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# Base-promoted lipase-catalyzed kinetic resolution of atropisomeric 1,1'-biaryl-2,2'-diols†

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Herein we report a dramatic acceleration of the lipase-catalyzed kinetic resolution of atropisomeric 1,1′-biaryl-2,2′-diols by the addition of sodium carbonate. This result likely originates from the increased nucleophilicity of the phenolic hydroxyl group toward the acyl-enzyme intermediate. Under these conditions, various substituted  $C_2$ -symmetric and non- $C_2$ -symmetric binaphthols and biphenols were efficiently resolved with  $\sim$ 50% conversion in only 13–30 h with excellent enantioselectivity.

#### Introduction

Axially chiral biaryls are ubiquitous structural motifs in various catalysts, natural products, and pharmaceuticals.1 In particular, optically active atropisomeric 1,1'-biaryl-2,2'-diols (e.g. 1,1'-bi-2naphthols (BINOLs)) have been widely used as chiral ligands for asymmetric transformations and as privileged scaffolds for designing numerous important chiral catalysts/ligands.2 Consequently, the development of efficient enantioselective syntheses of 1,1'-biaryl-2,2'-diols has attracted considerable attention from various research groups.3 Although the enantioselective oxidative coupling of 2-naphthols using chiral transition metals is an atom-economical route, it is mainly applicable to homochiral binaphthols with specific substitution patterns.4 Apart from the kinetic resolution (KR) of racemic precursors via non-enzymatic routes, the lipase-catalyzed KR of racemic atropisomeric 1,1'-biaryl-2,2'-diols has been intensively studied.6 At the core of this, racemic BINOL and its derivatives have been resolved via either hydrolytic (in aqueous media)<sup>7</sup> or acylative (in non-aqueous media) approaches.8,9 In the latter cases, the acylative KR of racemic BINOLs using a lipoprotein lipase from *Pseudomonas* sp. requires long reaction times (3–14 days) to afford the corresponding (R)-mono-esters in 32-53% yields with 90-95% ee and the recovery of (S)-BINOLs with 55-89% ee (E values: 10,11 41-117). 8a,b We believe that acceleration of the resolution process and the expansion of substrate scope are highly demanded to establish a more practical KR. Notably, to the best of our knowledge, none of the existing enzymatic KR protocols has been applied to  $C_1$ -symmetric, i.e. non- $C_2$ symmetric biaryl diols. Therefore, we studied the development modular that a enhances enzymatic

#### Results and discussion

We began this study by investigating the KR parameters of BINOL  $(\pm)$ -1a as a model substrate using either vinyl acetate (10 equiv.) or isopropenyl acetate (10 equiv.) as an acyl donor and the commercially available immobilized *Pseudomonas* sp. lipoprotein lipase (Toyobo LIP301). As shown in Table 1, only 4-30% conversions were achieved after 24 h at the temperature of 35 or 50 °C with lipase loading of 1-3 w/w in spite of the high enantioselectivity (E value = 58->200) (entries 1-6). To realize the requisite rate enhancement, we envisioned that the addition of some basic additives would promote the reaction by enhancing the nucleophilicity of the phenolic hydroxyl group towards an acyl-enzyme intermediate. To our delight, the addition of Na2CO3 (1.5 mol equiv.) at 35 °C dramatically increased the acylation rate while maintaining a substantial level of enantio-discrimination (E value = >200) giving the monoacetate (R)-2a in 50% NMR yield with 99% ee and the recovered (S)-1a in 50% NMR yield with 98% ee (entry 8). This result was reproduced on a larger scale (0.5 mmol of  $(\pm)$ -1a) leading to perfect conversion after 24 h with the formation of (R)-2a (51% isolated yield, 96% ee) and (S)-1a (48% isolated yield, >99% ee) (E = >200) (entry 9). Reducing the amount of Na<sub>2</sub>CO<sub>3</sub> to 0.3 mol equiv. resulted in only 8% conversion after 24 h (entry 10). We could reduce the lipase loading further to 1 w/w and the acyl donor to 5 equiv. at 50 °C to afford both (R)-2a and (S)-1a in high optical purities with 50% conversion (entries 11-12) (cf. previous studies required 4 w/w lipase and 20 equiv. of vinyl acetate<sup>8a,b</sup>). The use of isopropenyl acetate led to a similar rate enhancement with high enantioselectivity (E value = 149) (entry 14).12 In all cases, the formation of diacetate 3a was not observed.

transesterification and also covers a broader range of substituted biaryl diols. In this article, we show that the addition of sodium carbonate dramatically accelerates the KR for a broad range of  $C_1$ -symmetric and  $C_2$ -symmetric atropoisomeric 1,1'-biaryl-2,2'-diols, while maintaining excellent enantiocontrol.

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We also examined the effects of other types of organic and inorganic bases at 35 °C for 24 h (Table 2). Both the conversions and enantioselectivities dropped off sharply when pyridine or Hünig's base were added (entries 2 and 3). Although 48% conversion was attained by adding triethylamine, the enantioselectivity was very poor (entry 4). The conversions did not exceed 13% when Li<sub>2</sub>CO<sub>3</sub>, MgCO<sub>3</sub>, and CaCO<sub>3</sub> were examined despite the high enantioselectivity (entries 5, 7, and 9, respectively). Very low conversion and poor enantioselectivity were obtained upon using Cs<sub>2</sub>CO<sub>3</sub> (entry 10). The use of K<sub>2</sub>CO<sub>3</sub> resulted in 46% conversion with moderate enantiocontrol (E =43) (entry 8). Other sodium salts like NaHCO<sub>3</sub> and Na<sub>2</sub>HPO<sub>4</sub> led to poor conversions after 24 h, albeit in the high E values (>200) (entries 11, 12 and 14). Although Na<sub>3</sub>PO<sub>4</sub> afforded a 52% conversion (entry 13), the resultant enantioselectivity (E = 99)was inferior to that obtained with  $Na_2CO_3$  (E = >200, entry 6).

We found that the poor enantioselectivity caused by triethylamine, K<sub>2</sub>CO<sub>3</sub>, or Cs<sub>2</sub>CO<sub>3</sub>, in comparison to the excellent enantiocontrol in the case of Na<sub>2</sub>CO<sub>3</sub>, was due to the competitive non-enzymatic acetylation. Thus, a similar reaction of  $(\pm)$ -1a in the presence of these bases, while omitting the lipase, resulted in the formation of a mixture of  $(\pm)$ -2a and the diacetate ( $\pm$ )-3a (Table 3, entries 1, 3, and 4), while the formation of diacetate 3a was not detected in the presence of lipase (Table 2, entries 4, 8, and 10). On the other hand, Na<sub>2</sub>CO<sub>3</sub> did not promote any non-enzymatic acylation (entry 2) and has been identified as the ideal base for the enzymatic transformation in terms of both reaction rate and enantioselectivity.

**Table 2** Effect of basic additives on the KR of  $(\pm)$ -1a

Entry	Base	Conv. (%) <sup>a</sup>	(R)-2a (% ee) <sup>b</sup>	(S)-1a (% ee) <sup>b</sup>	E
1 <sup>c</sup>	None	7	>99	8	>200
2	Pyridine	13	91	13	24
3	EtN(iPr) <sub>2</sub>	24	60	19	5
$4^d$	Et <sub>3</sub> N	48	52	48	5
5	Li <sub>2</sub> CO <sub>3</sub>	4	99	4	>200
$6^e$	Na <sub>2</sub> CO <sub>3</sub>	50	99	98	>200
7	$MgCO_3$	13	99	15	>200
$8^d$	$K_2CO_3$	46	90	75	43
9	CaCO <sub>3</sub>	5	99	5	>200
$10^d$	$Cs_2CO_3$	10	18	2	1.5
11	NaHCO <sub>3</sub>	12	99	13	>200
$12^f$	$NaHCO_3$	17	99	20	>200
13	$Na_3PO_4$	52	90	99	99
14	$Na_2HPO_4$	20	99	20	>200

<sup>&</sup>lt;sup>a</sup> Calculated based on the optical purities of (R)-2a and (S)-1a, see ref. 10 and 11a. b Determined by chiral HPLC. From Table 1, entry 2. The formation of diacetate 3a was not observed under these conditions. From Table 1, entry 8. f 3 mol equiv. of NaHCO<sub>3</sub> was added.

