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Cobalt–Bisoxazoline-Catalyzed Asymmetric Kumada Cross-Coupling of Racemic α-Bromo Esters with Aryl Grignard Reagents

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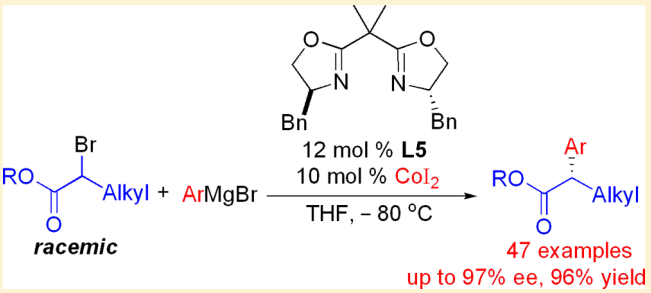
Supporting Information

ABSTRACT: The first cobalt-catalyzed asymmetric Kumada cross-coupling with high enantioselectivity has been developed. The reaction affords a unique strategy for the enantioselective arylation of α-bromo esters catalyzed by a cobalt–bisoxazoline complex. A variety of chiral α-arylalkanoic esters were prepared in excellent enantioselectivity and yield (up to 97% ee and 96% yield). The arylated products were transformed into α-arylcarboxylic acids and primary alcohols without erosion of ee. The new enantioenriched α-arylpropionic esters synthesized herein are potentially useful in the development of nonsteroidal anti-inflammatory drugs. This method was conducted on gram-scale and applied to the synthesis of highly enantioenriched (*S*)-fenoprofen and (*S*)-*ar*-turmerone.



INTRODUCTION

The catalytic cross-coupling of Grignard reagents with organic electrophiles under transition-metal catalysis (Kumada coupling) is an excellent method for the formation of carbon–carbon bonds.[1] The popularity of the Kumada coupling is, in part, due to the ready availability of organomagnesium reagents. Recent improvements in Kumada coupling reactions have focused on development of more active catalyst systems based on nickel,[2] palladium,[3] cobalt,[4] copper,[5] and iron[6] and on the introduction of more functional-group-tolerant organomagnesium reagents by Knochel and Hu.[7,8] These advances have enabled Kumada coupling under very mild reaction conditions.

Despite significant progress, opportunities in Kumada coupling reactions remain clear. This is particularly apparent in the application of the Kumada cross-coupling to enantioselective transformations and desymmetrization reactions,[9,10] which have witnessed little success compared to related coupling reactions employing organozinc (Negishi coupling)[11] and organoboron (Suzuki–Miyaura coupling) reagents.[12] Furthermore, very few enantioselective Kumada cross-coupling reactions generate products with synthetically useful levels of enantioselectivity.[9e,f,i] Impressive and highly enantioselective examples of such reactions include Kumada, Hayashi, Ito, and their co-workers' early demonstration of a palladium-catalyzed asymmetric Grignard cross-coupling (eq 1),[9c] and a nickel–ferrocenylphosphine-catalyzed asymmetric biaryl coupling to furnish (*R*)-2,2′-dimethy-1,1′-binaphthyl (eq 2).[9e] More recently, Lou and Fu reported a highly enantioselective nickel–bisoxazoline-catalyzed cross-coupling of racemic α-bromo ketones with aryl Grignard reagents (eq 3).[9i]

In a complementary approach, Jarvo and co-workers reported stereospecific nickel-catalyzed Kumada cross-coupling reactions.[9j–l,n,o]

Our interest in the asymmetric synthesis of α-aryl carboxylic acid derivatives stems from their potential applications toward the preparation of enantioenriched α-aryl propionic acids, which are the most important class of nonsteroidal anti-inflammatory drugs (NSAIDs) and are also useful synthetic intermediates.[13] Although a number of approaches to these compounds have been reported,[12g,14] it remains a challenge to devise more efficient and convenient asymmetric syntheses. Cobalt complexes are inexpensive and exhibit lower toxicity in comparison with other transition metals.[15] Despite the recent attention to cobalt-catalyzed reactions,[4] no examples of cobalt-catalyzed asymmetric Kumada coupling reactions that give even moderate enantioselectivity have been reported to our knowledge.[4b,c] Herein, we disclose the first highly enantioselective cobalt-catalyzed Kumada cross-coupling reaction (eq 4) and demonstrate its scalability in the synthesis of (*S*)-fenoprofen and (*S*)-*ar*-turmerone.

RESULTS AND DISCUSSION

Catalyst Identification and Reaction Optimization in the Cobalt-Catalyzed Asymmetric Kumada Cross-Cou-

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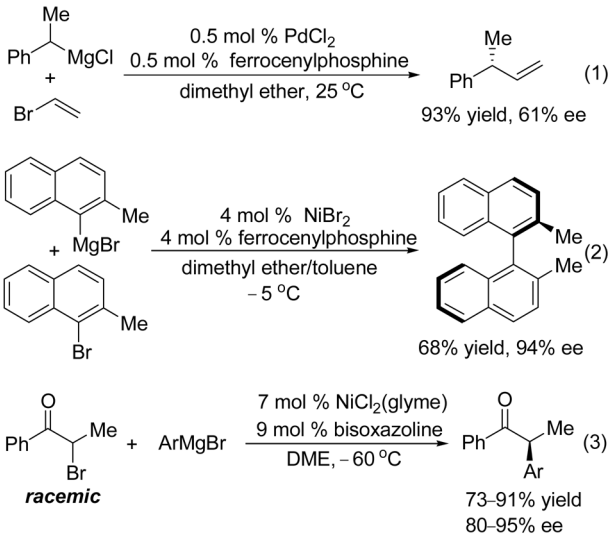
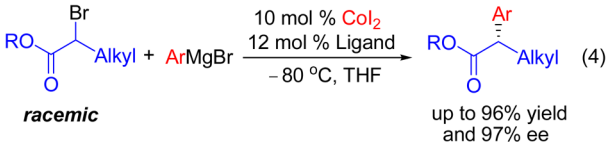
***Previous work*: Nickel and Palladium catalyzed asymmetric Kumada coupling**



