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Structure influence of chiral 1,1′-biscarboline-*N*,*N*′-dioxide on the enantioselective allylation of aldehydes with allyltrichlorosilanes

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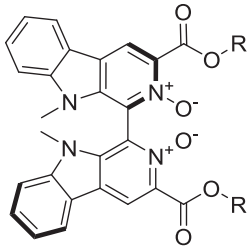
ABSTRACT

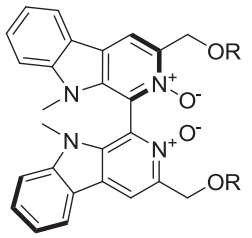
A series of new axially chiral 1,1′-biscarboline-*N*,*N*′-dioxide Lewis base organocatalysts were examined in the asymmetric allylation of aldehydes with allyltrichlorosilane. The chiral catalysts (*R*)-**1a**–**e** bearing ester groups in 3,3′ position provided good yields of the homoallyl alcohols with excellent enantioselectivities up to 99% for a broad substrate scope that covers aliphatic, aromatic, heteroaromatic, and α,β-unsaturated aldehydes. Solvent effects on the conversion and enantioselectivity were elucidated, and CH_2Cl_2 proved to be the optimal solvent for the reactions. In addition, the allylation with crotyltrichlorosilane was explored and the result showed that *anti*-isomer was favored from (*E*)-crotyltrichlorosilane with complete diastereoselectivity.

1. Introduction

Asymmetric allylation of aldehydes has been one of the most efficient methods to form chiral homoallylic alcohols since allylation of carbonyl compound with allylsilane was first reported by Sakurai.[1] In the pioneer studies, Hoffmann, Roush, Brown, Masamune, and Corey have made important contributions to this field utilizing chiral allylboranes and allylboronates.[2] In recent years, chiral catalysts such as binaphthyl-derivatives, chiral phosphoramides, chiral formamides, and chiral *N*-oxide have been engaged in enantioselective allylation of aldehydes and ketones.[3,4] Bipyridine *N*,*N*′-dioxides are of special interest in cases where the bipyridine moiety is a part of a rigid skeleton and the *N*-oxides are powerful electron-pair donors. Since Nakajima's report that axially chiral 2,2′-bipyridine *N*,*N*′-dioxides are effective as catalysts for the asymmetric allylation,[5] the class of 2,2′-bipyridine *N*,*N*′-dioxide derivatives has attracted considerable attention by Hayashi,[6] Malkov,[7] Denmark,[8] Kotora,[9] and others.[10] In our previous work, we have developed a new axially chiral Lewis base catalysts (*R*)-**1a** with the biscarboline framework for enantioselective allylation (Fig. 1).[11] The use of this type of the catalyst could overcome the common problem of the Lewis base catalyzed allylation: the substrate scope. A wide range of aliphatic, aromatic, heteroaromatic, and α,β-unsaturated aldehydes can be catalyzed by (*R*)-**1a** and high enantioselectivity (up to 91–99% ee) with low catalyst loading (1 mol%)



(*R*)-**1a** R = Me
(*R*)-**1b** R = Et
(*R*)-**1c** R = *i*-Pr
(*R*)-**1d** R = n-Bu
(*R*)-**1e** R = *i*-Pentyl



(*R*)-**1f** R = H
(*R*)-**1g** R = Ac
(*R*)-**1h** R = Bz
(*R*)-**1i** R = *t*-Butylacetyl
(*R*)-**1j** R = Me
(*R*)-**1k** R = Bn

Fig. 1. Chiral biscarboline *N*,*N*′-dioxide derivatives (*R*)-**1a**–**k**.

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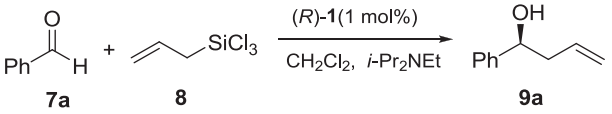
were achieved. In this work we will examine the effect of substituent R in the catalysts on the catalytic activity of asymmetric allylation of aldehydes. Meanwhile, the crotylation of benzaldehyde with crotyltrichlorosilane was investigated as well.