Under the optimal conditions obtained using Na<sub>2</sub>CO<sub>3</sub> as the base, various substituted  $C_2$ -symmetric biaryl diols ( $\pm$ )-1b-e were successfully resolved with  $\sim$ 50% conversion in only 16-

**Table 1** Optimization of the lipase-catalyzed KR of BINOL  $(\pm)$ -1 $a^a$ 

Entry	Na <sub>2</sub> CO <sub>3</sub> (mol equiv.)	$LIP301^{b}$ (w/w)	Acyl donor (equiv.)	Temp (°C)	Time (h)	Conv. (%) <sup>c</sup>	$(R)$ -2a $(\% \text{ ee})^d$	(S)-1a (% ee) <sup>d</sup>	$E^e$
1	0	1	Vinyl acetate (10)	35	24	4	>99	4	>200
2	0	3	Vinyl acetate (10)	35	24	7	>99	8	>200
3	0	3	Vinyl acetate (10)	50	24	30	95	40	58
4	0	1	Isopropenyl acetate (10)	35	24	7	98	7	106
5	0	3	Isopropenyl acetate (10)	35	24	8	98	9	108
6	0	3	Isopropenyl acetate (10)	50	24	16	98	18	118
7	1.5	1	Vinyl acetate (10)	35	24	36	99	56	>200
8	1.5	3	Vinyl acetate (10)	35	24	50	99	98	>200
9 <sup>f</sup>	1.5	3	Vinyl acetate (10)	35	24	51	96 (51% yield) <sup>g</sup>	>99 (48% yield) <sup>g</sup>	>200
10	0.3	3	Vinyl acetate (10)	35	24	8	99	8	>200
11	1.5	1	Vinyl acetate (10)	50	24	50	95	94	139
12	1.5	1	Vinyl acetate (5)	50	24	50	96	95	138
13	1.5	1	Isopropenyl acetate (10)	35	24	33	98	49	161
14	1.5	3	Isopropenyl acetate (10)	35	17	50	98	94	149

<sup>&</sup>lt;sup>a</sup> Except for entry 9, the screening was done using ca. 0.03 mmol of  $(\pm)$ -1a. <sup>b</sup> Commercially available immobilized *Pseudomonas* sp. lipoprotein lipase (Toyobo LIP301). Calculated based on the optical purities of (R)-2a and (S)-1a, see ref. 10 and 11a. Determined by chiral HPLC. For E value, see ref. 10 and 11a. f Reaction conducted using 0.5 mmol of  $(\pm)$ -1a. f Isolated yields.

Table 3 Testing the non-enzymatic acetylation of  $(\pm)$ -1a in the presence of bases

Entry	Base	<b>1a</b> (Yield%) <sup>a</sup>	<b>2a</b> (Yield%) <sup>a</sup>	<b>3a</b> (Yield%) <sup>a</sup>
1	$\mathrm{Et_{3}N}$	48	48	4
2	$Na_2CO_3$	100	0	0
3	$K_2CO_3$	0	2	98
4	$Cs_2CO_3$	25	56	19

<sup>&</sup>lt;sup>a</sup> Determined by <sup>1</sup>H NMR analysis of the crude mixture.

30 h with excellent enantioselectivity (E = > 100) (Table 4, entries 1, 2, 4 and 5). Particularly, 6,6'-dimethoxy-1,1'-biphenol (1d) underwent highly enantioselective KR with  $\sim$ 50% conversion after 24 h using lower amounts of lipase (2 w/w) and vinyl acetate (5 equiv.), thus offering an advantage over the reported enzymatic method that required three days using 4 w/w of lipase PS-IM and 1.5 equiv. of vinyl acetate to achieve 41% conversion.8c Notably, the reaction of 1c proceeded very slowly in absence of Na<sub>2</sub>CO<sub>3</sub>; only 10% yield of (R)-2c was obtained after 24 h (entry 3), which again confirms the significance of Na<sub>2</sub>CO<sub>3</sub> in accelerating the resolution process as seen in entry 2. All these reactions led only to the formation of monoacetates (R)-2 without any detectable amount of the corresponding diacetates 3. On the other hand, 3,3'-dibromo-1,1'-binaphthol (1f) did not react at all (entry 6); similar results were obtained using different types of immobilized lipases under different conditions probably due to the steric bulkiness imparted by the substituents at the 3,3'-positions that may retard the acyl transfer from the acyl-enzyme intermediate to the substrate.

The successful application of our method to  $C_1$ -symmetric biaryl diols ( $\pm$ )-1g-k is noteworthy (Table 5). Although they produced a mixture of regioisomeric acetates (R)-2g-k, we found that each isomer has the same (R) absolute configuration and high optical purity. For instance, two acetates (R)-2i were obtained; each of them with 91% ee, and their mixture was subjected to methanolysis to give a single product (R)-1i with 91% ee (Table 5, entry 3). In a similar manner, simple methanolysis of the mixtures of regioisomeric acetates (R)-2g-h and (R)-2j-k afforded (R)-diols (R)-1g-h and (R)-1i-k with complete retention of optical purity (entries 1, 2, 5, and 6). While the reported asymmetric oxidative cross coupling of 2-naphthols afforded (R)-1h with a maximum optical purity of 72% ee, 4e the optimized KR protocol discussed here afforded much higher optical purities for both (R)-1h (95% ee) and (S)-1h (>99%) (entry 2). Importantly, the acetylation of 1i did not proceed in absence of Na<sub>2</sub>CO<sub>3</sub>, reconfirming the necessity to add this base to promote the KR (entry 4). Notably, the reaction worked well for substrates

possessing only one substituent at the 3-position (Table 5, entries 3, 5, and 6).

We further examined the applicability of our method to the biaryl methanol derivative 4a (Table 6). However, the addition of  $Na_2CO_3$  in this case was deleterious to the enantioselectivity, affording the optically inactive product 5a (2% ee, 100% NMR yield) in which the primary hydroxyl group is acetylated (Table 6, entry 1). The 100% conversion is probably due to a concomitant non-enzymatic acetylation of the primary alcohol. The omission of  $Na_2CO_3$  dramatically improved the enantioselectivity (E=34) (entry 2). Lowering the reaction temperature to 25 °C afforded better E value (65) (entry 3); such high enantioselectivity was not realized in previously reported lipase-catalyzed resolution. The protocol was also applied successfully to diol 4b, resulting in high enantioselectivity (E=127) with 50% conversion after 32 h (entry 4).