***This work*: Cobalt catalyzed asymmetric Kumada coupling**

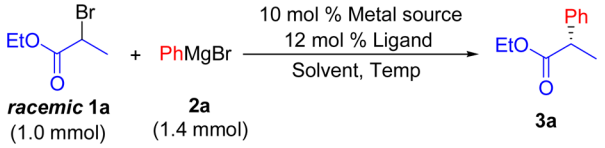


pling Reaction. We initially employed CoI_2 and examined the impact of reaction parameters on the asymmetric cross-coupling of racemic ethyl α-bromopropanoate with phenyl magnesium bromide (Table 1). Bisoxazoline (Box)[16] ligands were initially chosen because bisoxazolines have been successfully used in the nickel-catalyzed cross-coupling of racemic α-bromo ketones with aryl Grignard reagents.[9i] Diamine ligand **L8** has been applied to cobalt-catalyzed cross-coupling reactions,[4e,f,i] and diamine **L9** was successfully used in the enantioselective Hiyama cross-coupling of racemic α-bromo esters (Chart 1).[14e]

Due to the known reactivity of organomagnesium reagents with esters, we conducted reactions at −80 °C in THF. No α-arylation was observed in the absence of metal source (entry 1), and the cross-coupling product **3a** was obtained in only 22% yield when chiral ligand was omitted (entry 2). The phenyl-substituted bisoxazoline ligand **L1**, which is the best ligand for the coupling reaction reported by Lou and Fu (eq 3),[9i] resulted in the formation of **3a** in 61% yield with 72% ee (entry 3). Based on this promising result, other bisoxazoline ligands were examined. Bisoxazoline ligands with isopropyl, isobutyl, and phenethyl substituents (entries 4–6) generated product **3a** with 71–83% ee and indicated that varying the substitution on oxazoline significantly influenced the enantioselectivity of the catalyst. We were pleased to find that benzyl-substituted bisoxazoline ligand (**L5**) exhibited excellent yield (92%) and enantioselectivity (92%, entry 7). Introduction of a cyclopentane backbone into the bisoxazoline ligand reduced enantioselectivities and yields (entries 8 and 9) relative to the parent ligands (entries 3 and 4). Diamine ligands **L8** and **L9** afforded only 3–10% ee of the cross-coupling product (entries 10 and 11).

Previous reports[4h,i] demonstrating a marked effect of the cobalt halides and related complexes on the reactivity of cross-coupling of organic halides with aryl Grignard reagents

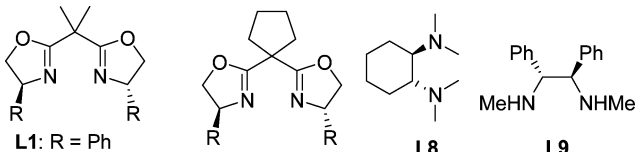
Table 1. Effect of Reaction Parameters on the Asymmetric Kumada Cross-Coupling Reaction[a]



entry	L	metal	solvent	T (°C)	yield (%)[b]	ee (%)[c]
1	**L5**	–	THF	−80	2[d]	–
2	–	CoI_2	THF	−80	22	0
3	**L1**	CoI_2	THF	−80	61	72
4	**L2**	CoI_2	THF	−80	73	74
5	**L3**	CoI_2	THF	−80	53	71
6	**L4**	CoI_2	THF	−80	49	83
7	**L5**	CoI_2	THF	−80	92	92
8	**L6**	CoI_2	THF	−80	51	58
9	**L7**	CoI_2	THF	−80	54	50
10	**L8**	CoI_2	THF	−80	68	10
11	**L9**	CoI_2	THF	−80	67	3
12	**L5**	$CoBr_2$	THF	−80	82	89
13	**L5**	$CoCl_2$	THF	−80	49	69
14	**L5**	$Co(OAc)_2$	THF	−80	16	85
15	**L5**	$Co(acac)_2$	THF	−80	61	52
16	**L5**	$Co(acac)_3$	THF	−80	42	79
17	**L5**	$Co(dppe)Cl_2$	THF	−80	36	75
18	**L5**	$Co(PPh_3)_2Cl_2$	THF	−80	27	50
19	**L5**	$NiCl_2(glyme)$	THF	−80	83	22
20	**L5**	CoI_2	Tol	−80	44	12
21	**L5**	CoI_2	DCM	−80	32	70
22	**L5**	CoI_2	Et_2O	−80	29	14
23	**L5**	CoI_2	DME	−60	70	86
24	**L5**	CoI_2	THF	−60	89	88
25	**L5**	CoI_2	THF	−70	92	90
26	**L5**	CoI_2	THF	−90	73	90
27[e]	**L5**	CoI_2	THF	−80	46	83
28[f]	**L5**	CoI_2	THF	−80	88	89

[a]All reactions were run for 5 h. [b]Isolated yields after chromatographic purification. [c]Determined by chiral HPLC on a R&C OD column. [d]Determined by GC analysis. [e]Ethyl 2-chloropropanoate as the electrophile. [f]Phenyl magnesium bromide **2a** was added in 5 min.

Chart 1. Ligands Screening in the Asymmetric Kumada Cross-Coupling Reaction



prompted further investigation of cobalt salts. Varying the cobalt source from CoI_2 to $CoBr_2$ resulted in a small drop in the yield (82%) and ee (89%, entry 12 vs 7), while use of $CoCl_2$ caused a significant decrease in both the yield (49%) and enantioselectivity (69%, entry 13). Use of $Co(OAc)_2$, $Co(acac)_2$, or $Co(acac)_3$ resulted in 52–85% enantioselectivities (entries 14–16), with the most enantioselective catalyst giving only 16% yield. Cobalt sources bearing phosphine ligands, such as $Co(dppe)Cl_2$ and $Co(PPh_3)_2Cl_2$, had a detrimental impact

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on the enantioselectivity of the coupling (entries 17 and 18 vs 7). Using $NiCl_2$(glyme), only 22% ee was obtained (entry 19).

