-4.17$ (m, 2H), 4.22–4.30 (m, 2H), 4.33–4.46 (m, 4H), 4.60–4.68 (m, 2H), 5.99 (s, 2H), 7.06–7.14 (m, 2H), 7.14–7.28 (m, 4H), 7.41–7.49 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 66.8$, 66.9, 68.0, 68.2, 68.6, 92.7, 127.0, 127.6, 128.5, 129.1, 131.9, 141.3; IR (KBr): $\tilde{\nu} = 3271$, 1469, 1434, 1016, 821, 747 cm^{-1}; m.p. 159.9–160.6 °C; elemental analysis calcd (%) for $C_{24}H_{20}O_2Cl_2Fe$: C 61.70, H 4.32; found: C 61.71, H 4.09. HPLC: Daicel Chiralpak AD-H (5% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 12.2 min (minor), 13.1 min (major), 15.5 min (*meso*); $[\alpha]_D^{23} = -47.3°$ ($c = 1.61$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxy-*o*-bromophenylmethyl)ferrocene (17h)**: ^{1}H NMR ($CDCl_3$): $\delta = 3.94-3.99$ (m, 2H), 4.14–4.19 (m, 2H), 4.26–4.30 (m, 2H), 4.39–4.45 (m, 4H), 6.00 (s, 2H), 7.03–7.10 (m, 2H), 7.21–7.28 (m, 2H), 7.44–7.49 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 67.0$, 67.2, 68.0, 68.4, 71.2, 92.8, 122.3, 127.7, 128.1, 128.9, 132.5, 143.0; IR (KBr): $\tilde{\nu} = 3284$, 1467, 1434, 1015, 745 cm^{-1}; m.p. 150.4–151.3 °C; elemental analysis calcd (%) for $C_{24}H_{20}O_2Br_2Fe$: C 51.84, H 3.63; found: C 51.58, H 3.61. HPLC: Daicel Chiralpak AD-H (10% propan-2-ol in hexane, flow 0.5 mL min^{-1}), 13.2 min (minor), 15.5 min (major), 17.9 min (*meso*); $[\alpha]_D^{23} = -10.6°$ ($c = 0.72$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxypropyl)ferrocene (17i)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.90$ (t, 6H, $J = 7.3$ Hz), 1.52–1.72 (m, 4H), 3.65 (br, 2H), 4.10–4.18 (m, 6H), 4.20–4.24 (m, 2H), 4.40 (t, 2H, $J = 6.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 9.9$, 32.7, 66.2, 66.6, 67.48, 67.51, 71.4, 93.7; IR (neat): $\tilde{\nu} = 3340$, 2965, 1463, 1036, 810, 489 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{22}O_2Fe$: C 63.59, H 7.34; found: C 63.83, H 7.31. HPLC: Daicel Chiralpak AD-H (10% Ethanol in hexane, flow 1.0 mL min^{-1}), 7.2 min (minor), 14.9 min (*meso*), 25.3 min (major); $[\alpha]_D^{23} = +49.9°$ ($c = 1.33$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxybutyl)ferrocene (17j)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.89$ (t, 6H, $J = 7.3$ Hz), 1.24–1.72 (m, 8H), 3.26 (br, 2H), 4.11–4.19 (m, 6H), 4.20–4.24 (m, 2H), 4.44 (dd, 2H, $J = 5.4$, 7.3 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.0$, 18.9, 42.1, 66.1, 66.5, 67.51, 67.55, 69.9, 94.2; IR (neat): $\tilde{\nu} = 3339$, 2957, 1465, 1020, 810, 488 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{26}O_2Fe$: C 65.47, H 7.94; found: C 65.43, H 7.88. HPLC: Daicel Chiralpak AD-H (10% Ethanol in hexane, flow 1.0 mL min^{-1}), 6.6 min (minor), 13.5 min (*meso*), 21.4 min (major); $[\alpha]_D^{23} = +33.9°$ ($c = 1.29$ in $CHCl_3$).

***dl*-1,1′-Bis(α-hydroxyhexyl)ferrocene (17k)**:[37c] HPLC: Daicel Chiralpak AD-H (2% Ethanol in hexane, flow 1.0 mL min^{-1}), 13.8 min (minor), 28.2 min (major), 33.8 min (*meso*).

***dl*-1,1′-Bis(α-hydroxyoctyl)ferrocene (17l)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.87$ (t, 6H, $J = 6.8$ Hz), 1.08–1.46 (m, 20H), 1.48–1.70 (m, 4H), 3.27 (br, 2H), 4.10–4.17 (m, 6H), 4.19–4.22 (m, 2H), 4.43 (dd, 2H, $J = 5.6$, 7.1 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.1$, 22.7, 25.7, 29.3, 29.6, 31.9, 40.0, 66.1, 66.6, 67.50, 67.54, 71.1, 94.2; IR (neat): $\tilde{\nu} = 3339$, 2926, 1465, 1044, 809, 488 cm^{-1}; elemental analysis calcd (%) for $C_{26}H_{42}O_2Fe$: C 70.58, H 9.57; found: C 70.48, H 9.28. HPLC: Daicel Chiralpak AD-H (2% Ethanol in hexane, flow 1.0 mL min^{-1}), 11.0 min (minor), 18.1 min (major), 21.6 min (*meso*); $[\alpha]_D^{23} = +16.4°$ ($c = 1.55$ in $CHCl_3$).

Preparation of 1,3-diaryl-2-alkyl-1,3-propanediones: The 1,3-dialkyl-1,3-propanediones were prepared by conventional Claisen condensation of the corresponding ArCOMe and $ArCO_2Et$, and then their sodium enolates were treated with the corresponding alkyl halide (RX) to obtain the 1,3-diaryl-2-alkyl-1,3-propanediones.

1,3-Diphenyl-2-methyl-1,3-propanedione (18a):[71] ^{1}H NMR ($CDCl_3$): $\delta = 1.61$ (d, 3H, $J = 6.9$ Hz), 5.27 (q, 1H, $J = 6.9$ Hz), 7.41–7.50 (m, 4H), 7.53–7.60 (m, 2H), 7.90–8.01 (m, 4H).

1,3-Di(*p*-methylphenyl)-2-methyl-1,3-propanedione (18b): ^{1}H NMR ($CDCl_3$): $\delta = 1.58$ (d, 3H, $J = 6.9$ Hz), 2.39 (s, 6H), 5.21 (q, 1H, $J = 6.9$ Hz), 7.24 (d, 4H, $J = 8.3$ Hz), 7.86 (d, 4H, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.5$, 21.7, 50.9, 128.5, 129.4, 133.0, 144.2, 196.6; IR (KBr): $\tilde{\nu} = 2992$, 2944, 1684, 1664, 1605, 1336, 1294, 1238, 1179, 966, 824, 565 cm^{-1}; m.p. 132.8–133.7 °C; elemental analysis calcd (%) for $C_{18}H_{18}O_2$: C 81.17, H 6.81; found: C 81.25, H 6.59.

1,3-Di(2-naphthyl)-2-methyl-1,3-propanedione (18c): ^{1}H NMR ($CDCl_3$): $\delta = 1.75$ (d, 3H, $J = 7.0$ Hz), 5.57 (q, 1H, $J = 7.0$ Hz), 7.51–7.57 (m, 2H), 7.58–7.64 (m, 2H), 7.84–7.93 (m, 6H), 8.02–8.07 (m, 2H), 8.54 (s, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 14.8$, 51.4, 124.0, 126.8, 127.6, 128.6, 128.7, 129.6, 130.2, 132.4, 132.9, 135.6, 197.0; IR (KBr): $\tilde{\nu} = 3058$, 2985, 2937, 1687, 1675, 1623, 1361, 1315, 1280, 1171, 801, 760 cm^{-1}; m.p. 132.3–132.9 °C; HRMS: m/z: calcd for $C_{24}H_{18}O_2$: 338.1307; found: 338.1329 [M^+].