Based on the results that produced acceleration of the reaction by the addition of Na<sub>2</sub>CO<sub>3</sub> in the case of phenolic substrates 1a-e and 1g-k, we considered the lipase-mediated catalytic cycle for the enantioselective esterification. In principle, the KR cycle begins with the transfer of acyl group from the acyl donor (e.g. vinyl acetate) to the hydroxyl group of serine in the reactive site of lipase to form an acyl-enzyme intermediate,16 which is subsequently attacked by the phenolic hydroxyl group of 1 in an enantioselective manner. Since *Pseudomonas* sp. lipoprotein lipase has been used in the KR of secondary alcohols without Na<sub>2</sub>CO<sub>3</sub> leading to ~50% conversion in shorter time,17 the formation of the acyl-enzyme intermediate is probably not the rate-limiting step. Instead, steric hindrance in the biaryl skeleton of 1 may decelerate the acyl transfer to 1. Moreover, the phenolic hydroxyl groups in 1 are more acidic with less nucleophilicity toward the acylenzyme than the alcoholic hydroxyl groups. This assumption was supported by the results obtained for alcohols 4, in which the addition of Na<sub>2</sub>CO<sub>3</sub> was not required and the acylation occurred on their primary hydroxyl groups with perfect chemoselectivity.

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Table 4 KR of  $C_2$ -symmetric biaryl diols ( $\pm$ )-1b- $\mathbf{f}^a$ 

			(R)-2 <b>b</b> - <b>g</b>		(S)- <b>1b</b> - <b>g</b>		
Entry	Substrate	Temp. and time	Isolated yield (%)	% ee <sup>b</sup>	Isolated yield (%)	% ee <sup>b</sup>	E
1	Br OH OH	50 °C, 29 h	49	95	50	99	>200
2 3 <sup>c</sup>	MeO OH OH	50 °C, 30 h 50 °C, 30 h	54 10	97 99	43 86	99 11	>200 >200
$4^d$	MeO OH OH	35 °C, 24 h	53	89	47	>99	101
5 <sup><i>d</i>,<i>e</i></sup>	OH OH	35 °C, 16 h	52	95	47	97	165
6	OH OH	50 °C, 24 h	No reaction				

<sup>&</sup>lt;sup>a</sup> Reaction was conducted using ( $\pm$ )-**1b-f**(0.1 mmol). <sup>b</sup> Determined by chiral HPLC. <sup>c</sup> In absence of Na<sub>2</sub>CO<sub>3</sub>. <sup>d</sup> 2 w/w LIP301 and 5 equiv. vinyl acetate were used. <sup>e</sup> i-Pr<sub>2</sub>O was used instead of toluene.

It is worth mentioning that the dynamic kinetic resolution (DKR) of secondary alcohols using a combination of ruthenium complexes and lipases has often been performed in the presence of Na<sub>2</sub>CO<sub>3</sub>.<sup>18</sup> Similarly, we also noted the importance of Na<sub>2</sub>CO<sub>3</sub> addition in our recent chemoenzymatic DKR of certain 2,2'-dihydroxy-1,1'-biaryls using a combination of a ruthenium complex and LIP301;<sup>9</sup> however, no clear explanation of the role of such additive has been proposed until now. Herein, we have partially elucidated the impact of this additive in enhancing the KR rate. In addition, the optical purities (76–89% ee) of the compounds 1b, 1c, 1g, and 1i, obtained by our DKR protocol,<sup>9</sup> have been improved to 91–97% ee in this study by modification of the KR conditions.

#### Conclusions

In contrast to the former lipase-catalyzed KRs of atropisomeric 2,2'-dihydroxy-1,1'-biaryls that required long reaction times (3–14 days) and were of limited scope,<sup>8</sup> we have improved the rate of enzymatic KR and expanded its applicability to a range of this class of compounds, such as 1a-e and 1g-k, with  $\sim$ 50% conversions within 30 h and with excellent enantioselectivity (E=101->200). The rate enhancement, realized by the addition of Na<sub>2</sub>CO<sub>3</sub>, is probably due to an improvement in the nucleophilicity of the phenolic hydroxyl group of 1 towards an acylenzyme intermediate. Since there is only one report describing an organocatalyzed resolution of non- $C_2$ -symmetric

Table 5 KR of non- $C_2$ -symmetric biaryl diols ( $\pm$ )- $1g-k^a$ 

			(R)-1g-k		(S)-1g-k			
Entry	Substrate	Temp. and time	Isolated yield (%) <sup>b</sup>	% ee <sup>b</sup>	Isolated yield (%)	% ee <sup>c</sup>	E	
$1^d$	EtO <sub>2</sub> C OH OH	35 °C, 14 h	48	95	51	93	126	
2	F <sub>3</sub> C OH OH	35 °C, 24 h	47	95	40	>99	>200	
$3^{d,e}$ $4^f$	Th Br OH OH	35 °C, 13 h 35 °C, 24 h	48 No reaction	91	44	>99	114	
5	Me OH OH	50 °C, 24 h	45	92	41	99	126	
6	MeO CI OH OH	50 °C, 14 h	43	96	44	99	>200	

<sup>&</sup>lt;sup>a</sup> Reaction was conducted using  $(\pm)$ -1g-k (0.1 mmol). <sup>b</sup> Obtained by methanolysis of a mixture of two regioisomers (R)-2 (for details, see Experimental section), and the optical purity was determined by chiral HPLC after methanolysis. <sup>c</sup> Determined by chiral HPLC. <sup>d</sup> Using 3 mol equiv. Na<sub>2</sub>CO<sub>3</sub>. <sup>e</sup> Using 4 w/w LIP301. <sup>f</sup> In absence of Na<sub>2</sub>CO<sub>3</sub>.

axially chiral dihydroxy biaryl **1i** with moderate enantiose-lectivity (S value = 38),  $^{5a}$  our method shows broader applicability to non- $C_2$ -symmetric dihydroxy biaryls with higher enantioselectivities. The finding described here will also expand

the efficiency of DKR of atropisomers particularly when combined with efficient racemization catalysts. Detailed mechanistic investigation of the effect of  $Na_2CO_3$  is in progress in our laboratory.

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Table 6 KR of biaryl methanol derivatives  $(\pm)$ -4a-b<sup>a</sup>

Entry	Substrate	Na <sub>2</sub> CO <sub>3</sub> (mol equiv.)	Temp. (°C)	Time (h)	Conv. (%) <sup>b</sup>	(R)-5 <b>a</b> - <b>b</b> <sup>c</sup>	$(S)$ -4a- $\mathbf{b}^c$	E
1 2 3	4a 4a 4a 4b	1.5 0 0	35 35 25 25	24 24 48 32	100 57 52 50	2% ee, quant. 68% ee, 57% NMR yield 88% ee, 55% isolated yield 93% ee, 49% isolated yield	ND >99% ee, 43% NMR yield 97% ee, 43% isolated yield 98% ee, 51% isolated yield	ND 34 65 127

<sup>&</sup>lt;sup>a</sup> Reaction was conducted using (±)-4a-b (0.1 mmol). <sup>b</sup> Determined by <sup>1</sup>H NMR analysis of the crude mixture. <sup>c</sup> Optical purity was determined by chiral HPLC. ND: not determined.