Given the solvated structures of Grignard reagents, it is not surprising that solvent had a significant impact on these reactions. Less coordinating diethyl ether and noncoordinating toluene and CH_2Cl_2 resulted in dramatic drops in the product ee to 12−70% (entries 20−22). In contrast, the reaction in DME was only slightly less enantioselective than in THF (86 vs 92% ee, entry 23 vs 7).

The impact of temperature on the reactivity and enantioselectivity with CoI_2 and **L5** was next explored (entries 7 and 24−26). As the temperature was decreased from −60 to −90 °C, the enantioselectivity increased to 92% at −80 °C, then decreased slightly to 90% at −90 °C. The reactivity at −90 °C, however, also decreased, as reflected in the lower yield (73%, entry 26). Our screening of other reaction parameters indicated that the optimum molar ratio of Grignard reagent **2a** to bromo ester **1a** was 1.4:1, and the most suitable catalyst loading was 10 mol % (see Supporting Information for details).

The optimized reaction conditions in entry 7 involved 1.0 equiv of ethyl α-bromopropanoate and 1.4 equiv of phenyl magnesium bromide in THF at −80 °C for 5 h, catalyzed by 10 mol % of CoI_2 and 12 mol % of bisoxazoline **L5**. The cross-coupling product **3a** was generated in 92% yield and 92% ee, favoring the *S* enantiomer (based on comparison with reported optical rotation values).[17] These conditions were applied to subsequent substrates, as outlined below.

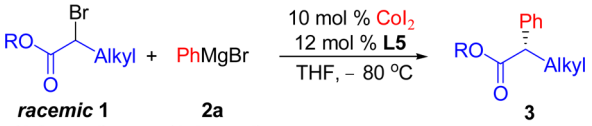
Scope of the α-Bromo Ester in the Asymmetric Kumada Cross-Coupling Reaction. With the optimized conditions outlined above, coupling reactions with a variety of racemic α-bromo esters and phenyl magnesium bromide in the presence of CoI_2 and bisoxazoline ligand **L5** were explored (Table 2). Initial studies examined α-bromo propionic esters derived from different alcohols (entries 1−11). It is noteworthy that ester OR substituents, from R = methyl to isopropyl to the bulky *tert*-butyl, exhibited only minor variance in product ee (89−95%, entries 1−5). Likewise, esters derived from phenol, cyclic alcohols, and cyclohexylmethanol gave uniformly high enantioselectivities (86−92% ee, entries 6−9). Alkyl bromide containing **1j** (entry 10) and prenol derivative **1k** (entry 11) underwent arylation in 91−92% enantioselectivity. Interestingly, the high enantioselectivities of our catalyst with a wide range of OR substituents stand in sharp contrast to the trend reported by Fu et al.[14e] in the catalytic asymmetric Hiyama cross-coupling of racemic α-bromo esters with a nickel-based diamine catalyst. They observed very high enantioselectivities with racemic α-bromo esters derived from sterically hindered 2,6-di-*tert*-butyl-4-methylphenol (BHT) esters (95% ee). In contrast, when OR was OEt or O-*t*Bu, the enantioselectivities were 23 and 33%, respectively.

The scope of the alkyl group attached to the α-carbon of the α-bromo ester was next investigated. α-Bromo butyric acid derivatives with various OR groups (R = methyl, ethyl, isopropyl, or benzyl) gave enantioselectivities ranging from 89 to 93% ee and yields in the 90−94% range (entries 12−15). Excellent enantioselectivities were obtained with primary alkyl groups (Me, Et, *n*-Bu, *i*-Bu, entries 1−15, 17, and 18) attached to the α-carbon. Secondary substituents, such as isopropyl and cyclopentyl, exhibited poor enantioselectivities and are not tolerated by this catalyst (entries 16 and 19).

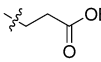
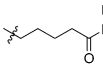
Cross-coupling of α-bromo ester substrates bearing functionalized alkyl groups attached to the α-carbon were next examined. When ester substrates containing a primary alkyl bromide or chloride were utilized, enantioselectivities of 87−90% were obtained with good yields (80−82%, entries 20 and 21). Although an ester with an olefin in the side chain exhibited slightly lower reactivity and enantioselectivity (82% ee and 63% yield, entry 22), the ester with a benzyl group at this position underwent coupling in 90% enantioselectivity and good yield (81% yield, entry 23). Likewise, a benzyl ester in the side chain also proved to be a good substrate, giving 90% ee and 82% yield (entry 24).

Substrates bearing heterocyclic side chains containing 2-furyl and 2-thiophenyl groups both underwent coupling in 83−88% yield with slightly reduced enantioselectivities (85−87% ee,

Table 2. Asymmetric Kumada Phenylations of Racemic α-Bromo Esters[a]



***racemic* 1** (1.0 mmol) **2a** (1.4 mmol) **3**

entry	R	alkyl	product	yield (%)[b]	ee (%)[c]
1	Et	Me	**3a**	92	92
2	Me	Me	**3b**	89	89
3	*i*-Pr	Me	**3c**	93	95
4	*t*-Bu	Me	**3d**	89	90
5	Bn	Me	**3e**	95	94
6	Ph	Me	**3f**	93	92
7		Me	**3g**	83	91
8		Me	**3h**	81	91
9		Me	**3i**	79	86
10		Me	**3j**	81	92
11		Me	**3k**	73	91
12	Me	Et	**3l**	90	89
13	Et	Et	**3m**	92	92
14	*i*-Pr	Et	**3n**	94	93
15	Bn	Et	**3o**	90	93
16[d]	Bn	*i*-Pr	**3p**	83	23
17	Bn	*n*-Bu	**3q**	72	90
18	Bn	*i*-Bu	**3r**	78	91
19[d]	Et		**3s**	83	33
20	Et		**3t**	82	90
21	Bn		**3u**	80	87
22[d]	Bn		**3v**	63	82
23	Bn		**3w**	81	90
24	Bn		**3x**	82	90
25[e]	Me		**3y**	83	87
26[e]	Me		**3z**	88	85
27[e]	Bn		**3za**	89	91
28[e]	Me		**3zb**	79	81

[a]All reactions were run for 5 h. [b]Isolated yields after chromatographic purification. [c]Determined by chiral HPLC analysis. [d]2.0 mmol phenyl magnesium bromide was used. [e]1.8 mmol phenyl magnesium bromide was used.