1,3-Di(*p*-methoxyphenyl)-2-methyl-1,3-propanedione (18d): ^{1}H NMR ($CDCl_3$): $\delta = 1.58$ (d, 3H, $J = 6.9$ Hz), 3.85 (s, 6H), 5.13 (q, 1H, $J = 6.9$ Hz), 6.92 (d, 4H, $J = 9.3$ Hz), 7.95 (d, 4H, $J = 9.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.6$, 51.1, 55.5, 113.9, 128.6, 130.7, 163.5, 195.6; IR (KBr): $\tilde{\nu} = 2973$, 2940, 2917, 1674, 1658, 1598, 1570, 1511, 1338, 1263, 1169, 1021, 973, 855, 565 cm^{-1}; m.p. 78.4–79.4 °C; elemental analysis calcd (%) for $C_{18}H_{18}O_4$: C 72.47, H 6.08; found: C 72.41, H 5.85.

1,3-Di(*p*-bromophenyl)-2-methyl-1,3-propanedione (18e): ^{1}H NMR ($CDCl_3$): $\delta = 1.59$ (d, 3H, $J = 7.1$ Hz), 5.12 (q, 1H, $J = 7.1$ Hz), 7.60 (d, 4H, $J = 8.5$ Hz), 7.79 (d, 4H, $J = 8.5$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.4$, 51.4, 128.9, 129.9, 132.2, 134.1, 195.7; IR (KBr): $\tilde{\nu} = 2986$, 2935, 1697, 1671, 1583, 1281, 1195, 1068, 970, 797, 590 cm^{-1}; m.p. 112.9–113.8 °C; elemental analysis calcd (%) for $C_{16}H_{12}Br_2O_2$: C 48.52, H 3.05; found: C 48.24, H 2.77.

1,3-Diphenyl-2-ethyl-1,3-propanedione (18f): ^{1}H NMR ($CDCl_3$): $\delta = 1.06$ (t, 3H, $J = 7.3$ Hz), 2.13–2.23 (m, 2H), 5.12 (t, 1H, $J = 6.4$ Hz), 7.41–7.49 (m, 4H), 7.53–7.60 (m, 2H), 7.93–8.01 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 13.0$, 23.0, 58.7, 128.4, 128.7, 133.3, 136.0, 195.9; IR (KBr): $\tilde{\nu} = 2972$, 2941, 1686, 1665, 1595, 1578, 1448, 1355, 1281, 1226, 1201, 991, 701, 692 cm^{-1}; m.p. 88.1–88.6 °C; elemental analysis calcd (%) for $C_{17}H_{16}O_2$: C 80.93, H 6.39; found: C 80.88, H 6.17.

2-Allyl-1,3-diphenyl-1,3-propanedione (18g): ^{1}H NMR ($CDCl_3$): $\delta = 2.88$ (t, 2H, $J = 6.8$ Hz), 5.04 (dd, 1H, $J = 1.5$, 10.3 Hz), 5.11 (dd, 1H, $J = 1.5$, 17.1 Hz), 5.30 (t, 1H, $J = 6.8$ Hz), 5.81–5.94 (m, 1H), 7.42–7.50 (m, 4H), 7.55–7.60 (m, 2H), 7.92–7.99 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 33.6$, 56.8, 117.2, 128.5, 128.8, 133.4, 135.0, 135.8, 195.3; IR (KBr): $\tilde{\nu} = 3060$, 2916, 1695, 1671, 1594, 1447, 1333, 1208, 908, 761, 685 cm^{-1}; m.p. 65.9–66.6 °C; elemental analysis calcd (%) for $C_{18}H_{16}O_2$: C 81.79, H 6.10; found: C 82.01, H 6.01.

2-Benzyl-1,3-diphenyl-1,3-propanedione (18h): ^{1}H NMR ($CDCl_3$): $\delta = 3.45$ (d, 2H, $J = 6.5$ Hz), 5.52 (t, 1H, $J = 6.5$ Hz), 7.13–7.26 (m, 5H), 7.36–7.45 (m, 4H), 7.50–7.56 (m, 2H), 7.85–7.92 (m, 4H); ^{13}C NMR (C_6D_6): $\delta = 35.6$, 59.6, 126.7, 128.7, 128.80, 128.82, 129.4, 133.1, 136.6, 139.7, 194.9; IR (KBr): $\tilde{\nu} = 3037$, 2905, 1695, 1664, 1594, 1446, 1350, 1214, 948, 760, 711, 696 cm^{-1}; m.p. 106.4–107.4 °C; elemental analysis calcd (%) for $C_{22}H_{18}O_2$: C 84.05, H 5.77; found: C 84.24, H 5.82.

1,3-Diphenyl-2-isopropyl-1,3-propanedione (18i): ^{1}H NMR ($CDCl_3$): $\delta = 1.02$ (d, 6H, $J = 6.4$ Hz), 2.85–2.98 (m, 1H), 5.05 (d, 1H, $J = 9.3$ Hz), 7.39–7.49 (m, 4H), 7.51–7.59 (m, 2H), 7.96–8.05 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 21.4$, 30.4, 64.9, 128.55, 128.64, 133.2, 136.9, 195.4; IR (KBr): $\tilde{\nu} = 2965$, 2935, 2876, 1696, 1657, 1448, 1292, 1224, 1204, 998, 705, 685 cm^{-1}; m.p. 82.1–83.0 °C; elemental analysis calcd (%) for $C_{18}H_{18}O_2$: C 81.17, H 6.81; found: C 81.10, H 6.63.

Typical procedure for the reductive desymmetrization of 1,3-diaryl-2-alkyl-1,3-propanedione: Under a dry nitrogen atmosphere in a precooled vessel at −20 °C were placed the (*R*,*R*)-**3b** catalyst (7.2 mg, 0.0125 mmol), 1,3-diphenyl-2-methyl-1,3-propanedione (59.4 mg, 0.25 mmol), and $CHCl_3$ (12 mL). To this solution was added the solution of premodified $NaBH_4$ (2.0 mL), and stirred for 10 h at −20 °C. The reaction was quenched by precooled aqueous THF solution at −20 °C and pH 7 buffer solution and the crude products were extracted with AcOEt. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to give 1,3-diphenyl-3-hydroxy-2-methyl-1-propanone (55.5 mg, 93%). The *anti*-selectivity was determined by ^{1}H NMR analysis to be 99%. The enantiomeic excess was determined by HPLC analysis to be 99% *ee*.

***anti*-1,3-Diphenyl-3-hydroxy-2-methyl-1-propanone (19a)**:[72, 73] ^{1}H NMR ($CDCl_3$): $\delta = 1.05$ (d, 3H, $J = 7.6$ Hz), 3.05 (br, 1H), 3.83 (quin, 1H, $J = 7.6$ Hz), 4.98 (d, 1H, $J = 7.6$ Hz), 7.24–7.49 (m, 7H), 7.52–7.59 (m, 1H), 7.93–7.99 (m, 2H); HPLC: Daicel Chiralpak AD (5% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 23.6 min (major), 26.4 min (minor); $[\alpha]_D^{24} = +111.4°$ ($c = 0.489$ in $CHCl_3$).