#### **Experimental**

#### General considerations

Melting points were determined on a Yanagimoto Melting Point Apparatus and are uncorrected. Infrared (IR) absorption spectra were recorded on a SHIMADZU FTIR-8400S spectrophotometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured on a JEOL JNM-ECA500 (1H: 500 MHz, 13C: 125 MHz) or JEOL JNM-ECS400 (1H: 400 MHz, <sup>13</sup>C: 100 MHz) instrument with chemical shifts reported in  $\delta$  (ppm) relative to the residual nondeuterated solvent signal for  ${}^{1}$ H (CHCl<sub>3</sub>:  $\delta = 7.26$  ppm) and relative to the deuterated solvent signal for <sup>13</sup>C (CDCl<sub>3</sub>:  $\delta = 77.0$  ppm). The mass spectra (MS) were measured on a JEOL JMS-S3000 (MALDI) with TOF mass analyser. HPLC analyses were carried out using a JASCO LC-2000Plus system (HPLC pump: PU-2080, UV detector: MD-2018) equipped with a Daicel CHIRALPAK IC-3, CHIRALPAK AD-3, CHIRALCEL OD-3, CHIRALCEL OZ-3 or CHIRALPAK IE column; each with a size of 4.6 mm × 250 mm. Optical rotations were measured on a JASCO P-1020 polarimeter. Gel permeation chromatography was carried out on LaboACE LC-5060 with JAIGEL-2HR columns (Japan Analytical Industry). The lipase from Pseudomonas sp. (TOYOBO lipoprotein lipase GradeIII LPL-311) immobilized on Hyflo Super-Cel (commercial name: TOYOBO LIP301) was gifted from TOYOBO CO., LTD. Kanto silica gel 60N was used for column chromatography. In general, the reactions were carried out in anhydrous solvents. Racemic substrates 1b, 19 1c, 20 1d, 21 1e, 22 1f, 23 1g, 9 1h, 4e 1i, 24 1j, 23 1k,25 4a,14 and 4b14 were prepared according to reported procedure.

#### Kinetic resolution of $(\pm)$ -1a (Table 1, entry 9)

To a stirred solution of ( $\pm$ )-1a (143 mg, 0.50 mmol) and vinyl acetate (0.46 mL, 5.0 mmol) in anhydrous PhCH<sub>3</sub> (5.0 mL, 0.10 M) were added LIP301 (0.43 g, 3 w/w) and Na<sub>2</sub>CO<sub>3</sub> (80 mg, 0.75 mmol). After being stirred for 24 h at 35 °C, the reaction mixture was filtered through a Celite pad. The Celite pad was washed

with EtOAc and the combined filtrate was evaporated *in vacuo*. The residue was purified by flash column chromatography (hexanes/EtOAc = 8:1) to give ester (R)-2a (84 mg, 51% yield, 96% ee) and recovered (S)-1a (68 mg, 48% yield, >99% ee).

(*R*)-2'-Hydroxy-(1,1'-binaphthalen)-2-yl acetate (*R*)-2a. White solid; mp 56–57 °C (lit.9 mp 55–58 °C);  $[\alpha]_{\rm D}^{22}$  + 84.7 (c 1.01, CHCl<sub>3</sub>) (lit.9 $[\alpha]_{\rm D}^{20}$  + 76 (c 1.08, CHCl<sub>3</sub>) for (*R*)-2a with 99% ee); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.07 (d, J = 8.5 Hz, 1H), 7.97 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 8.5 Hz, 1H), 7.51 (td, J = 7.5, 1.5 Hz, 1H), 7.40 (d, J = 9.0 Hz, 1H), 7.31–7.36 (m, 3H), 7.23–7.26 (m, 3H), 7.03 (d, J = 7.5 Hz, 1H), 5.20 (s, 1H), 1.87 (s, 3H). The spectroscopic data are in good agreement with those reported.9 Its optical purity (96% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min $^{-1}$ ; retention times: 8.0 min (*R*), 10.7 min (*S*)).

(*S*)-1,1'-Bi-2-naphthol (*S*)-1a. White solid; mp 205–207 °C (lit.²6 mp 207–210 °C);  $[\alpha]_{\rm D}^{22} - 34.7$  (c 1.02, THF) (lit.²6  $[\alpha]_{\rm D}^{21} - 34$  (c 1.00, THF) for (*S*)-1a with 99% ee); ¹H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.99 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.0 Hz, 2H), 7.36–7.40 (m, 4H), 7.30–7.33 (m, 2H), 7.16 (d, J = 8.5 Hz, 2H), 5.06 (s, 2H). The spectroscopic data are in good agreement with those reported.²7 Its optical purity (>99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 14.5 min (R), 20.8 min (S)).

#### Kinetic resolution of $C_2$ -symmetric biaryl diols ( $\pm$ )-1b-f (Table 4)

Representative procedure A (Table 4, entry 2). To a stirred solution of ( $\pm$ )-1c (34.6 mg, 0.10 mmol) and vinyl acetate (93 µL, 1.0 mmol) in anhydrous PhCH $_3$  (1.0 mL, 0.10 M) were added LIP301 (133 mg, 3 w/w) and Na $_2$ CO $_3$  (15.9 mg, 0.15 mmol). After being stirred for 30 h at 50 °C, the reaction mixture was filtered through a Celite pad. The Celite pad was washed with EtOAc and the combined filtrate was evaporated *in vacuo*. The residue was purified by preparative thin layer chromatography (PTLC)

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(PhCH<sub>3</sub>/EtOAc = 8:1) to give ester (R)-2c (21 mg, 54% yield, 97% ee) and recovered (S)-1c (14.8 mg, 43% yield, 99% ee).

(R)-2'-Hydroxy-7,7'-dimethoxy-(1,1'-binaphthalen)-2-yl acetate (R)-2c. White solid; mp 47-49 °C;  $[\alpha]_D^{20}$  - 40.8 (c 0.24, CHCl<sub>3</sub>); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.00 (d, J = 9.0 Hz, 1H), 7.88 (d, J =9.0 Hz, 1H), 7.83 (d, I = 9.0 Hz, 1H), 7.76 (d, I = 9.0 Hz, 1H), 7.28 (d, J = 1.0 Hz, 1H), 7.17-7.20 (m, 2H), 7.01 (dd, J = 9.0, 3.0 Hz,1H), 6.59 (d, I = 2.0 Hz, 1H), 6.40 (d, I = 2.0 Hz, 1H), 5.17 (s, 1H), 3.58 (s, 3H), 3.57 (s, 3H), 1.85 (s, 3H); <sup>13</sup>C-NMR (100 MHz,  $CDCl_3$ )  $\delta$  170.3, 158.9, 158.3, 152.1, 148.6, 134.8, 134.7, 130.4, 130.1, 129.8, 129.5, 127.6, 124.3, 121.7, 119.3, 118.8, 115.50, 115.46, 113.2, 104.0, 103.6, 55.1, 55.0, 20.4; IR (CHCl<sub>3</sub>)  $\nu$  3545, 1755 cm<sup>-1</sup>; HRMS (MALDI) m/z calcd for  $C_{24}H_{20}O_5$  [M]<sup>+</sup>: 388.1305, found: 388.1304. Its optical purity (97% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 92.5:7.5; flow rate: 1.0  $mL min^{-1}$ ; retention times: 8.6 min (R), 12.4 min (S)).

(S)-7,7'-Dimethoxy-1,1'-bi-2-naphthol (S)-1c. White solid; mp 62-63 °C;  $[\alpha]_D^{20}$  + 152.5 (c 0.31, CHCl<sub>3</sub>) (lit. <sup>28</sup>  $[\alpha]_D^{22}$  + 122.3 (c 1.0, CHCl<sub>3</sub>) for (S)-1c with 94% ee);  ${}^{1}$ H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.88 (d, J = 9.0 Hz, 2H), 7.79 (d, J = 9.0 Hz, 2H), 7.22 (d, J = 9.0 Hz, 2H)2H), 7.04 (dd, J = 9.0, 3.0 Hz, 2H), 6.48 (d, J = 3.0 Hz, 2H), 5.07 (s, 2H), 3.58 (s, 6H). The spectroscopic data are in good agreement with those reported.28 Its optical purity (99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 80:20; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 7.3 min (R), 9.4 min (S)).