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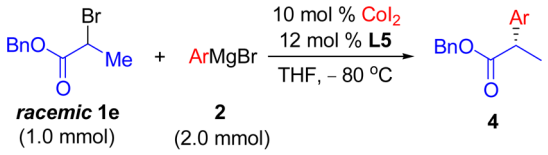
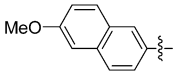
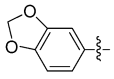
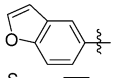
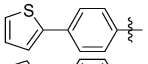
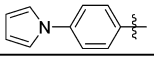
entries 25 and 26). A substrate with a pendent amide afforded coupling product with 91% ee in 89% yield (entry 27). Silyloxy-substituted ester coupled in 79% yield with 81% ee (entry 28). With a wide range of α-bromo esters coupling with PhMgBr and affording products with high enantioselectivities, we next moved to examine a range of aryl Grignard reagents.

Scope of the Aryl Grignard Reagent in the Asymmetric Kumada Cross-Coupling Reaction. The asymmetric cross-coupling reaction in Table 2 was not limited to phenyl magnesium bromide. As outlined in Table 3, a range of

Table 3. Asymmetric Kumada Arylations of Racemic α-Bromo Esters with Various Aryl Grignard Reagents[a]



racemic **1e** (1.0 mmol) **2** (2.0 mmol) **4**

entry	Ar	product	y (%)[b]	ee (%)[c]
1	4-MeO-C_6H_4	**4b**	81	91
2	4-Me-C_6H_4	**4c**	88	91
3	4-F-C_6H_4	**4d**	82	90
4	4-Cl-C_6H_4	**4e**	80	93
5	4-Ph-C_6H_4	**4f**	83	91
6[d]	4-CO_2Et-C_6H_4	**4g**	65	91
7	3-MeO-C_6H_4	**4h**	80	93
8	3-Cl-C_6H_4	**4i**	82	96
9	3-CF_3-C_6H_4	**4j**	75	93
10	3,4-F_2-C_6H_3	**4k**	96	97
11	3-BnO-C_6H_4	**4l**	64	87
12	2-Naphthyl	**4m**	74	87
13		**4n**	57	90
14		**4o**	71	95
15[d]		**4p**	58	92
16[d]		**4q**	68	86
17[d]		**4r**	70	86

[a]All reactions were run for 24 h. [b]Isolated yields after chromatographic purification. [c]Determined by chiral HPLC analysis. [d]4.0 mmol aryl magnesium bromide and 20 mol % of catalyst were used.

arylmagnesium reagents also furnished cross-coupling products with high enantioselectivities. In general, arylmagnesium reagents bearing electron-neutral and electron-donating groups (4-OMe, 4-Me, 4-Ph) or electron-withdrawing groups (4-F, 4-Cl, 4-CO_2Et, 3-OMe, 3-Cl, 3-CF_3, 3,4-F_2, 3-OBn) consistently exhibited excellent enantioselectivities (87–97%) and good to excellent yields (64–96%, entries 1–11). In particular, (3,4-difluorophenyl)magnesium bromide was an outstanding reagent, furnishing product **4k** with 97% ee in 96% yield (entry 10). Furthermore, enantioselectivities of 87–90% were observed for 2-naphthyl and 6-methoxy-2-naphthyl magnesium bromides (entries 12 and 13).

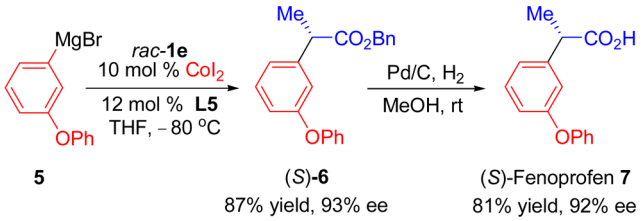
It is noteworthy that functionalized aryl Grignard reagents bearing ether, halide, ester, and acetal functional groups smoothly coupled with α-bromo propionic esters to yield the corresponding cross-coupling products with high ee (entries 1, 3, 4, 6, 7, 8, 10, 11, 13, and 14). Functionalized Grignard reagents possessing halides provided the cross-coupling products in 80–96% yield (entries 3, 4, 8, and 10). These results indicate that the coupling reactions occurred chemoselectively at the sp^3 C–Br bond. Moreover, heteroaryl nucleophiles, such as 4-thiophenyl benzene, 4-pyrrolyl benzene, and benzofuran-based Grignard reagents, gave 86–92% enantioselectivities (entries 15–17). These functionalized coupling partners required increased catalyst loading (20 mol %) and 4 equiv of aryl magnesium bromide.

Despite the wide scope of substrates and coupling partners employed above, some limitations should be discussed. The catalyst proved particularly sensitive to steric effects from substituents on the aryl Grignard reagents, as both 2-methyl- and 2-methoxy-substituted phenyl magnesium bromides did not react with α-bromo ester **1e**. Similar limitations have been reported in the use of congested Grignard reagents with catalytic $CoCl_2$(dppe),[4a] Fe(acac)$_3$,[6h] and nickel(II) pincer complexes.[7i]

Taken together, the results in Tables 2 and 3 suggest that the cobalt catalyst exhibits high enantioselectivity with a wide variety of α-bromo esters and aryl Grignard reagents. It is noteworthy that the β-hydride elimination product, benzyl acrylate, was not detected by GC-MS in the representative coupling between α-bromo ester **1e** and phenyl magnesium bromide **2a**.