2. Results and discussion

General synthetic route to biscarboline *N*,*N*′-dioxide derivatives is illustrated in Scheme 1. In synthesis of **2**, the core precursor to (*R*)-**1**, was previously described by us in detail.[11] Hydrolysis of the **2** afforded carboxylic acid **3**, which was esterified with different alcohols to form **4a**–**d**. The reduction of **2** using lithium aluminum hydride afforded **5**. Esterification of **5** produced the corresponding **6a**, similarly, etherification of **5** produced the corresponding **6b**–**c**. Oxidation of **4a**–**d** with *m*-chloroperoxybenzoic acid (*m*-CPBA) afforded dioxide and monoxide (about ratio of 3:2) along with traces of the unreacted biscarboline (<5%). Unlike **4a**–**d**, compounds **6a**–**c** could be oxidized completely. The racemates were resolved into enantiomers by using HPLC with a chiral column. Absolute configuration of enantiomer was assigned by comparing the experimental optical rotation (OR) values with the one that was calculated using density functional theory (DFT), and (+)-**1a**–**k** were assigned as (*R*) configuration.

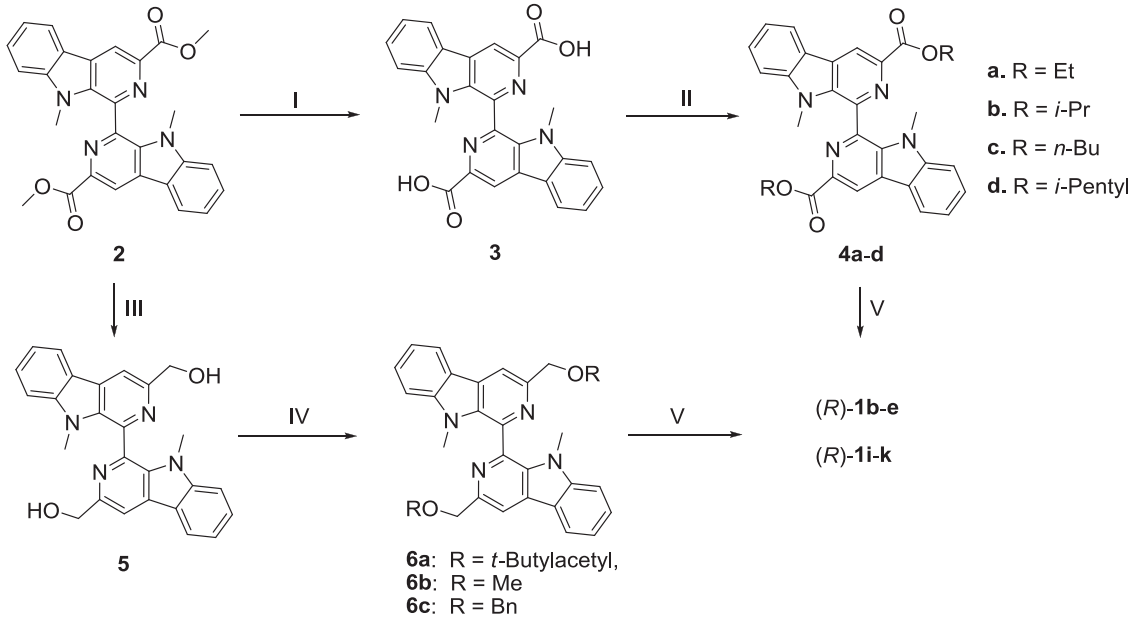
Table 1
Screening of catalysts[a]



7a 8 9a

Entry	Cat.	Conv.[b] (%)	ee[c] (%)	Config.[d]
1	(*R*)-**1a**	100	95	*S*
2	(*R*)-**1b**	100	95	*S*
3	(*R*)-**1c**	100	95	*S*
4	(*R*)-**1d**	100	95	*S*
5	(*R*)-**1e**	100	95	*S*
6	(*R*)-**1f**	100	60	*S*
7	(*R*)-**1g**	100	77	*S*
8	(*R*)-**1h**	100	79	*S*
9	(*R*)-**1i**	100	82	*S*
10	(*R*)-**1j**	100	78	*S*
11	(*R*)-**1k**	100	81	*S*

[a] Reaction condition **7a** (0.5 mmol), **8** (0.6 mmol), (*R*)-**1** (1 mol %) as catalyst.
[b] Estimated by recovering unreacted PhCHO.
[c] ee was determined by chiral HPLC.
[d] The configuration was determined by comparing optical rotation data and HPLC retention times with literature.