**Table 4, entry 1.** Following the above-mentioned procedure A for KR,  $(\pm)$ -1b (44.4 mg, 0.10 mmol) was converted to (R)-2b (24 mg, 49% yield, 95% ee) and (S)-1b (22 mg, 50% yield, 99% ee), after purification of the crude reaction mixture by PTLC  $(PhCH_3/EtOAc = 8:1).$ 

(R)-7,7'-Dibromo-2'-hydroxy-(1,1'-binaphthalen)-2-yl acetate (R)-**2b.** White solid; mp 65–67 °C;  $[\alpha]_D^{23}$  – 75.7 (c 0.63, CHCl<sub>3</sub>); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.05 (d, J = 9.0 Hz, 1H), 7.89 (d, J =9.0 Hz, 1H), 7.85 (d, J = 9.0 Hz, 1H), 7.73 (d, J = 9.0 Hz, 1H), 7.61 (dd, J = 9.0, 2.0 Hz, 1H), 7.33-7.44 (m, 4H), 7.13 (d, J = 2.0 Hz, 1.00 Hz)1H), 5.25 (s, 1H), 1.87 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.3, 152.6, 148.9, 134.54, 134.50, 131.1, 130.73, 130.68, 130.03, 130.01, 129.8, 127.4, 127.2, 126.2, 122.4, 122.2, 121.9, 121.5, 118.9, 112.7, 20.4 (two peaks are overlapped); IR (CHCl<sub>3</sub>)  $\nu$  $3529, 1754 \text{ cm}^{-1}$ ; HRMS (MALDI) m/z calcd for  $C_{22}H_{12}O_3Na^{79}Br_2$  $[M + Na]^+$ : 506.9202, found: 506.9198. Its optical purity (95% ee) was determined by chiral HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol) = 97.5 : 2.5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 8.3 min for (R)-2b, 11.4 min for (S)-2b.

(S)-7,7'-Dibromo-1,1'-bi-2-naphthol (S)-1b. White solid; mp 136–138 °C;  $[\alpha]_D^{23}$  + 263 (c 0.75, CHCl<sub>3</sub>) (lit.<sup>28</sup>  $[\alpha]_D^{21}$  + 129.1 (c 1.8, CHCl<sub>3</sub>) for (S)-1b with 73% ee);  ${}^{1}$ H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 (d, J = 9.0 Hz, 2H), 7.77 (d, J = 9.0 Hz, 2H), 7.48 (dd, J = 9.0,2.0 Hz, 2H, 7.38 (d, J = 9.0 Hz, 2H), 7.23 (d, J = 2.0 Hz, 2H), 5.04(s, 2H). The spectroscopic data are in good agreement with those reported.28 Its optical purity (99% ee) was determined by chiral HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 97.5:2.5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 29.2 min for (R)-1b; 31.6 min for (S)-1b).

Table 4, entry 4. Following the above-mentioned procedure A for KR,  $(\pm)$ -1d (24.6 mg, 0.10 mmol) was converted to (R)-2d (15.0 mg, 53% yield, 89% ee) and (S)-1d (12.0 mg, 47% yield, >99% ee), after purification of the crude reaction mixture by flash column chromatography ( $CH_2Cl_2/Et_2O = 20:1$ ).

(R)-2'-Hydroxy-6,6'-dimethoxy-(1,1'-biphenyl)-2-yl acetate (R)-**2d.** Colorless oil;  $[\alpha]_D^{21}$  + 93.4 (c 0.63, CHCl<sub>3</sub>) (lit. \*c  $[\alpha]_D^{20}$  + 91.2 (c 0.70, CHCl<sub>3</sub>) for (R)-2d with 98% ee); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.42 (t, J = 8.0 Hz, 1H), 7.24 (t, J = 8.0 Hz, 1H), 6.92–6.94 (m, 1H), 6.83–6.85 (m, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.55 (dd, J = 8.0, 1.0 Hz, 1H), 5.01 (s, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.96 (s, 3H). The spectroscopic data are in good agreement with those reported.8c Its optical purity (89% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2propanol = 92:8; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 29.1 min (R), 32.2 min (S)).

(S)-2,2'-Dihydroxy-6,6'-dimethoxy-1,1'-biphenyl (S)-1d. White solid; mp 138–140 °C;  $[\alpha]_D^{21}$  – 102 (c 0.64, CHCl<sub>3</sub>) (lit.<sup>21</sup>  $[\alpha]_D^{20}$  –  $144 (c 0.77, CHCl_3)$  for (S)-1d with 98.6% ee);  $^{1}$ H-NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.31 (t, J = 8.0 Hz, 2H), 6.72 (d, J = 8.0 Hz, 2H), 6.62 (d, J= 8.0 Hz, 2H, 5.05 (s, 2H), 3.77 (s, 6H). The spectroscopic data are in good agreement with those reported.21 Its optical purity (>99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 85:15; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 12.9 min (R), 18.9 min (S)).

Table 4, entry 5. Following the above-mentioned procedure A for KR,  $(\pm)$ -1e (21.4 mg, 0.10 mmol) was converted to (R)-2e (13.5 mg, 52% yield, 95% ee) and (S)-1e (10.1 mg, 47% yield, 97% ee), after purification of the crude reaction mixture by flash column chromatography (hexanes/EtOAc = 8:1).

(R)-2,2'-Dihydroxy-6,6'-dimethyl-1,1'-biphenyl (R)-2e. Colorless oil;  $[\alpha]_D^{22}$  + 36.8 (c 0.63, CHCl<sub>3</sub>); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.37 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.17 (t, J = 8.0 Hz, 2H)1H), 7.00 (d, J = 8.0 Hz, 1H), 6.83-6.86 (m, 2H), 4.82 (s, 1H), 2.04(s, 3H), 1.94 (s, 3H), 1.91 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.5, 153.0, 149.6, 140.1, 137.6, 129.5, 129.1, 128.5, 128.3, 122.7, 122.1, 120.0, 113.9, 20.3, 19.6, 19.4; IR (CHCl<sub>3</sub>) ν 3532, 1744 cm<sup>-1</sup>; HRMS (MALDI) m/z calcd for  $C_{16}H_{16}O_3Na [M + Na]^+$ : 279.0997, found: 279.0992. Its optical purity (95% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 99 : 1; flow rate: 1.0 mL min<sup>-1</sup>; retention times:  $13.7 \min(R)$ ,  $16.9 \min(S)$ ).

(S)-2'-Hydroxy-6,6'-dimethyl-(1,1'-biphenyl)-2-yl acetate (S)-1e. White solid; mp 122–124 °C (lit.<sup>29</sup> mp 159–160 °C);  $[\alpha]_D^{21}$  – 54.3 (c 0.50, CHCl<sub>3</sub>) (lit.<sup>23</sup>  $[\alpha]_D^{20}$  –60.5 (c 1.0, CHCl<sub>3</sub>) for (S)-1e with >99% ee); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.21–7.27 (m, 2H), 6.86–6.92 (m, 4H), 4.71 (brs, 2H), 2.01 (s, 6H). The spectroscopic data are in good agreement with those reported.29 Its optical purity (97% ee) was determined by HPLC analysis at 20 °C using a CHIRALCEL OZ-3 column (hexanes/2-propanol = 95:5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 7.5 min (R), 10.4 min (S)).