Demonstration of the Scalability and Utility of the Catalytic Asymmetric Coupling. To demonstrate the scalability and utility of our method, (*S*)-fenoprofen, a member of the well-known NSAIDs, was synthesized with high enantioselectivity (Scheme 1). Only three syntheses of the

Scheme 1. Enantioselective Synthesis of (*S*)-Fenoprofen



5 (*S*)-**6** 87% yield, 93% ee (*S*)-Fenoprofen **7** 81% yield, 92% ee

more active enantiomer, (*S*)-fenoprofen,[18] have been reported.[14g,19] After we prepared the Grignard reagent **5**,[20] it was coupled with 2.0 mmol racemic α-bromo ester **1e** under our standard conditions to afford (*S*)-fenoprofen ester (**6**) with 93% ee in 87% yield. Debenzylation with hydrogen over Pd/C[21] furnished (*S*)-fenoprofen (**7**) in 92% ee with 81% yield (overall 70% yield from *rac*-**1e**).

We also applied our method to the synthesis of (*S*)-*ar*-turmerone **10** (Scheme 2), a sesquiterpene isolated from rhizomes of *Curcuma longa*[22] that is reported to exhibit cytotoxic, anti-inflammatory, and anti-venom activity.[23] Only a limited number of enantioselective synthetic strategies for (*S*)-*ar*-turmerone have been reported.[24] Our synthesis began with gram-scale asymmetric cross-coupling of racemic benzyl 2-bromopropanoate (**1e**, 6 mmol) and *p*-tolylmagnesium bromide (**2c**) catalyzed by *ent*-**L5** and CoI_2, providing 1.34 g of (*R*)-benzyl 2-(*p*-tolyl)propanoate **4c** with 93% ee and 88% yield. Treatment of (*R*)-**4c** with diisobutylaluminum hydride (DIBAl-H)[25] in DCM furnished alcohol (*R*)-**8** with no racemization in 94% yield. After tosylation, nucleophilic displacement with cyanide and reduction with DIBAl-H

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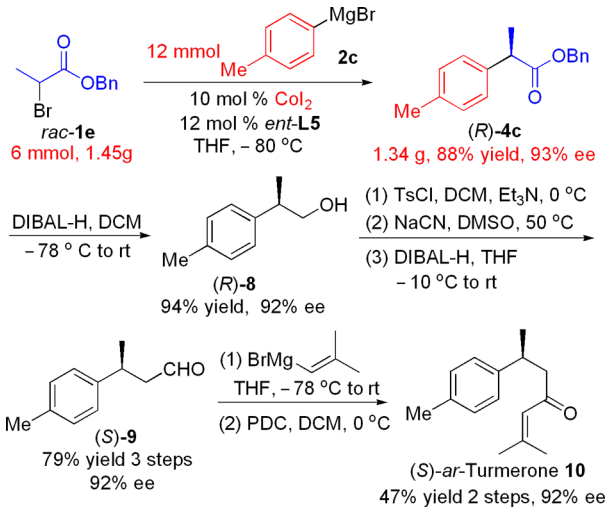
Scheme 2. Total Synthesis of (*S*)-*ar*-Turmerone



afforded (*S*)-3-*p*-tolylbutanal (**9**) in 92% ee with 79% yield over the three steps.[26] Finally, carbonyl addition of the isobutenylmagnesium reagent and subsequent oxidation with PDC[24f] gave the target compound **10** with 92% ee.

CONCLUSIONS

In summary, we have developed the first highly enantioselective cobalt-catalyzed Kumada cross-coupling reaction. A range of readily available aryl Grignard reagents couple with 28 different α-bromo esters to afford α-arylated esters with high enantioselectivity in most cases. The cross-coupling reactions could easily be conducted on gram-scale, and the cross-coupling products transformed into enantioenriched α-arylcarboxylic acids and primary alcohols without erosion of the ee. Furthermore, new enantioenriched α-arylpropionic esters were synthesized, with potential utility in the discovery of NSAIDs. This novel method has been applied to the asymmetric synthesis of (*S*)-fenoprofen (3 steps) and the total synthesis of (*S*)-*ar*-turmerone. Advantages of this system are the lower toxicity of cobalt relative to nickel and the low cost compared to palladium. The use of Grignard reagents with a variety of α-bromo esters without need of preparing esters with very bulky OR groups is also advantageous. We are currently applying our cobalt–bisoxazoline-based catalysts to other asymmetric cross-coupling reactions.

EXPERIMENTAL SECTION

Typical Procedure for the Asymmetric Kumada Cross-Coupling Reaction. Anhydrous cobalt(II) iodide (31.2 mg, 0.1 mmol) was placed in a 50 mL Schlenk tube and was heated with a heat gun in vacuo for 2 h. Anhydrous THF (3 mL) and **L5** (43.5 mg, 0.12 mmol) were added sequentially under argon. After being stirred for 1 h at room temperature, racemic α-bromo ester (1.0 mmol) was added via syringe. The Schlenk tube was then cooled to −80 °C, and arylmagnesium bromide was then added over 1 h to the mixture at −80 °C. The reaction mixture was stirred for 5 h at the same temperature and quenched with saturated NH_4Cl solution (5 mL). The aqueous phase was extracted with Et_2O (4 × 15 mL), then the combined organic layers were dried over Na_2SO_4, filtered, and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford the corresponding Kumada cross-coupling product.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data for all compounds, ^1H and $^{13}C\{^1H\}$ NMR spectra, HPLC chromatography of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Negishi, E.-i. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley-Interscience: New York, 2002. (b) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2004. (c) Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1439. Metal-catalyzed cross-coupling reactions, special issue: (d) Desai, K. R. *Organic Name Reactions*; Oxford: Jaipur India, 2008. (e) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417.