***anti*-1,3-Di(*p*-methylphenyl)-3-hydroxy-2-methyl-1-propanone (19b)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.05$ (d, 3H, $J = 7.4$ Hz), 2.34 (s, 3H), 2.41 (s, 3H), 2.94 (d, 1H, $J = 4.6$ Hz), 3.79 (quin, 1H, $J = 7.4$ Hz), 4.95 (dd, 1H, $J = 4.6$, 7.4 Hz), 7.17 (d, 2H, $J = 7.9$ Hz), 7.27 (d, 2H, $J = 7.9$ Hz), 7.30 (d, 2H, $J = 7.9$ Hz), 7.88 (d, 2H, $J = 7.9$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 15.9$, 21.2, 21.7, 47.8, 76.6, 126.5, 128.5, 129.0, 129.2, 134.1, 137.4, 139.1, 144.0, 204.3; IR (KBr): $\tilde{\nu} = 3385$, 2980, 2950, 1663, 1605, 1453, 1186, 999, 966, 818 cm^{-1}; m.p. 95.0–95.6 °C; elemental analysis calcd (%) for $C_{18}H_{20}O_2$: C 80.56, H 7.51; found: C 80.57, H 7.62. HPLC: Daicel Chiralpak AD-H (15% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 13.7 min (minor), 15.5 min (major); $[\alpha]_D^{24} = +126.1°$ ($c = 1.077$ in $CHCl_3$).

***anti*-1,3-Di(2-naphthyl)-3-hydroxy-2-methyl-1-propanone (19c)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.17$ (d, 3H, $J = 7.6$ Hz), 3.12 (d, 1H, $J = 4.4$ Hz), 4.11 (quin, 1H, $J = 7.6$ Hz), 5.24 (dd, 1H, $J = 4.4$, 7.6 Hz), 7.45–7.66 (m, 5H), 7.81–7.93 (m, 6H), 7.95–7.99 (m, 1H), 8.03–8.08 (m, 1H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 16.2$, 48.0, 77.1, 124.0, 124.3, 125.88, 125.92, 126.1, 126.7, 127.59, 127.65, 127.9, 128.3, 128.49, 128.53, 129.6, 130.2, 132.4, 133.05, 133.08, 133.9,

135.6, 139.4, 204.5; IR (KBr): $\tilde{\nu}$ = 3446, 3052, 2980, 1664, 1188, 823, 748, 477 cm^{-1}; m.p. 120.7–121.6 °C; HRMS: *m*/*z*: calcd for $C_{24}H_{20}O_2$: 340.1463; found: 340.1456 [M^+]. HPLC: Daicel Chiralpak AD (25% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 20.2 min (minor), 22.4 min (major); $[\alpha]_D^{24}$ = +96.2° (*c* = 1.083 in $CHCl_3$).

***anti*-1,3-Di(*p*-bromophenyl)-3-hydroxy-2-methyl-1-propanone (19d)**: ^{1}H NMR ($CDCl_3$): δ = 1.05 (d, 3H, *J* = 7.5 Hz), 2.92 (d, 1H, *J* = 4.4 Hz), 3.70 (quin, 1H, *J* = 7.5 Hz), 4.95 (dd, 1H, *J* = 4.4, 7.5 Hz), 7.29 (d, 2H, *J* = 8.7 Hz), 7.50 (d, 2H, *J* = 8.7 Hz), 7.62 (d, 2H, *J* = 8.7 Hz), 7.83 (d, 2H, *J* = 8.7 Hz); ^{13}C NMR ($CDCl_3$): δ = 15.6, 47.9, 76.1, 121.8, 128.3, 128.6, 129.8, 131.5, 131.9, 135.1, 140.9, 203.3; IR (KBr): $\tilde{\nu}$ = 3494, 2978, 1661, 1581, 1396, 1244, 1069, 1009, 964, 822, 742 cm^{-1}; m.p. 114.2–114.9 °C; HRMS: *m*/*z*: calcd for $C_{16}H_{14}Br_2O_2$: 395.9362; found: 395.9390 [M^+]. HPLC: Daicel Chiralpak AD-H (10% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 22.5 min (minor), 24.9 min (major); $[\alpha]_D^{24}$ = +97.8° (*c* = 1.038 in $CHCl_3$).

***anti*-1,3-Di(*p*-methoxyphenyl)-3-hydroxy-2-methyl-1-propanone (19e)**: ^{1}H NMR ($CDCl_3$): δ = 1.06 (d, 3H, *J* = 7.5 Hz), 2.98 (d, 1H, *J* = 4.4 Hz), 3.75 (quin, 1H, *J* = 7.5 Hz), 3.81 (s, 3H), 3.88 (s, 3H), 4.94 (dd, 1H, *J* = 4.4, 7.5 Hz), 6.89 (d, 2H, *J* = 8.9 Hz), 6.94 (d, 2H, *J* = 8.9 Hz), 7.34 (d, 2H, *J* = 8.9 Hz), 7.97 (d, 2H, *J* = 8.9 Hz); ^{13}C NMR ($CDCl_3$): δ = 16.0, 47.6, 55.3, 55.5, 76.4, 113.71, 113.73, 127.7, 129.6, 130.7, 134.4, 159.0, 163.5, 203.2; IR (KBr): $\tilde{\nu}$ = 3366, 2977, 2934, 1664, 1599, 1516, 1252, 1174, 1032, 973, 825, 576 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{20}O_4$: C 71.98, H 6.71; found: C 71.86, H 6.72; m.p. 80.8–81.7 °C. HPLC: Daicel Chiralcel OD-H (10% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 21.3 min (major), 26.4 min (minor); $[\alpha]_D^{24}$ = +124.8° (*c* = 1.079 in $CHCl_3$).

***anti*-1,3-Diphenyl-2-ethyl-3-hydrodxy-1-propanone (19f)**:[72, 73] ^{1}H NMR ($CDCl_3$): δ = 0.82 (t, 3H, *J* = 7.3 Hz), 1.48–1.61 (m, 1H), 1.66–1.80 (m, 1H), 3.07 (d, 1H, *J* = 6.4 Hz), 3.78 (q, 1H, *J* = 6.4 Hz), 5.03 (t, 1H, *J* = 6.4 Hz), 7.22–7.49 (m, 7H), 7.51–7.58 (m, 1H), 7.88–7.95 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 11.8, 23.8, 54.3, 75.7, 126.3, 127.7, 128.2, 128.4, 128.5, 133.1, 138.1, 142.6, 205.4; IR (KBr): $\tilde{\nu}$ = 3411, 3061, 2958, 2877, 1671, 1447, 1269, 1207, 1001, 768, 703 cm^{-1}; m.p. 63.0–63.8 °C; elemental analysis calcd (%) for $C_{17}H_{18}O_2$: C 80.28, H 7.13; found: C 80.24, H 7.28. HPLC: Daicel Chiralpak AD (1.5% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 59.1 min (major), 67.5 min (minor); $[\alpha]_D^{24}$ = +90.7° (*c* = 1.046 in $CHCl_3$).

***anti*-2-Allyl-1,3-diphenyl-3-hydrodxy-1-propanone (19g)**: ^{1}H NMR ($CDCl_3$): δ = 2.24–2.35 (m, 1H), 2.37–2.50 (m, 1H), 3.17 (d, 1H, *J* = 5.4 Hz), 3.90 (q, 1H, *J* = 6.8 Hz), 4.88–5.06 (m, 3H), 5.55–5.69 (m, 1H), 7.23–7.47 (m, 7H), 7.51–7.58 (m, 1H), 7.85–7.91 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 34.8, 52.6, 75.5, 117.5, 126.3, 127.8, 128.2, 128.4, 128.5, 133.1, 134.2, 137.7, 142.2, 204.5; IR (KBr): $\tilde{\nu}$ = 3374, 3073, 1671, 1448, 1241, 1209, 1012, 916, 767, 704, 607 cm^{-1}; m.p. 79.3–80.2 °C; elemental analysis calcd (%) for $C_{18}H_{18}O_2$: C 81.17, H 6.81; found: C 81.07, H 6.78. HPLC: Daicel Chiralcel OD-H (3% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 17.7 min (minor), 19.1 min (major); $[\alpha]_D^{24}$ = +74.7° (*c* = 1.053 in $CHCl_3$).