#### Kinetic resolution of non $C_2$ -symmetric biaryl diols ( $\pm$ )-1g-k (Table 5)

Representative procedure B (Table 5, entry 3). To a stirred solution of ( $\pm$ )-1i (36.5 mg, 0.10 mmol) and vinyl acetate (93  $\mu$ L, **RSC Advances** 

1.0 mmol) in anhydrous PhCH<sub>3</sub> (1.0 mL, 0.10 M) were added LIP301 (146 mg, 4 w/w) and Na<sub>2</sub>CO<sub>3</sub> (32 mg, 0.30 mmol). After being stirred for 13 h at 35 °C, the reaction mixture was filtered through a Celite pad. The Celite pad was washed with EtOAc and the combined filtrate was evaporated in vacuo. The residue was purified by PTLC (PhCH<sub>3</sub>/EtOAc = 10:1) to give a 3:2mixture of two regioisomeric esters (R)-2i (19.5 mg, 48% yield, 91% ee for each regioisomer) in addition to recovered (S)-1i (16.0 mg, 44% yield, >99% ee). The mixture of regioisomers (R)-2i was subjected to methanolysis as follows: to a stirred solution of (R)-2i (19.5 mg, 0.048 mmol, 91% ee) in MeOH (1.0 mL) was added  $K_2CO_3$  (28 mg, 0.20 mmol). After being stirred for 15 min at room temperature, the reaction mixture was acidified with 1 N HCl and diluted with CH2Cl2. The mixture was transferred to a separating funnel and the organic layer was washed with brine. The organic layer was separated, dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo to give (R)-1i (17.4 mg, 48% yield from  $(\pm)$ -1i, 91% ee) as a pure pale-yellow solid.

(*R*)-3-Bromo-2'-hydroxy-(1,1'-binaphthalen)-2-yl acetate and (*R*)-3'-bromo-2'-hydroxy-(1,1'-binaphthalen)-2-yl acetate (*R*)-2i. Pale yellow solid; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ 8.35 (s, 0.4H), 8.22 (s, 0.6H), 8.07 (d, J = 9.0 Hz, 0.6H), 7.97 (d, J = 8.0 Hz, 0.6H), 7.92 (d, J = 9.0 Hz, 0.4H), 7.89 (d, J = 9.0 Hz, 0.4H), 7.86 (d, J = 8.0 Hz, 0.4H), 7.78 (d, J = 8.0 Hz, 0.6H), 7.51 (m, 1H), 7.43 (d, J = 9.0 Hz, 0.6H), 7.32–7.37 (m, 2.4H), 7.25–7.28 (m, 1H), 7.22 (d, J = 9.0 Hz, 0.6H) 7.20 (d, J = 9.0 Hz, 0.4H), 7.04 (d, J = 9.0 Hz, 0.6H), 7.01 (d, J = 9.0, 0.4H), 5.30–5.64 (brs, 1H), 1.97 (s, 1.2H), 1.88 (s, 1.8H). Its optical purity (91% ee) was determined by HPLC analysis at 20 °C using a CHIRALCEL IC-3 column (hexanes/2-propanol) = 95:5; flow rate: 1.0 mL min<sup>-1</sup>; retention times for (*R*)-regioisomers of 2i: 6.7 min and 8.9 min; retention times for (*S*)-regioisomers of 2i: 8.0 min and 10.0 min.

(*R*)-3-*Bromo-1*, 1'-bi-2-naphthol (*R*)-1i. White solid; mp 82–89 °C (lit.9 mp 130–132 °C);  $[\alpha]_D^{23}$  + 56.5 (*c* 0.28, CHCl<sub>3</sub>) (lit.9  $[\alpha]_D^{20}$  + 38.3 (*c* 0.23, CHCl<sub>3</sub>) for (*R*)-1i with 86% ee); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.28 (s, 1H), 7.98 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.28–7.42 (m, 5H), 7.14 (d, J = 7.0 Hz, 1H), 7.10 (d, J = 9.0 Hz, 1H), 5.58 (s, 1H), 4.95 (s, 1H). The spectroscopic data are in good agreement with those reported.9 Its optical purity (91% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min  $^{-1}$ ; retention times: 10.1 min (*R*), 27.0 min (*S*)).

(S)-3-Bromo-1,1'-bi-2-naphthol (S)-1i. White solid; mp 64-68 °C;  $[\alpha]_D^{24}$  – 64.1 (c 0.39, CHCl<sub>3</sub>). Its spectroscopic data are in good agreement with those described above for (R)-1i. Its optical purity (>99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 11.4 min (R), 26.5 min (S)).

**Table 5, entry 1.** Following the above-mentioned procedure B,  $(\pm)$ -1g (36 mg, 0.10 mmol) was treated with vinyl acetate (93  $\mu$ L, 1.0 mmol) and LIP301 (108 mg, 3 w/w) and Na<sub>2</sub>CO<sub>3</sub> (32 mg, 0.30 mmol) to give (*R*)-2g (19.2 mg, 48% yield) and (*S*)-1g (18.0 mg, 51% yield, 93% ee) after purification of the crude reaction mixture by PTLC (PhCH<sub>3</sub>/EtOAc = 10 : 1). Methanolysis

of (*R*)-2g (19.2 mg, 0.048 mmol), as described above, afforded (*R*)-1g (17.0 mg, 48% yield from  $(\pm)$ -1g, 95% ee).

Ethyl (R)-2-acetoxy-2'-hydroxy-(1,1'-binaphthalene)-6-carboxylate and ethyl (R)-2'-acetoxy-2-hydroxy-(1,1'-binaphthalene)-6-carboxylate (R)-2g. Pale yellow solid; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ 8.58 (d, J=2.0 Hz, 0.3H), 8.48 (d, J=1.0 Hz, 0.7H), 8.04 (d, J=9.0 Hz, 0.3H), 7.95 (d, J=9.0 Hz, 0.7H), 7.88 (d, J=9.0 Hz, 0.7H), 7.84 (d, J=9.0 Hz, 0.7H), 7.76-7.79 (m, 0.6H), 7.73 (d, J=8.0 Hz, 0.3H), 7.70 (dd, J=9.0, 2.0 Hz, 0.7H), 7.37-7.40 (m, 0.7H), 7.33 (d, J=9.0 Hz, 0.3H), 7.19-7.28 (m, 1.7H), 7.16 (d, J=9.0 Hz, 0.3H), 7.07-7.13 (m, 1H), 6.93 (d, J=9.0 Hz, 0.7H), 6.84 (d, J=8.0 Hz, 0.3H), 5.07-5.26 (m, 1H), 4.24-4.31 (m, 2H), 1.74 (s, 0.9H), 1.72 (s, 2.1H), 1.27 (m, 3H).

Ethyl (R)-2,2'-dihydroxy-(1,1'-binaphthalene)-6-carboxylate (R)-1g. White solid; mp 83–85 °C (lit.9 mp 98–100 °C);  $[\alpha]_D^{22}$  – 72.8 (c 0.39, CHCl<sub>3</sub>) (lit.9  $[\alpha]_D^{21}$  – 54.6 (c 0.7, CHCl<sub>3</sub>) for (R)-1g with 89% ee); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.60 (s, 1H), 8.06 (d, J = 9.0 Hz, 1H), 7.98 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 9.0 Hz, 1H), 7.84 (dd, J = 9.0, 2.0 Hz, 1H), 7.43 (d, J = 9.0 Hz, 1H), 7.36–7.39 (m, 2H), 7.31 (td, J = 7.0, 2.0 Hz, 1H), 7.16 (d, J = 9.0 Hz, 1H), 7.09 (d, J = 9.0 Hz, 1H), 5.31 (s, 2H), 5.21 (s, 1H), 4.38 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H). The spectroscopic data are in good agreement with those reported.9 Its optical purity (95% ee) was determined by HPLC analysis at 20 °C using a CHIRALCEL OD-3 column (hexanes/2-propanol = 85 : 15; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 19.5 min (R), 14.0 min (S)).

Ethyl (S)-2,2'-dihydroxy-(1,1'-binaphthalene)-6-carboxylate (S)-1g. White solid; mp 93–95 °C;  $[\alpha]_D^{21}$  + 67.5 (c 0.82, CHCl<sub>3</sub>). Its spectroscopic data are in good agreement with those described above for (R)-1g. Its optical purity (93% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 85 : 15; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 18.8 min (R), 12.9 min (S)).