(2) For examples and leading references of nickel-catalyzed Kumada cross-coupling reactions, see: (a) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374. (b) Böhm, V. P. W.; Gstöttmayr, C. W. K.; Weskamp, T.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3387. (c) Ackermann, L.; Born, R.; Spatz, J. H.; Meyer, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 7216. (d) Csok, Z.; Vechorkin, O.; Harkins, S. B.; Scopelliti, R.; Hu, X. *J. Am. Chem. Soc.* **2008**, *130*, 8156. (e) Vechorkin, O.; Csok, Z.; Scopelliti, R.; Hu, X. *Chem.—Eur. J.* **2009**, *15*, 3889. (f) Vechorkin, O.; Hu, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 2937. (g) Xie, L.-G.; Wang, Z.-X. *Chem.—Eur. J.* **2010**, *16*, 10332. (h) Tennyson, A. G.; Lynch, V. M.; Bielawski, C. W. *J. Am. Chem. Soc.* **2010**, *132*, 9420. (i) Ren, P.; Vechorkin, O.; von Allmen, K.; Scopelliti, R.; Hu, X. *J. Am. Chem. Soc.* **2011**, *133*, 7084. (j) Joshi-Pangu, A.; Wang, C.-Y.; Biscoe, M. R. *J. Am. Chem. Soc.* **2011**, *133*, 8478. (k) Liu, N.; Wang, Z.-X. *J. Org. Chem.* **2011**, *76*, 10031. (l) Wu, J.-C.; Gong, L.-B.; Xia, Y.; Song, R.-J.; Xie, Y.-X.; Li, J.-H. *Angew. Chem., Int. Ed.* **2012**, *51*, 9909. (m) Soulé, J.-F.; Miyamura, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2013**, *135*, 10602. (n) Breitenfeld, J.; Ruiz, J.; Wodrich, M. D.; Hu, X. *J. Am. Chem. Soc.* **2013**, *135*, 12004. (o) Guo, W.-J.; Wang, Z.-X. *J. Org. Chem.* **2013**, *78*, 1054. (p) Zheng, B.; Tang, F.; Luo, J.; Schultz, J. W.; Rath, N. P.; Mirica, L. M. *J. Am. Chem. Soc.* **2014**, *136*, 6499.

(3) For recent examples and leading references of palladium-catalyzed Kumada cross-coupling reactions, see: (a) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889. (b) Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 8704. (c) Terao, J.; Naitoh, Y.; Kuniyasu, H.; Kambe, N. *Chem. Commun.* **2007**, 825. (d) Wolf, C.; Xu, H. *J. Org. Chem.* **2008**, *73*, 162. (e) López-Pérez, A.; Adrio, J.; Carretero, J. C. *Org. Lett.* **2009**, *11*, 5514. (f) Shu, C.; Sidhu, K.; Zhang, L.; Wang, X.-j.; Krishnamurthy, D.; Senanayake, C. H. *J. Org. Chem.* **2010**, *75*, 6677. (g) Sugita, N.; Hayashi, S.; Hino, F.; Takanami, T. *J. Org. Chem.* **2012**, *77*, 10488. (h) Krasovskiy, A. L.; Haley, S.; Voigtritter, K.; Lipshutz, B. H. *Org. Lett.* **2014**, *16*, 4066.

(4) For recent examples and leading references of cobalt-catalyzed Kumada cross-coupling reactions, see: (a) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374. (b) Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 4137. (c) Ohmiya, H.; Tsuji, T.; Yorimitsu, H.; Oshima, K. *Chem.—Eur. J.*

dx.doi.org/10.1021/ja5109084 | *J. Am. Chem. Soc.* XXXX, XXX, XXX–XXX

2004, *10*, 5640. (d) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2006**, *8*, 3093. (e) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2006**, *128*, 1886. (f) Cahiez, G.; Chaboche, C.; Duplais, C.; Giulliani, A.; Moyeux, A. *Adv. Synth. Catal.* **2008**, *350*, 1484. (g) Hatakeyama, T.; Hashimoto, S.; Ishizuka, K.; Nakamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 11949. (h) Hsu, S.-F.; Ko, C.-W.; Wu, Y.-T. *Adv. Synth. Catal.* **2011**, *353*, 1756. (i) Nicolas, L.; Angibaud, P.; Stansfield, I.; Bonnet, P.; Meerpoel, L.; Reymond, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 11101. (j) Gülak, S.; Stepanek, O.; Malberg, J.; Rad, B. R.; Kotora, M.; Wolf, R.; von Wangelin, A. J. *Chem. Sci.* **2013**, *4*, 776. (k) Iwasaki, T.; Takagawa, H.; Singh, S. P.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2013**, *135*, 9604. (l) Przyojski, J. A.; Arman, H. D.; Tonzetich, Z. J. *Organometallics* **2013**, *32*, 723.

(5) For recent examples and leading references of copper-catalyzed Kumada cross-coupling reactions, see: (a) Dohle, W.; Lindsay, D. M.; Knochel, P. *Org. Lett.* **2001**, *3*, 2871. (b) Terao, J.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2003**, *125*, 5646. (c) Terao, J.; Todo, H.; Begum, S. A.; Kuniyasu, H.; Kambe, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 2086. (d) Hintermann, L.; Xiao, L.; Labonne, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 8246. (e) Cahiez, G.; Gager, O.; Buendia, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 1278. (f) Shen, R.; Iwasaki, T.; Terao, J.; Kambe, N. *Chem. Commun.* **2012**, *48*, 9313. (g) Yang, C.-T.; Zhang, Z.-Q.; Liang, J.; Liu, J.-H.; Lu, X.-Y.; Chen, H.-H.; Liu, L. *J. Am. Chem. Soc.* **2012**, *134*, 11124. (h) Kim, J. H.; Chung, Y. K. *Chem. Commun.* **2013**, *49*, 11101.