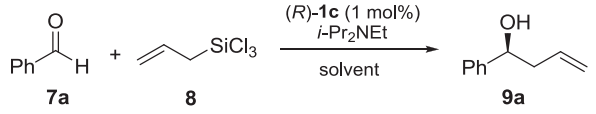
Scheme 1. Synthesis of axially chiral catalysts. Conditions: (I) NaOH, CH_3OH/H_2O, reflux, 6 h; (II) $SOCl_2$, ROH, 60 °C, 12 h; (III) $LiAlH_4$, THF, rt 1 h; (IV) for **6a**: acyl halides, Et_3N, CH_2Cl_2, rt, 12 h; for **6b** and **6c**: halides, NaH, DMF, rt, 12 h; (V) *m*-CPBA, CH_2Cl_2, rt, 6–12 h.

Addition of allyltrichlorosilane **8** to benzaldehyde **7a** was carried out to test the enantioselectivity and reactivity of organocatalysts (*R*)-**1a**–**k** in CH_2Cl_2 at about −80 °C. Conversion and ee value, as determined by HPLC, are summarized in Table 1. The results indicated that the chiral catalysts (*R*)-**1a**–**k** showed surprising differences in chiral induction, although each of them possesses biscarboline framework with a C_2-symmetric axis. The parent catalyst (*R*)-**1a**, bearing methyl ester substituent in 3,3′-position, gave product **9a** in 100% conversion and 95% ee (entry 1). This exciting effect suggested that there be a connection between ester group and selectivity. As expected, catalysts (*R*)-**1b**–**e**, bearing larger substituents like ethyl ester and isopropyl ester, afforded the product in comparable conversion and ee to (*R*)-**1a**. Subsequently, we turned our attention to catalyst (*R*)-**1f**, which is a reductive product of ester and characterized by its alcohol group. Surprisingly, the enantioselectivity decreased to 60% even though 100% conversion was recorded using (*R*)-**1f**. Considering the poor selectivity of (*R*)-**1f**, its esterifiable and etherifiable products (*R*)-**1g**–**k** were employed as a remedy. However, 77–82% ee could not be a mark of an excellent catalyst. Although more substituent has yet to be investigated, the observed results reveals that the ester group in 3,3′ position plays an important role in the catalysis.

We had found that the (*R*)-**1a**–**e** were the best catalysts in the tests using *N*,*N*′-dioxides, further optimization of the reaction conditions were conducted by examining the effect of solvents (Table 2). At the outset we studied the allylation of benzaldehyde in commonly used solvent CH_2Cl_2 (entry 1) and CH_3CN (entry 4) with

(*R*)-**1c**. It proceeded with full conversion to give product (*S*)-**9a** with ee of 95% and 90%, respectively. THF, toluene, Et_2O, and EtOAc provided the similarly good enantioselectivities as CH_2Cl_2 and CH_3CN but in low yields. Thus, CH_2Cl_2 was used to test the effect of temperature on the ee. When the reaction temperature was elevated from −80 °C to −20 °C, the enantioselectivity declined from 95% to 91% ee. From the results obtained so far, it seems that the addition of allyltrichlorosilane **8** to benzaldehyde carried out in CH_2Cl_2 at about −80 °C is an optimal condition.