***anti*-2-Benzyl-1,3-diphenyl-3-hydrodxy-1-propanone (19h)**:[73] ^{1}H NMR ($CDCl_3$): δ = 2.91 (dd, 1H, *J* = 7.0, 13.3 Hz), 3.05 (dd, 1H, *J* = 7.0, 13.3 Hz), 3.45 (d, 1H, *J* = 7.0 Hz), 4.09 (q, 1H, *J* = 7.0 Hz), 4.97 (t, 1H, *J* = 7.0 Hz), 7.07–7.37 (m, 12H), 7.42–7.48 (m, 1H), 7.63–7.68 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 36.7, 54.7, 75.4, 126.0, 126.3, 127.6, 128.0, 128.2, 128.3, 128.4, 128.9, 133.0, 137.8, 138.4, 142.5, 205.3; IR (KBr): $\tilde{\nu}$ = 3434, 3062, 3035, 1674, 1456, 1206, 1047, 1010, 751, 703 cm^{-1}; m.p. 115.6–116.5 °C; HRMS: *m*/*z*: calcd for $C_{22}H_{20}O_2$: 316.1463; found: 316.1481 [M^+]. HPLC: Daicel Chiralcel OD-H (5% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 15.4 min (major), 17.3 min (minor); $[\alpha]_D^{24}$ = −8.7° (*c* = 1.024 in $CHCl_3$).

***anti*-1,3-Diphenyl-3-hydrodxy-2-isopropyl-1-propanone (19i)**: ^{1}H NMR ($CDCl_3$): δ = 0.87 (d, 3H, *J* = 6.8 Hz), 1.15 (d, 3H, *J* = 6.8 Hz), 2.24–2.35 (m, 1H), 3.59 (dd, 1H, *J* = 4.4, 8.3 Hz), 4.04 (d, 1H, *J* = 8.1 Hz), 5.17 (dd, 1H, *J* = 4.4, 8.1 Hz), 7.08–7.14 (m, 1H), 7.18–7.35 (m, 6H), 7.42–7.48 (m, 1H), 7.60–7.66 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 21.1, 21.3, 29.6, 58.7, 73.5, 125.5, 127.1, 127.9, 128.2, 128.3, 133.0, 138.6, 143.0, 207.1; IR (KBr): $\tilde{\nu}$ = 3435, 2952, 1666, 1447, 1271, 1207, 1010, 768, 700, 570 cm^{-1}; m.p. 84.0–85.2 °C; HRMS: *m*/*z*: calcd for $C_{18}H_{20}O_2$: 268.1463; found: 268.1502 [M^+]. HPLC: Daicel Chiralpak AD-H (15% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 8.3 min (minor), 11.2 min (major); $[\alpha]_D^{24}$ = +40.1° (*c* = 0.261 in $CHCl_3$).

Chemoselective reduction of 2-undecanone and 2-acetonaphthone in the presence of *β*-ketoiminato cobalt complex catalyst (Scheme 6): To the $CHCl_3$ solution (20 mL) of 2-undecanone **20a** (85.2 mg, 0.5 mmol), 2-acetonaphthone **20b** (85.1 mg, 0.5 mmol), and catalyst **22** (18.6 mg, 0.05 mmol) was added the solution of the premodified borohydride (3.2 mL, 0.4 mmol) under a dry nitrogen atmosphere at −20 °C. After stirring for 12 h at −20 °C, the reaction was quenched by a precooled aqueous THF solution at −20 °C and pH 7 buffer solution; then the crude products were extracted with AcOEt. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to give undecan-2-ol **21a** (4.0 mg, 5%) and 1-(2-naphthyl)-1-ethanol **21b** (38.3 mg, 45%).

Preparation of 1,2-dialkyl-3-aryl-1,3-diketones: The 1-alkyl-3-aryl-1,3-diketones ($RC(O)CH_2C(O)Ar$) were prepared by conventional Claisen condensation of the corresponding RCOMe and $ArCO_2Et$, and then their sodium enolates were treated with the corresponding R′X to obtain the 1,2-dialkyl-3-aryl-1,3-propanediones ($RC(O)CH(R')C(O)Ar$).

2,4-Dimethyl-1-phenyl-1,3-pentanedione (23a):[74] ^{1}H NMR ($CDCl_3$): δ = 1.03 (d, 3H, *J* = 6.9 Hz), 1.10 (d, 3H, *J* = 6.9 Hz), 1.45 (d, 3H, *J* = 7.0 Hz), 2.77 (sept, 1H, *J* = 6.9 Hz), 4.64 (q, 1H, *J* = 7.0 Hz), 7.46–7.53 (m, 2H), 7.56–7.64 (m, 1H), 7.93–8.00 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.8, 18.6, 19.2, 39.5, 54.4, 128.5, 128.8, 133.5, 135.9, 197.5, 210.8; HRMS: *m*/*z*: calcd for $C_{13}H_{16}O_2$: 204.1150; found: 204.1131 [M^+].

2-Ethyl-4-methyl-1-phenyl-1,3-pentanedione (23b):[75] ^{1}H NMR ($CDCl_3$): δ = 0.95 (t, 3H, *J* = 7.3 Hz), 0.99 (d, 3H, *J* = 6.8 Hz), 1.06 (d, 3H, *J* = 6.8 Hz), 2.02 (double quint, 2H, *J* = 7.3, 14.6 Hz), 2.75 (sept, 1H, *J* = 6.8 Hz), 4.49 (t, 1H, *J* = 7.3 Hz), 7.46–7.53 (m, 2H), 7.57–7.63 (m, 1H), 7.94–8.01 (m, 2H); IR (neat): $\tilde{\nu}$ = 2971, 1721 ($\nu_{C=O}$), 1674 ($\nu_{C=O}$), 1448, 1273, 1209, 694 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{14}H_{18}O_2$: 218.1307; found: 218.1281 [M^+].

2-Allyl-4-methyl-1-phenyl-1,3-pentanedione (23c): ^{1}H NMR ($CDCl_3$): δ = 1.01 (d, 3H, *J* = 6.8 Hz), 1.06 (d, 3H, *J* = 6.8 Hz), 2.64–2.81 (m, 3H), 4.68 (t, 1H, *J* = 7.1 Hz), 5.02 (d, 1H, *J* = 10.3 Hz), 5.08 (d, 1H, *J* = 17.1 Hz), 5.69–5.82 (m, 1H), 7.46–7.54 (m, 2H), 7.58–7.64 (m, 1H), 7.95–8.01 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 18.4, 19.0, 33.1, 39.8, 60.4, 117.2, 128.5, 128.8, 133.6, 134.7, 136.4, 195.8, 208.9; IR (neat): $\tilde{\nu}$ = 2974, 1722 ($\nu_{C=O}$), 1675 ($\nu_{C=O}$), 1448, 1000, 919, 693 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{15}H_{18}O_2$: 230.1307; found: 230.1300 [M^+].

2,4,4-Trimethyl-1-phenyl-1,3-pentanedione (23d): ^{1}H NMR ($CDCl_3$): δ = 1.14 (s, 9H), 1.42 (d, 3H, *J* = 7.1 Hz), 4.93 (q, 1H, *J* = 7.1 Hz), 7.47–7.54 (m, 2H), 7.57–7.64 (m, 1H), 7.94 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 15.4, 26.8, 44.7, 49.3, 128.4, 128.8, 133.4, 135.4, 197.2, 211.1; IR (KBr): $\tilde{\nu}$ = 2970, 1716 ($\nu_{C=O}$), 1663 ($\nu_{C=O}$), 1451, 1345, 1217, 972, 694cm^{-1}; m.p. 93.5–94.2 °C; HRMS: *m*/*z*: calcd for $C_{14}H_{18}O_2$: 218.1307; found: 218.1321 [M^+].