Table 5, entry 2. Following the above-mentioned procedure B, ( $\pm$ )-1h (49.8 mg, 0.10 mmol) was treated with vinyl acetate (93 μL, 1.0 mmol) and LIP301 (149 mg, 3 w/w) and Na<sub>2</sub>CO<sub>3</sub> (16.0 mg, 0.15 mmol) to give to (R)-2h (25.4 mg, 47% yield) and (S)-1h (20.1 mg, 40% yield, >99% ee), after purification of the crude reaction mixture by flash column chromatography (PhCH<sub>3</sub>/EtOAc = 20 : 1). Methanolysis of (R)-2h (25.4 mg, 0.047 mmol), as described above, afforded (R)-1h (23.0 mg, 47% yield from ( $\pm$ )-1h, 95% ee).

(R)-6-(3,5-Bis(trifluoromethyl)phenyl)-2'-hydroxy-(1,1'-binaphthalen)-2-yl acetate and (R)-6'-(3,5-bis(trifluoromethyl)phenyl)-2'-hydroxy-(1,1'-binaphthalen)-2-yl acetate (R)-2h. Pale yellow solid.  $^{1}$ H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.85–8.22 (m, 7H), 7.35–7.58 (m, 5H), 7.25–7.30 (m, 1H), 7.18 (d, J=9.0 Hz, 0.7H), 7.04 (d, J=8.0 Hz, 0.3H), 5.32 (s, 0.7H), 5.23 (s, 0.3H), 1.91 (s, 2H), 1.90 (s, 1H).

(*R*)-6-(3,5-Bis(trifluoromethyl)phenyl)-1,1'-bi-2-naphthol (*R*)-1*h*. White solid; mp 94–95 °C;  $[\alpha]_D^{22}$  – 71.2 (*c* 0.86, CHCl<sub>3</sub>) (lit.<sup>4e</sup>  $[\alpha]_D^{22}$  – 39.8 (*c* 5.53, CHCl<sub>3</sub>) for (*R*)-1*h* with 72% ee); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 8.06–8.12 (m, 4H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.87 (s, 1H), 7.53 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.40 (d, *J* = 9.0 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 1H), 5.18

(s, 1H), 5.06 (s, 1H). The spectroscopic data are in good agreement with those reported. Its optical purity (95% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95:5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 9.4 min (R), 11.9 min (S)).

(*S*)-6-(3,5-*Bis*(trifluoromethyl)phenyl)-1,1'-bi-2-naphthol (*S*)-1*h*. White solid; mp 91–93 °C;  $[\alpha]_D^{22}$  + 69.1 (*c* 0.97, CHCl<sub>3</sub>). Its spectroscopic data are in good agreement with those described above for (*R*)-1*h*. Its optical purity (>99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 9.7 min (*R*), 11.6 min (*S*)).

**Table 5, entry 5.** Following the above-mentioned procedure B,  $(\pm)$ -1j (30.0 mg, 0.10 mmol) was treated with vinyl acetate (93  $\mu$ L, 1.0 mmol) and LIP301 (90 mg, 3 w/w) and Na<sub>2</sub>CO<sub>3</sub> (16.0 mg, 0.15 mmol) to give to (*R*)-2j (15.4 mg, 45% yield) and (*S*)-1j (12.4 mg, 41% yield, 99% ee) after purification of the crude reaction mixture by gel permeation chromatography using chloroform as an eluent. Methanolysis of (*R*)-2j (15.4 mg, 0.045 mmol) as described above, afforded (*R*)-1j (13.4 mg, 45% yield from  $(\pm)$ -1j, 92% ee).

(*R*)-2-Hydroxy-3'-methyl-(1,1'-binaphthalen)-2-yl acetate and (*R*)-2'-hydroxy-3'-methyl-(1,1'-binaphthalen)-2-yl acetate (*R*)-2*j*. White solid; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.07 (d, J = 9.0 Hz, 0.7H), 7.97 (d, J = 8.0 Hz, 0.7H), 7.85–7.92 (m, 1H), 7.78 (d, J = 8.0 Hz, 0.7H), 7.53–7.16 (m, 6.2H), 7.03 (d, J = 8.6 Hz, 0.3H), 6.97 (d, J = 9.0 Hz, 0.7H), 5.21 (s, 1H), 2.50 (s, 2.1H), 2.44 (s, 0.9H), 1.87 (s, 2.1H), 1.86 (s, 0.9H).

(*R*)-3-Methyl-1,1'-bi-2-naphthol (*R*)-1*j*. White solid; mp 94–96 °C;  $[\alpha]_D^{22} + 17.4$  (c 0.75, CDCl<sub>3</sub>) (lit.<sup>30</sup>  $[\alpha]_D^{20} + 22.1$  (c 1.5, CDCl<sub>3</sub>) for (*R*)-1*j* with 95% ee); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.98 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.81–7.83 (m, 2H), 7.29–7.40 (m, 4H), 7.23–7.26 (m, 1H), 7.15 (d, J = 9.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 5.12 (brs, 1H), 5.07 (brs, 1H), 2.52 (s, 3H). The spectroscopic data are in good agreement with those reported.<sup>30</sup> Its optical purity (92% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 6.0 min (*R*), 9.3 min (*S*)).

(*S*)-3-Methyl-1,1'-bi-2-naphthol (*S*)-1j. White solid; mp 93–99 °C;  $[\alpha]_D^{22}$  – 19.4 (*c* 0.75, CDCl<sub>3</sub>). Its spectroscopic data are in good agreement with those described above for (*R*)-1j. Its optical purity (99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IC-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 6.1 min (*R*), 9.4 min (*S*)).

**Table 5, entry 6.** Following the above-mentioned procedure B,  $(\pm)$ -**1k** (41.4 mg, 0.10 mmol) was treated with vinyl acetate (93 μL, 1.0 mmol) and LIP301 (124 mg, 3 w/w) and Na<sub>2</sub>CO<sub>3</sub> (16 mg, 0.15 mmol) to give to (R)-**2k** (19.6 mg, 43% yield) and (S)-**1k** (18.2 mg, 44% yield, 99% ee), after purification of the crude reaction mixture by PTLC (PhCH<sub>3</sub>/EtOAc = 10:1). Methanolysis of (R)-**2k** (19.6 mg, 0.043 mmol), as described above, afforded (R)-**1k** (17.9 mg, 43% yield from ( $\pm$ )-**1k**, 96% ee).

(R)-6-Bromo-1-(2,5-dichloro-6-hydroxy-3-methoxyphenyl)naphthalen-2-yl acetate and (R)-2-(6-bromo-2-hydroxynaphthalen-1-yl)-3,6-dichloro-4-methoxyphenyl acetate (R)-2k. Pale yellow solid;  $^1$ H-NMR (500 MHz, CDCl $_3$ )  $\delta$  8.08 (d, J=2.0 Hz, 0.2H),

8.96 (d, J = 2.0 Hz, 0.8H), 7.89 (d, J = 9.0 Hz, 0.2H), 7.74 (d, J = 9.0 Hz, 0.8H), 7.49 (dd, J = 9.0, 2.0 Hz, 0.2H), 7.38–7.43 (m, 1H), 7.25–7.27 (m, 0.8H), 7.21 (s, 0.8H), 7.19 (d, J = 8.0 Hz, 0.2H), 7.10 (s, 0.2H), 7.01 (d, J = 9.0 Hz, 0.8H), 5.23–5.30 (brs, 1H), 3.99 (s, 2.4H), 3.93 (s, 0.6H), 2.11 (s, 0.6H), 1.86 (s, 2.4H).