(6) For reviews and leading references of iron-catalyzed Kumada cross-coupling reactions, see: (a) Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686. (b) Robin, B. B.; Duncan, W. B.; Robert, M. F.; Michael, H. *Chem. Commun.* **2005**, 4161. (c) Cahiez, G.; Habiak, V.; Duplais, C.; Moyeux, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4364. (d) Dongol, K. G.; Koh, H.; Sau, M.; Chai, C. L. L. *Adv. Synth. Catal.* **2007**, *349*, 1015. (e) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500. (f) Noda, D.; Sunada, Y.; Hatakeyama, T.; Nakamura, M.; Nagashima, H. *J. Am. Chem. Soc.* **2009**, *131*, 6078. (g) Czaplik, W. M.; Mayer, M.; Cvengroš, J.; von Wangelin, A. J. *ChemSusChem* **2009**, *2*, 396. (h) Denmark, S. E.; Cresswell, A. J. *J. Org. Chem.* **2013**, *78*, 12593. (i) Guisán-Ceinos, M.; Tato, F.; Buñuel, E.; Calle, P.; Cárdenas, D. J. *Chem. Sci.* **2013**, *4*, 1098. (j) Bedford, R. B.; Brenner, P. B.; Carter, E.; Cogswell, P. M.; Haddow, M. F.; Harvey, J. N.; Murphy, D. M.; Nunn, J.; Woodall, C. H. *Angew. Chem., Int. Ed.* **2014**, *53*, 1804.

(7) For leading references of functionalized Grignard reagents in Kumada cross-coupling reactions, see: (a) Bonnet, V.; Mongin, F.; Trecourt, F.; Queguiner, G.; Knochel, P. *Tetrahedron Lett.* **2001**, *42*, 5717. (b) Dohle, W.; Kopp, F.; Cahiez, G.; Knochel, P. *Synlett* **2001**, 1901. (c) Bonnet, V.; Mongin, F.; Trécourt, F.; Quéguiner, G.; Knochel, P. *Tetrahedron* **2002**, *58*, 4429. (d) Bonnet, V.; Mongin, F.; Trecourt, F.; Breton, G.; Marsais, F.; Knochel, P.; Queguiner, G. *Synlett* **2002**, 1008. (e) Sapountzis, I.; Knochel, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 1610. (f) Kofink, C. C.; Knochel, P. *Org. Lett.* **2006**, *8*, 4121. (g) Martin, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3844. (h) Manolikakes, G.; Knochel, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 205. (i) Vechorkin, O.; Proust, V.; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 9756. (j) Steib, A. K.; Kuzmina, O. M.; Fernandez, S.; Flubacher, D.; Knochel, P. *J. Am. Chem. Soc.* **2013**, *135*, 15346.

(8) For reviews of functionalized Grignard reagents, see: (a) Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 4302. (b) Adrio, J.; Carretero, J. C. *ChemCatChem* **2010**, *2*, 1384.

(9) For asymmetric and stereospecific Kumada cross-coupling of Grignard reagents under nickel or palladium catalysis, see: (a) Kiso, Y.; Tamao, K.; Miyake, N.; Yamamoto, K.; Kumada, M. *Tetrahedron Lett.* **1974**, *15*, 3. (b) Hayashi, T.; Tajika, M.; Tamao, K.; Kumada, M. *J. Am. Chem. Soc.* **1976**, *98*, 3718. (c) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180. (d) Consiglio, G.; Morandini, F.; Piccolo, O. *Tetrahedron* **1983**, *39*, 2699. (e) Hayashi, T.; Hayashizaki, K.; Kiyoi, T.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8153. (f) Hayashi, T.; Hayashizaki, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 215. (g) Pellet-Rostaing, S.; Saluzzo, C.; Ter Halle, R.; Breuzard, J.; Vial, L.; Le Guyader, F.; Lemaire, M. *Tetrahedron: Asymmetry* **2001**, *12*, 1983. (h) Horibe, H.; Fukuda, Y.; Kondo, K.; Okuno, H.; Murakami, Y.; Aoyama, T. *Tetrahedron* **2004**, *60*, 10701. (i) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264. (j) Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389. (k) Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed* **2012**, *51*, 7790. (l) Greene, M. A.; Yonova, I. M.; Williams, F. J.; Jarvo, E. R. *Org. Lett.* **2012**, *14*, 4293. (m) Wu, L.; Salvador, A.; Ou, A.; Shi, M. W.; Skelton, B. W.; Dorta, R. *Synlett* **2013**, *24*, 1215. (n) Yonova, I. M.; Johnson, A. G.; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jarvo, E. R. *Angew. Chem., Int. Ed.* **2014**, *126*, 2454. (o) Tollefson, E. J.; Dawson, D. D.; Osborne, C. A.; Jarvo, E. R. *J. Am. Chem. Soc.* **2014**, *136*, 14951.

(10) For examples of desymmetrization reactions via Kumada coupling, see: (a) Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9101. (b) Kamikawa, T.; Hayashi, T. *Tetrahedron* **1999**, *55*, 3455.

(11) For recent examples and leading references of catalytic asymmetric Negishi cross-coupling reactions, see: (a) Arp, F. O.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 10482. (b) Fischer, C.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 4594. (c) Smith, S. W.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 12645. (d) Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 2756. (e) Lundin, P. M.; Esquivias, J.; Fu, G. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 154. (f) Lin, X.; Sun, J.; Xi, Y.; Lin, D. *Organometallics* **2011**, *30*, 3284. (g) Binder, J. T.; Cordier, C. J.; Fu, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 17003. (h) Choi, J.; Fu, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 9102. (i) Do, H.-Q.; Chandrashekar, E. R. R.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 16288. (j) Cordier, C. J.; Lundgren, R. J.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 10946. (k) Liang, Y.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 5520. (l) Choi, J.; Martín-Gago, P.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 12161.