2-Methyl-1-phenyl-1,3-dodecanedione (23e):[76] ^{1}H NMR ($CDCl_3$): δ = 0.87 (t, 3H, *J* = 7.1 Hz), 1.12–1.33 (m, 12H), 1.45 (d, 3H, *J* = 7.1 Hz), 1.47–1.57 (m, 2H), 2.38 (dt, 1H, *J* = 7.3, 17.6 Hz), 2.51 (dt, 1H, *J* = 7.3, 17.6 Hz), 4.49 (q, 1H, *J* = 7.1 Hz), 7.46–7.52 (m, 2H), 7.57–7.62 (m, 1H), 7.95–8.00 (m, 2H).

2,5-Dimethyl-1-phenyl-1,3-hexanedione (23f): ^{1}H NMR ($CDCl_3$): δ = 0.80 (d, 3H, *J* = 6.8 Hz), 0.86 (d, 3H, *J* = 6.8 Hz), 1.44 (d, 3H, *J* = 7.0 Hz), 2.13 (nonet, 1H, *J* = 6.8 Hz), 2.27 (dd, 1H, *J* = 6.8, 17.1 Hz), 2.39 (dd, 1H, *J* = 6.8, 17.1 Hz), 4.47 (q, 1H, *J* = 7.0 Hz), 7.45–7.53 (m, 2H), 7.56–7.63 (m, 1H), 7.93–8.00 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.6, 22.4, 24.0, 49.4, 56.8, 128.6, 128.8, 133.5, 136.0, 197.1, 206.5; IR (neat): $\tilde{\nu}$ = 2958, 1717 ($\nu_{C=O}$), 1677 ($\nu_{C=O}$), 1449, 1226, 969, 689 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{14}H_{18}O_2$: 218.1307; found: 218.1307 [M^+].

2-Methyl-1,4-diphenyl-1,3-butanedione (23g): ^{1}H NMR ($CDCl_3$): δ = 1.44 (d, 3H, *J* = 7.1 Hz), 3.71 (d, 1H, *J* = 15.9 Hz), 3.82 (d, 1H, *J* = 15.9 Hz), 4.57 (q, 1H, *J* = 7.1 Hz), 7.09–7.16 (m, 2H), 7.18–7.31 (m, 3H), 7.39–7.46 (m, 2H), 7.53–7.60 (m, 1H), 7.77–7.85 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.8, 48.2, 54.6, 127.1, 128.4, 128.6, 128.7, 129.6, 133.4, 133.5, 135.7, 197.4, 204.4; IR (neat): $\tilde{\nu}$ = 1718 ($\nu_{C=O}$), 1675 ($\nu_{C=O}$), 1449, 1330, 1215, 970, 702 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{17}H_{16}O_2$: 252.1150; found: 252.1113 [M^+].

Chemo-, diastereo-, and enantioselective reduction of 2,4-dimethyl-1-phenyl-1,3-pentanedione (Scheme 7): Under a dry nitrogen atmosphere in a precooled vessel at −20 °C were placed the (*R*,*R*)-catalyst **3b** (7.2 mg, 0.0125 mmol), 2,4-dimethyl-1-phenyl-1,3-pentanedione (51.0 mg, 0.25 mmol), and $CHCl_3$ (12.0 mL). The five portions of the 0.1 equiv of the premodified borohydride (0.2 mL, 0.025 mmol) were successively added at 1 h intervals to the reaction mixture, and stirred for 24 h at −20 °C. The reaction was quenched by a precooled aqueous THF solution

at −20 °C and pH 7 buffer solution; then the crude products were extracted with AcOEt. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to give the corresponding 2-substituted-3-hydroxyketone (22.2 mg,43 %). The chemo-selectivity and diastereoselectivity were determined by ^{1}H NMR analysis to be 97 % aryl/alcohol selectivity and 99 % *anti*-selectivity. The enantiomeric excess of the *anti*-form was determined by HPLC analysis to be 94 %.

Analysis of the *ee* values of the remaining 2,4-dimethyl-1-phenyl-1,3-pentanedione after kinetic resolution: The above-mentioned reaction mixture, before the reaction was quenched by a precooled aqueous THF solution, was directly injected into HPLC chiral column (Daicel Chiralpak AD, 5 % propan-2-ol in hexane, 1 mL min^{-1}) to determine the *ee* of 2,4-dimethyl-1-phenyl-1,3-pentanedione to be 99 % *ee* (7.1 min (minor), 7.6 min (major)). Since racemization of 2-substituted-1,3-diketones gradually proceeded at room temperature, the substrate isolated by silica gel column chromatography was of low *ee*.

Optimized procedure of highly chemo-, diastereo-, and enantioselective reduction, example for the reaction of 2,4,4-trimethyl-1-phenyl-1,3-pentanedione: Under a dry nitrogen atmosphere in a precooled vessel at −20 °C were placed the (*R*,*R*)-catalyst **3b** (7.2 mg, 0.0125 mmol), 2,4,4-trimethyl-1-phenyl-1,3-pentanedione **23d** (54.7 mg, 0.25 mmol), and $CHCl_3$ (12.0 mL). The four portions of the 0.1 equiv of the premodified borohydride (0.2 mL, 0.025 mmol) were successively added at 2 h intervals to the reaction mixture, and stirred for 12 h at −20 °C. The reaction was quenched by a precooled aqueous THF solution at −20 °C and pH 7 buffer solution; then the crude products were extracted with AcOEt. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to give the corresponding 2-substituted-3-hydroxyketone **24d** in (26.6 mg, 48 %). The chemo- and diastereoselectivity were determined by ^{1}H NMR analysis to be 99 % aryl/alcohol selectivity and 99 % *anti*-selectivity. The enantiomeric excess of the *anti*-form was determined by HPLC analysis to be 97 %.

***anti*-1-Hydroxy-2,4-dimethyl-1-phenyl-3-pentanone (24a)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.97$ (d, 3H, $J = 7.3$, 3.4 Hz), 0.98 (d, 3H, $J = 6.9$ Hz), 1.07 (d, 3H, $J = 6.9$ Hz), 2.64 (sept, 1H, $J = 6.9$ Hz), 3.07 (quin, 1H, $J = 7.3$ Hz), 4.75 (dd, 1H, $J = 3.4$, 7.3 Hz), 7.25–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta =$ 15.0, 17.70, 17.73, 41.3, 51.0, 76.7, 126.3, 127.7, 128.3, 142.3, 219.2; IR (neat): $\tilde{\nu} = 3456$, 2972, 2933, 1707 ($\nu_{C=O}$), 1456, 1375, 1009, 756, 702 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{13}H_{18}O_2$: 206.1307; found: 206.1309 [M^+]. HPLC: Daicel Chiralcel OD-H, 3.0 % propan-2-ol in hexane, 1 mL min^{-1}, 9.0 min (minor), 12.7 min (major), Daicel chiralpak AD-H, 2 % propan-2-ol, 1 mL min^{-1}, 17.2 min (major), 20.0 min (minor); $[\alpha]_D^{29} = +97.1°$ ($c = 1.04$ in $CHCl_3$).