(*R*)-6-Bromo-1-(2,5-dichloro-6-hydroxy-3-methoxyphenyl)naphthalen-2-ol (*R*)-1*k*. White solid; mp 72–74 °C;  $[\alpha]_D^{22}$  + 20.2 (c 0.83, CHCl<sub>3</sub>); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.00 (d, J = 2.0 Hz, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.44 (dd, J = 9.0, 2.0 Hz, 1H), 7.30 (d, J = 9.0 Hz, 1H), 7.14 (s, 1H), 7.08 (d, J = 9.0 Hz, 1H), 5.12 (s, 1H), 5.03 (s, 1H), 3.95 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  151.4, 149.9, 144.6, 130.9, 130.5, 130.3, 130.24, 130.20, 125.5, 123.3, 121.6, 119.0, 118.9, 117.7, 113.7, 113.0, 56.9; IR (neat)  $\nu$  3517 cm<sup>-1</sup>; HRMS (MALDI) m/z calcd for  $C_{17}H_{11}^{79}Br^{35}Cl_2O_3$  [M]\*: 411.9263, found: 411.9263. Its optical purity (96% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IE column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 22.3 min (*R*), 26.8 min (*S*)).

(S)-6-Bromo-1-(2,5-dichloro-6-hydroxy-3-methoxyphenyl)napht-halen-2-ol (S)-1k. White solid; mp 65–68 °C;  $[\alpha]_{\rm D}^{22}-22.7$  (c 0.81, CHCl<sub>3</sub>). Its spectroscopic data are in good agreement with those described above for (R)-1k. Its optical purity (99% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK IE column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 22.5 min (R), 24.7 min (S)).

# Kinetic resolution of biaryl methanol derivatives ( $\pm$ )-4a-b (Table 6)

Representative procedure C: Table 6, entry 3. To a stirred solution of ( $\pm$ )-4a (28 mg, 0.10 mmol) and vinyl acetate (93  $\mu$ L, 1.0 mmol) in anhydrous PhCH<sub>3</sub> (1.0 mL, 0.10 M) was added LIP301 (84 mg, 3 w/w). After being stirred for 48 h at 25 °C, the reaction mixture was filtered through a Celite pad. The Celite pad was washed with EtOAc and the combined filtrate was evaporated *in vacuo*. The residue was purified by flash column chromatography (hexanes/EtOAc = 3:1) to give ester (R)-5a (18.1 mg, 55% yield, 88% ee) and recovered (S)-4a (12.0 mg, 43% yield, 97% ee).

(*R*)-(1-(2-Hydroxy-4,6-dimethylphenyl)naphthalen-2-yl)methyl acetate (*R*)-5a. Colorless oil;  $[\alpha]_{\rm D}^{23} - 22.9$  (c 0.79, CHCl<sub>3</sub>); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ 7.95 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 8.5 Hz, 1H), 7.50–7.53 (m, 1H), 7.39–7.42 (m, 2H), 6.77 (s, 1H), 6.75 (s, 1H), 4.99 (d, J = 12.5 Hz, 1H), 4.96 (d, J = 12.5 Hz, 1H), 4.54 (s, 1H), 2.38 (s, 3H), 2.05 (s, 3H), 1.79 (s, 3H); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>) δ 170.9, 153.1, 139.4, 137.9, 133.6, 133.3, 132.5, 132.1, 129.0, 128.2, 127.1, 126.6, 126.1, 125.5, 123.3, 120.3, 113.9, 64.8, 21.3, 20.8, 19.7; IR (CHCl<sub>3</sub>)  $\nu$  3548, 1737 cm<sup>-1</sup>; HRMS (MALDI) *m/z* calcd for C<sub>21</sub>H<sub>20</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 343.1310, found: 343.1305. Its optical purity (88% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK AD-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 15.5 min (*R*), 17.5 min (*S*)).

(S)-2-(2-(Hydroxymethyl)naphthalen-1-yl)-3,5-dimethylphenol (S)-4a. White solid; mp 140–141 °C;  $[\alpha]_D^{23}$  + 32.6 (c 0.75, CHCl<sub>3</sub>) (lit.  $[\alpha]_D^{20}$  + 21.9 (c 0.8, CHCl<sub>3</sub>) for (S)-4a with 79% ee);  $^1$ H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.0 Hz,

1H), 7.72 (d, J = 8.0 Hz, 1H), 7.48–7.51 (m, 1H), 7.38–7.39 (m, 2H), 6.79 (s, 1H), 6.75 (s, 1H), 4.53 (s, 2H), 2.38 (s, 3H), 1.80 (s, 3H). The spectroscopic data are in good agreement with those reported. Its optical purity (97% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK AD-3 column (hexanes/2-propanol = 85 : 15; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 8.8 min (R), 11.2 min (S)).

**Table 6, entry 4.** Following procedure C described above,  $(\pm)$ -**4b** (27.8 mg, 0.10 mmol) was converted to (R)-**5b** (15.7 mg, 49% yield, 93% ee) and (S)-**4b** (14.2 mg, 51% yield, 98% ee), after purification of the crude reaction mixture by flash column chromatography (hexanes: EtOAc = 8:1).

(*R*)-(1-(2-Hydroxy-3,6-dimethylphenyl)naphthalen-2-yl)methyl acetate (*R*)-5**b**. Colorless oil;  $[\alpha]_D^{21} - 13.7$  (c 0.51, CHCl<sub>3</sub>); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.50–7.54 (m, 1H), 7.35–7.42 (m, 2H), 7.14 (d, J = 7.5 Hz, 1H), 6.84 (d, J = 7.5 Hz, 1H), 4.99 (d, J = 12.5 Hz, 1H), 4.94 (d, J = 12.5 Hz, 1H), 4.58 (s, 1H), 2.28 (s, 3H), 2.04 (s, 3H), 1.78 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.8, 151.3, 135.3, 133.6, 133.2, 132.4, 132.3, 130.6, 129.1, 128.2, 127.1, 126.7, 126.2, 125.5, 122.7, 121.9, 121.7, 64.8, 20.8, 19.6, 16.0; IR (CHCl<sub>3</sub>)  $\nu$  3553, 1737 cm<sup>-1</sup>; HRMS (MALDI) m/z calcd for C<sub>21</sub>H<sub>20</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 343.1310, found: 343.1305. Its optical purity (93% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK AD-3 column (hexanes/2-propanol = 95 : 5; flow rate: 1.0 mL min<sup>-1</sup>; retention times: 8.5 min (*S*), 10.6 min (*R*)).

(S)-2-(2-(Hydroxymethyl)naphthalen-1-yl)-3,6-dimethylphenol (S)-4b. Colorless oil;  $[\alpha]_D^{21} + 21.7$  (c 0.6, CHCl<sub>3</sub>) (lit.  $^{14}[\alpha]_D^{20} + 27.2$  (c 0.4, CHCl<sub>3</sub>) for (S)-4b with 87% ee);  $^{1}$ H-NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.98 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.49–7.52 (m, 1H), 7.34–7.41 (m, 2H), 7.16 (d, J = 7.5 Hz, 1H), 6.86 (d, J = 7.5 Hz, 1H), 4.52 (s, 2H), 2.29 (s, 3H), 1.79 (s, 3H). The spectroscopic data are in good agreement with those reported.  $^{14}$  Its optical purity (98% ee) was determined by HPLC analysis at 20 °C using a CHIRALPAK AD-3 column (hexanes/2-propanol = 90 : 10; flow rate: 1.0 mL min  $^{-1}$ ; retention times: 12.9 min (R), 29.8 min (S)).

#### Conflicts of interest

There are no conflicts to declare.

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