(12) For recent examples and leading references of catalytic asymmetric Suzuk−Miyaurai cross-coupling reactions, see: (a) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051. (b) Willis, M. C.; Powell, L. H. W.; Claverie, C. K.; Watson, S. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1249. (c) Bermejo, A.; Ros, A.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 15798. (d) Saito, B.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 6694. (e) Sawai, K.; Tatumi, R.; Nakahodo, T.; Fujihara, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6917. (f) Uozumi, Y.; Matsuura, Y.; Arakawa, T.; Yamada, Y. M. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 2708. (g) Lundin, P. M.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 11027. (h) Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 11908. (i) Shen, X.; Jones, G. O.; Watson, D. A.; Bhayana, B.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 11278. (j) Lu, Z.; Wilsily, A.; Fu, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 8154. (k) Yamamoto, T.; Akai, Y.; Nagata, Y.; Suginome, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 8844. (l) Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 5794. (m) Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 570. (n) Cong, H.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 3788.

(13) Landoni, M. F.; Soraci, A. *Curr. Drug Metab.* **2001**, *2*, 37.

(14) For recent and leading references of asymmetric synthesis of α-aryl carboxylic acid derivatives, see: (a) Alper, H.; Hamel, N. *J. Am. Chem. Soc.* **1990**, *112*, 2803. (b) Pai, C.-C.; Lin, C.-W.; Lin, C.-C.; Chen, C.-C.; Chan, A. S. C. *J. Am. Chem. Soc.* **2000**, *122*, 11513. (c) Spielvogel, D. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 3500. (d) Xie, X.; Yu, C.; Ma, D. *J. Am. Chem. Soc.* **2006**, *128*, 16050. (e) Dai, X.; Strotman, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 3302. (f) Bigot, A.; Williamson, A. E.; Gaunt, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 13778. (g) Stivala, C. E.; Zakarian, A. *J. Am. Chem. Soc.* **2011**, *133*, 11936. (h) Huang, Z.; Liu, Z.; Zhou, J. *J. Am. Chem. Soc.* **2011**, *133*, 15882. (i) Harvey, J. S.; Simonovich, S. P.; Jamison, C. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 13782.

(15) (a) Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1435. (b) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775.

(16) For reviews of bisoxazoline ligands in asymmetric catalysis, see: (a) Rechavi, D.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 3467. (b) Desimoni, G.; Faita, G.; Jørgensen, K. A. *Chem. Rev.* **2006**, *106*, 3561. (c) Hargaden, G. C.; Guiry, P. J. *Chem. Rev.* **2009**, *109*, 2505.

(d) Desimoni, G.; Faita, G.; Jørgensen, K. A. *Chem. Rev.* **2011**, *111*, PR284.
(17) Piccolo, O.; Spreafico, F.; Visentin, G.; Valoti, E. *J. Org. Chem.* **1985**, *50*, 3945.
(18) Rubin, A.; Knadler, M. P.; Ho, P. P. K.; Bechtol, L. D.; Wolen, R. L. *J. Pharm. Sci.* **1985**, *74*, 82.
(19) For synthetic approaches of (*S*)-fenoprofen, see: (a) Carde, L.; Davies, H.; Geller, T. P.; Roberts, S. M. *Tetrahedron Lett.* **1999**, *40*, 5421. (b) Smith, C. R.; RajanBabu, T. V. *J. Org. Chem.* **2009**, *74*, 3066.
(20) Tarui, A.; Kondo, S.; Sato, K.; Omote, M.; Minami, H.; Miwa, Y.; Ando, A. *Tetrahedron* **2013**, *69*, 1559.
(21) Martin, N. J. A.; Cheng, X.; List, B. *J. Am. Chem. Soc.* **2008**, *130*, 13862.
(22) Rupe, H.; Gassmann, A. *Helv. Chim. Acta* **1936**, *19*, 569.
(23) (a) Ferreira, L. A. F.; Henriques, O. B.; Andreoni, A. A. S.; Vital, G. R. F.; Campos, M. M. C.; Habermehl, G. G.; De Moraes, V. L. G. *Toxicon* **1992**, *30*, 1211. (b) Hong, C. H.; Noh, M. S.; Lee, W. Y.; Lee, S. K. *Planta Med.* **2002**, *68*, 545. (c) Ji, M.; Choi, J.; Lee, J.; Lee, Y. *Int. J. Mol. Med.* **2004**, *14*, 253.
(24) For asymmetry synthesis of (*S*)-*ar*-turmerone, see: (a) Meyers, A. I.; Smith, R. K. *Tetrahedron Lett.* **1979**, *20*, 2749. (b) Fuganti, C.; Serra, S.; Dulio, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 279. (c) Li, A.; Yue, G.; Li, Y.; Pan, X.; Yang, T.-K. *Tetrahedron: Asymmetry* **2003**, *14*, 75. (d) Rowe, B. J.; Spilling, C. D. *J. Org. Chem.* **2003**, *68*, 9502. (e) Kamal, A.; Malik, M. S.; Azeeza, S.; Bajee, S.; Shaik, A. A. *Tetrahedron: Asymmetry* **2009**, *20*, 1267. (f) Nave, S.; Sonawane, R. P.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2010**, *132*, 17096. (g) Afewerki, S.; Breistein, P.; Pirttilä, K.; Deiana, L.; Dziedzic, P.; Ibrahem, I.; Córdova, A. *Chem.—Eur. J.* **2011**, *17*, 8784. (h) Endo, K.; Hamada, D.; Yakeishi, S.; Shibata, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 606.
(25) Dineen, T. A.; Roush, W. R. *Org. Lett.* **2004**, *6*, 2043.
(26) Abate, A.; Brenna, E.; Negri, C. D.; Fuganti, C.; Serra, S. *Tetrahedron: Asymmetry* **2002**, *13*, 899.