***anti*-2-Ethyl-1-Hydroxy-4-methyl-1-phenyl-3-pentanone (24b)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.85$ (d, 3H, $J = 6.8$ Hz), 0.89 (d, 3H, $J = 7.6$ Hz), 1.01 (d, 3H, $J = 6.8$ Hz), 1.44–1.55 (m, 1H), 1.57–1.68 (m, 1H), 2.46 (sept, 1H, $J =$ 6.8 Hz), 2.98 (dt, 1H, $J = 6.1$, 7.6 Hz), 3.22 (d, 1H, $J = 6.1$ Hz), 4.82 (t, 1H, $J = 6.1$ Hz), 7.24–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 12.0$, 17.2, 17.3, 23.1, 42.4, 58.1, 75.2, 126.0, 127.6, 128.3, 142.9, 219.7; IR (neat): $\tilde{\nu} = 3464$, 2968, 1705 ($\nu_{C=O}$), 1456, 1031, 701 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{14}H_{20}O_2$: 220.1463; found: 220.1465 [M^+]. HPLC: Daicel Chiralcel OD-H, 2.0 % propan-2-ol in hexane, 1 mL min^{-1}, 18.1 min (major), 22.4 min (minor), Daicel chiralpak AD-H, 2 % propan-2-ol, 1 mL min^{-1}, 9.1 min (minor), 13.7 min (major); $[\alpha]_D^{27} = +86.2°$ ($c = 0.77$ in $CHCl_3$).

***anti*-2-Allyl-1-Hydroxy-4-methyl-1-phenyl-3-pentanone (24c)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.83$ (d, 3H, $J = 6.9$ Hz), 0.97 (d, 3H, $J = 6.9$ Hz), 2.18–2.35 (m, 2H), 2.42 (sept, 1H, $J = 6.9$ Hz), 3.11 (dt, 1H, $J = 6.3$, 8.3 Hz), 3.33 (d, 1H, $J = 6.3$ Hz), 4.81 (t, 1H, $J = 6.3$ Hz), 5.02 (d, 1H, $J = 9.5$ Hz), 5.03 (d, 1H, $J = 17.1$ Hz), 5.68 (ddt, 1H, $J = 7.3$, 9.5, 17.1 Hz), 7.25- 7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 17.0$, 17.2, 34.5, 42.5, 56.4, 75.1, 117.6, 126.0, 127.6, 128.3, 134.6, 142.6, 218.9; IR (neat): $\tilde{\nu} = 3465$, 2974, 2932, 1707 ($\nu_{C=O}$), 1445, 1042, 701 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{15}H_{20}O_2$: 232.1463; found: 232.1482 [M^+]. HPLC: Daicel Chiralcel OD-H, 1.0 % propan-2-ol in hexane, 1 mL min^{-1}, 18.1 min (minor), 28.0 min (major). Daicel chiralpak AD-H, 1 % propan-2-ol, 1 mL min^{-1}, 13.5 min (minor), 20.6 min (major); $[\alpha]_D^{25} =$ $+39.6°$ ($c = 1.26$ in $CHCl_3$).

***anti*-1-Hydroxy-2,4,4-trimethyl-1-phenyl-3-pentanone (24d)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.03$–1.04 (m, 12H), 3.17 (d, 1H, $J = 6.2$ Hz), 3.32 (quin, 1H, $J = 6.2$ Hz), 4.77 (t, 1H, $J = 6.2$ Hz), 7.25–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 16.7$, 26.0, 45.0, 46.7, 77.4, 126.3, 127.7, 128.3, 142.9, 220.9; IR (KBr): $\tilde{\nu} = 3506$, 2976, 1699 ($\nu_{C=O}$), 987, 700 cm^{-1}; m.p. 66.4–68.0 °C; HRMS: *m*/*z*: calcd for $C_{14}H_{20}O_2$: 220.1463; found: 220.1491 [M^+]. HPLC: Daicel Chiralcel OD-H, 3.0 % propan-2-ol in hexane, 1 mL min^{-1}, 6.8 min (minor), 15.8 min (major). Daicel chiralpak AD-H, 5 % propan-2-ol, 1 mL min^{-1}, 8.3 min (major), 9.5 min (minor); $[\alpha]_D^{26} = +99.4°$ ($c = 0.54$ in $CHCl_3$).

***anti*-1-Hydroxy-2-methyl-1-phenyl-3-dodecanone (24e)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.88$ (t, 3H, $J = 6.8$ Hz), 0.94 (d, 3H, $J = 7.5$ Hz), 1.20–1.32 (m, 12H), 1.50–1.57 (m, 2H), 2.41 (dt, 1H, $J = 7.2$, 17.3 Hz), 2.50 (dt, 1H, $J = 7.6$, 17.3 Hz), 2.92 (quin, 1H, $J = 7.5$ Hz), 2.94 (s, 1H), 4.75 (d, 1H, $J =$ 7.5 Hz), 7.27–7.37 (m, 5H); ^{13}C NMR ([D$_6$]DMSO): $\delta = 13.6$, 14.0, 22.1, 22.8, 28.6, 28.7, 28.9, 29.0, 31.3, 42.3, 52.8, 75.6, 126.7, 127.2, 127.9, 143.6, 213.0; IR (KBr): 3364, 3302, 2954, 2928, 2850, 1706 ($\nu_{C=O}$), 1467, 1009, 699 cm^{-1}; m.p. 41.6–43.8 °C; HRMS: *m*/*z*: calcd for $C_{19}H_{30}O_2$: 290.2246; found: 290.2948 [M^+]. HPLC: Daicel Chiralcel OD-H, 3.0 % propan-2-ol in hexane, 1 mL min^{-1}, 14.4 min (major), 16.0 min (minor). Daicel chiralpak AD-H, 1 % propan-2-ol, 1 mL min^{-1}, 15.7 min (minor), 19.7 min (major); $[\alpha]_D^{24} = +52.2°$ ($c = 0.86$ in $CHCl_3$).

***anti*-1-Hydroxy-2,5-dimethyl-1-phenyl-3-hexanone (24f)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.887$ (d, 1H, $J = 6.8$ Hz), 0.893 (d, 1H, $J = 6.3$ Hz), 0.93 (d, 1H, $J = 7.6$ Hz), 2.10–2.20 (m, 1H), 2.32 (dd, 1H, $J = 6.1$, 16.5 Hz), 2.38 (dd, 1H, $J = 7.3$, 16.5 Hz), 2.90 (quin, 1H, $J = 7.6$ Hz), 2.95 (d, 1H, $J =$ 3.1 Hz), 4.75 (dd, 1H, $J = 3.1$, 7.6 Hz), 7.27–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 14.3$, 22.5, 22.6, 24.0, 52.2, 53.1, 76.5, 126.5, 127.8, 128.4, 142.1, 215.1; IR (neat): $\tilde{\nu} = 3452$, 2958, 2933, 2871, 1707 ($\nu_{C=O}$), 1456, 1356, 702 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{14}H_{20}O_2$: 220.1463; found: 220.1449 [M^+]. HPLC: Daicel chiralpak AD-H, 5.0 % propan-2-ol, 1 mL min^{-1}, 9.1 min (major), 10.6 min (minor); $[\alpha]_D^{25} = +72.1°$ ($c = 0.64$ in $CHCl_3$).

***anti*-4-Hydroxy-3-methyl-1,4-diphenyl-2-pentanone (24g)**: ^{1}H NMR ($CDCl_3$): $\delta = 0.84$ (d, 3H, $J = 7.6$ Hz), 2.79 (br, 1H), 2.98 (quin, 1H, $J =$ 7.6 Hz), 3.68 (s, 2H), 4.66 (d, 1H, $J = 7.6$ Hz), 7.06 (d, 2H, $J = 7.3$ Hz), 7.16–7.28 (m, 8H); ^{13}C NMR ($CDCl_3$): $\delta = 14.6$, 50.6, 52.0, 76.8, 126.4, 126.9, 127.8, 128.4, 128.5, 129.5, 133.5, 142.0, 212.5; IR (neat): $\tilde{\nu} = 3448$, 3030, 1711 ($\nu_{C=O}$), 1454, 702 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{17}H_{18}O_2$: 254.1307; found: 254.1325 [M^+]. HPLC: Daicel chiralpak AD-H, 3.0 % propan-2-ol, 1 mL min^{-1}, 34.2 min (major), 39.0 min (minor); $[\alpha]_D^{28} = +101.8°$ ($c = 0.63$ in $CHCl_3$).

Preparation of the 2-alkyl-3-ketoesters: The 2-alkyl-3-ketoesters were prepared by the conventional Claisen condensation and alkylation, or by the reported methods.

2-Methyl-3-(2-naphthyl)-3-oxopropionic acid ethyl ester (25a):[77] ^{1}H NMR ($CDCl_3$): $\delta = 1.17$ (t, 3H, $J = 7.1$ Hz), 1.56 (d, 3H, $J = 7.0$ Hz), 4.09–4.21 (m, 2H), 4.55 (q, 1H, $J = 7.0$ Hz), 7.53–7.65 (m, 2H), 7.86–7.93 (m, 2H), 7.95–8.00 (m, 1H), 8.01–8.06 (m, 1H), 8.52 (s, 1H).

2-Methyl-3-phenyl-3-oxopropionic acid ethyl ester (25b):[71] ^{1}H NMR ($CDCl_3$): $\delta = 1.17$ (t, 3H, $J = 7.1$ Hz), 1.50 (d, 3H, $J = 7.1$ Hz), 4.15 (q, 2H, $J = 7.1$ Hz), 4.38 (q, 1H, $J = 7.1$ Hz), 7.45–7.52 (m, 2H), 7.56–7.62 (m, 1H), 7.95–8.01 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 13.8$, 14.0, 48.4, 61.3, 128.5, 128.6, 133.3, 135.7, 170.7, 195.7.

2-Methyl-3-(*p*-methylphenyl)-3-oxopropionic acid ethyl ester (25c): ^{1}H NMR ($CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 7.1$ Hz), 4.49 (d, 3H, $J = 7.0$ Hz), 2.42 (s, 3H), 4.15 (q, 2H, $J = 7.1$ Hz), 4.36 (q, 1H, $J = 7.0$ Hz), 7.28 (d, 2H, $J = 8.1$ Hz), 7.89 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 13.9$, 14.1, 21.7, 48.3, 61.3, 128.7, 129.3, 133.2, 144.3, 170.9, 195.3; IR (neat): $\tilde{\nu} = 2984$, 1739 ($\nu_{C=O}$), 1684 ($\nu_{C=O}$), 1607, 1186, 969, 833, 746 cm^{-1}; HRMS: *m*/*z* calcd for $C_{13}H_{16}O_3$: 220.1099; found: 220.1121 [M^+].

2-Methyl-3-(*p*-methoxyphenyl)-3-oxopropionic acid ethyl ester (25d): ^{1}H NMR ($CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 7.0$ Hz), 1.48 (d, 3H, $J = 7.1$ Hz), 3.88 (s, 3H), 4.15 (q, 2H, $J = 7.0$ Hz), 4.34 (q, 1H, $J = 7.1$ Hz), 6.95 (d, 2H, $J = 9.3$ Hz), 7.98 (d, 2H, $J = 9.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 13.9$, 14.1, 48.1, 55.5, 61.3, 113.8, 128.7, 130.9, 163.6, 171.0, 194.2; IR (neat): $\tilde{\nu} = 2983$, 1736 ($\nu_{C=O}$), 1677 ($\nu_{C=O}$), 1602, 1263, 1172, 1030, 971, 845 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{13}H_{16}O_4$: 236.1049; found: 236.1065 [M^+].

3-(*p*-Bromophenyl)-2-methyl-3-oxopropionic acid ethyl ester (25e): ^{1}H NMR ($CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 7.1$ Hz), 1.49 (d, 3H, $J = 7.0$ Hz), 4.15 (q, 2H, $J = 7.1$ Hz), 4.31 (q, 1H, $J = 7.0$ Hz), 7.63 (d, 2H, $J = 8.5$ Hz), 7.85 (d, 2H, $J = 8.5$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 13.7$, 14.0, 48.4, 61.5, 128.7, 130.0, 132.0, 134.5, 170.4, 194.6; IR (neat): $\tilde{\nu} = 2984$, 1739 ($\nu_{C=O}$), 1689

($\nu_{C=O}$), 1585, 1397, 1071, 842 cm^{-1}; HRMS: m/z: calcd for $C_{12}H_{13}BrO_3$: 284.0049; found: 284.0028 [M^+].

2-Ethyl-3-phenyl-3-oxopropionic acid ethyl ester (25 f):[78] ^{1}H NMR ($CDCl_3$): $\delta = 1.00$ (t, 3H, $J = 7.3$ Hz), 1.18 (t, 3H, $J = 7.1$ Hz), 2.05 (quintet, 2H, $J = 7.3$ Hz), 4.15 (q, 2H, $J = 7.1$ Hz), 4.22 (t, 1H, $J = 7.3$ Hz), 7.45–7.52 (m, 2H), 7.56–7.62 (m, 1H), 7.97–8.03 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta =$ 12.2, 14.1, 22.4, 55.9, 61.3, 128.5, 128.6, 133.3, 136.3, 169.9, 195.1; IR (neat): $\tilde{\nu} = 2974$, 1738 ($\nu_{C=O}$), 1687 ($\nu_{C=O}$), 1448, 1217, 1025, 691 cm^{-1}.

2-Allyl-3-phenyl-3-oxopropionic acid ethyl ester (25 g):[78b] ^{1}H NMR ($CDCl_3$): $\delta = 1.17$ (t, 3H, $J = 7.1$ Hz), 2.69–2.82 (m, 2H), 4.10–4.19 (m, 2H), 4.40 (t, 1H, $J = 7.1$ Hz), 5.05 (dd, 1H, $J = 1.2$, 10.3 Hz), 5.12 (dd, 1H, $J = 1.2$, 17.1 Hz), 5.76–5.88 (m, 1H), 7.45–7.52 (m, 2H), 7.56–7.62 (m, 1H), 7.97–8.03 (m, 2H); IR (neat): $\tilde{\nu} = 2982$, 1738 ($\nu_{C=O}$), 1687 ($\nu_{C=O}$), 1449, 1237, 1001, 921, 670 cm^{-1}; HRMS: m/z: calcd for $C_{14}H_{16}O_3$: 232.1099; found: 232.1092 [M^+].

Diastereo- and enantioselective reduction of the 2-alkyl-3-ketoester: Under a dry nitrogen atmosphere in a precooled vessel at $-10\,^\circ$C were placed the (*R*,*R*)-cobalt catalyst **3b** (5.7 mg, 0.01 mmol), sodium methoxide (13.5 mg, 0.25 mmol), the 2-alkyl-3-ketoester (0.25 mmol), and $CHCl_3$ (12.0 mL). The premodified $NaBH_4$ (2.4 mL, 0.30 mmol) was added to the reaction mixture, and stirred for 15 h at $-10\,^\circ$C. The reaction was quenched by a precooled aqueous THF solution at $-10\,^\circ$C and pH 7 buffer solution, then the crude products were extracted with AcOEt. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by silica gel column chromatography (hexane/AcOEt) to give the corresponding 2-alkyl-3-hydroxyester. The *anti*-selectivity was determined by ^{1}H NMR analysis. The enantiomer excess was determined by HPLC analysis.

***anti*-3-Hydroxy-2-methyl-3-(2-naphthyl)propionic acid ethyl ester (26 a)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.05$ (d, 3H, $J = 7.6$ Hz), 1.26 (t, 3H, $J = 7.1$ Hz), 2.92 (quin, 1H, $J = 7.6$ Hz), 3.14 (d, 1H, $J = 4.4$ Hz), 4.20 (q, 2H, $J = 7.1$ Hz), 4.93 (dd, 1H, $J = 4.4$, 7.6 Hz), 7.45–7.53 (m, 3H), 7.77–7.88 (m, 4H); ^{13}C NMR ($CDCl_3$): $\delta = 14.2$, 14.7, 47.0, 60.8, 76.5, 124.2, 125.9, 126.0, 126.1, 127.6, 127.9, 128.3, 133.0, 133.1, 138.9, 175.7; IR (neat): $\tilde{\nu} = 3461$, 2979, 1732 ($\nu_{C=O}$), 1376, 1182, 1034, 822, 749, 479 cm^{-1}; HRMS: m/z: calcd for $C_{16}H_{18}O_3$: 258.1256; found: 258.1236 [M^+]. HPLC: Daicel Chiralpak AD-H (5.0% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 24.9 min (minor), 27.3 (major); $[\alpha]_D^{21} = +33.9^\circ$ ($c = 0.45$ in $CHCl_3$).

***anti*-3-Hydroxy-2-methyl-3-phenylpropionic acid ethyl ester (26 b)**:[79] ^{1}H NMR ($CDCl_3$): $\delta = 1.02$ (d, 3H, $J = 7.3$ Hz), 1.26 (t, 3H, $J = 7.0$ Hz), 2.80 (quin, 1H, $J = 7.3$ Hz), 3.02 (d, 1H, $J = 4.2$ Hz), 4.19 (q, 2H, $J = 7.0$ Hz), 4.75 (dd, 1H, $J = 4.2$, 7.3 Hz), 7.23–7.43 (m, 5H); IR (neat): $\tilde{\nu} = 3461$, 2980, 1733 ($\nu_{C=O}$), 1455, 1376, 1181, 1025, 767, 703 cm^{-1}. HPLC: Daicel Chiralpak AD-H (2.0% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 27.5 min (major), 30.7 (minor); $[\alpha]_D^{21} = +48.7^\circ$ ($c = 0.63$ in $CHCl_3$).

***anti*-3-Hydroxy-2-methyl-3-(*p*-methylphenyl)propionic acid ethyl ester (26 c)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.01$ (d, 3H, $J = 7.5$ Hz), 1.27 (t, 3H, $J =$ 7.0 Hz), 2.35 (s, 3H), 2.79 (quin, 1H, $J = 7.5$ Hz), 2.89 (d, 1H, $J = 4.4$ Hz), 4.19 (q, 2H, $J = 7.0$ Hz), 4.72 (dd, 1H, $J = 4.4$, 7.5 Hz), 7.16 (d, 2H, $J =$ 7.1 Hz), 7.23 (d, 2H, $J = 7.1$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.2$, 14.6, 21.2, 47.2, 60.7, 76.2, 126.5, 129.1, 137.6, 138.5, 175.8; IR (neat): $\tilde{\nu} = 3471$, 2980, 1734 ($\nu_{C=O}$), 1458, 1376, 1249, 1179, 1035, 819, 539 cm^{-1}; HRMS: m/z: calcd for $C_{13}H_{18}O_3$: 222.1256; found: 222.1286 [M^+]. HPLC: Daicel Chiralcel OB-H (0.7% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 20.8 min (minor), 32.0 (major); $[\alpha]_D^{21} = +43.2^\circ$ ($c = 0.46$ in $CHCl_3$).

***anti*-3-Hydroxy-2-methyl-3-(*p*-methoxyphenyl)propionic acid ethyl ester (26 d)**:[79] ^{1}H NMR ($CDCl_3$): $\delta = 0.99$ (d, 3H, $J = 7.7$ Hz), 1.28 (t, 3H, $J =$ 7.2 Hz), 2.77 (quin, 1H, $J = 7.7$ Hz), 2.89 (d, 1H, $J = 3.9$ Hz), 3.81 (s, 3H), 4.20 (q, 2H, $J = 7.2$ Hz), 4.71 (dd, 1H, $J = 3.9$, 7.7 Hz), 6.89 (d, 2H, $J =$ 8.3 Hz), 7.27 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.2$, 14.6, 47.2, 55.3, 60.8, 76.0, 113.8, 127.8, 133.6, 159.2, 175.8; m.p. 66.5–67.5 °C. HPLC: Daicel Chiralcel OB-H (3% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 18.7 min (minor), 26.1 (major); $[\alpha]_D^{21} = +42.1^\circ$ ($c = 0.51$ in $CHCl_3$).

***anti*-3-(*p*-Bromophenyl)-3-hydroxy-2-methylpropionic acid ethyl ester (26 e)**: ^{1}H NMR ($CDCl_3$): $\delta = 1.04$ (d, 3H, $J = 7.4$ Hz), 1.26 (t, 3H, $J =$ 7.2 Hz), 2.75 (quin, 1H, $J = 7.4$ Hz), 3.15 (d, 1H, $J = 4.6$ Hz), 4.18 (q, 2H, $J = 7.2$ Hz), 4.72 (dd, 1H, $J = 4.6$, 7.4 Hz), 7.23 (d, 2H, $J = 8.3$ Hz), 7.49 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.2$, 14.5, 46.9, 60.9, 75.6, 121.7, 128.2, 131.5, 140.5, 175.5; IR (neat): $\tilde{\nu} = 3453$, 2980, 1732 ($\nu_{C=O}$), 1377, 1181, 1011, 823, 542 cm^{-1}; HRMS: m/z: calcd for $C_{12}H_{15}BrO_3$: 286.0205; found: 286.0203 [M^+]. HPLC: Daicel Chiralpak AD-H (5.0% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 16.8 min (minor), 18.5 (major); $[\alpha]_D^{21} = +36.0^\circ$ ($c = 0.44$ in $CHCl_3$).

***anti*-2-Ethyl-3-hydroxy-3-phenylpropionic acid ethyl ester (26 f)**:[79, 80] ^{1}H NMR ($CDCl_3$): $\delta = 0.87$ (t, 3H, $J = 7.6$ Hz), 1.23 (t, 3H, $J = 7.1$ Hz), 1.33–1.45 (m, 1H), 1.53–1.66 (m, 1H), 2.63–2.72 (m, 1H), 2.89 (d, 1H, $J =$ 5.5 Hz), 4.10–4.24 (m, 2H), 4.80 (dd, 1H, $J = 5.5$, 7.6 Hz), 7.25–7.40 (m, 5H). HPLC: Converted to acyl-form with Ac_2O, py, and DMAP. Daicel Chiralpak AD-H (0.7% propan-2-ol in hexane, flow 1.0 mL min^{-1}), 19.9 min (major), 31.1 (minor); $[\alpha]_D^{21} = +39.0^\circ$ ($c = 0.17$ in $CHCl_3$).

***anti*-2-Allyl-3-hydroxy-3-phenylpropionic acid ethyl ester (26 g)**:[81] ^{1}H NMR ($CDCl_3$): $\delta = 1.20$ (t, 3H, $J = 7.1$ Hz), 2.13–2.22 (m, 1H), 2.24–2.35 (m, 1H), 2.80–2.88 (m, 1H), 2.99 (d, 1H, $J = 5.9$ Hz), 4.08–7.21 (m, 2H), 4.83 (dd, 1H, $J = 5.9$, 7.3 Hz), 5.01 (d, 1H, $J = 9.8$ Hz), 5.04 (d, 1H, $J =$ 17.1 Hz), 5.64–5.76 (m, 1H), 7.27–7.39 (m, 5H). HPLC: Daicel Chiralpak AD-H (1.2% propan-2-ol in hexane, flow 1.0 mL min – 1), 48.6 min (major), 52.4 (minor); $[\alpha]_D^{21} = +32.1^\circ$ ($c = 0.46$ in $CHCl_3$).

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