Table 2
Optimization of solvents[a]



7a 8 9a

Entry	Solvent	*T* (°C)	Conv.[b] (%)	ee[c] (%)
1	CH_2Cl_2	−80	100	95
2	CH_2Cl_2	−40	100	93
3	CH_2Cl_2	−20	100	91
4	CH_3CN	−40	100	90
5	THF	−80	5	90
6	Toluene	−80	10	86
7	EtOAc	−60	10	85
8	Et_2O	−60	5	91

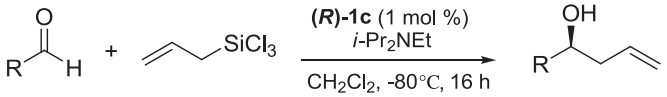
[a] Reaction condition: **7a** (0.5 mmol), **8** (0.6 mmol), (*R*)-**1c** (1 mol %) as catalyst.
[b] Estimated by recovering unreacted PhCHO.
[c] ee was determined by chiral HPLC.

In the next step, catalytic activity and enantioselectivity of the (*R*)-**1c** (1 mol %) were tested in the addition of allyltrichlorosilane to variously substituted aldehydes **7** under the optimal conditions (Table 3). To our delight, the reaction catalyzed by (*R*)-**1c** was found to be very applicable to a variety of aromatic, heteroaromatic, and aliphatic aldehydes, which was similar to (*R*)-**1a**. Aromatic aldehydes include electron-donating and electron-withdrawing substituents (entries 1–10) gave the expected products **9a**–**k** in good yields and excellent enantioselectivities up to 99%. Further additions to other aldehydes bearing heteroaromatic (entry 11), steric hindrance (entries 12–14), and α,β-unsaturated (entry 15) were also found to be efficient with high enantioselectivity of 93–98%. It was surprised to find that aliphatic aldehydes, especially saturated aldehydes, which always involves in low enantioselectivities and reaction rates,[6a,7a,8d] afforded the corresponding product in good yield with considerable 92% ee (entries 15–17). It is the highest reported to date for enantioselective allylation of aliphatic aldehydes catalyzed by a chiral *N*-oxide Lewis base.

Encouraged by the excellent results obtained from addition of allyltrichlorosilane to various aldehydes, the allylation with crotyltrichlorosilane (prepared as an 86:14 trans/cis mixture by the CuCl-catalyzed reaction of crotyl chloride with $HSiCl_3$) and various types of allyltrichlorosilanes was explored to expand the scope of the reaction and to explain the mechanism (Table 4). It was found that *anti*-isomer was produced from (*E*)-crotyltrichlorosilane with complete diastereoselectivity and good enantioselectivity (entries 1 and 2). γ-(*E*)-phenyltrichlorosilane gave a good enantioselectivity similar to (*E*)-crotyltrichlorosilane (entries 3 and 4). Meanwhile, γ-dimethyltrichlorosilane **10c**, which has steric hindrance between R^1 and R^2 position, gave the enantioselectivities about 96% ee (entries 5 and 6). However, when β-substituted allyltrichlorosilane **10d** was employed, the decrease of the enantioselectivities to 82% ee (entries 7 and 8) was observed.

The observed result above can be rationalized based on the Zimmerman–Traxler model, according to which the reaction proceeds through a six-membered chair-like transition state. The

Table 3
Asymmetric allylation to aldehydes **7** catalyzed by (*R*)-**1c**[a]

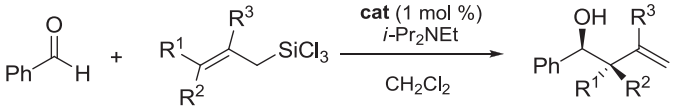


7 8 9

Entry	Aldehyde	R	Product	Yield[b] (%)	ee[c] (%)	Config.[d]
1	**7a**	Ph	**9a**	79	95	(*S*)-(−)
2	**7b**	4-MeO–Ph	**9b**	83	99	(*S*)-(−)
3	**7c**	3-MeO–Ph	**9c**	80	97	(*S*)-(−)
4	**7d**	3-Cl–Ph	**9d**	74	96	(*S*)-(−)
5	**7e**	4-Cl–Ph	**9e**	77	96	(*S*)-(−)
6	**7f**	3-NO_2–Ph	**9f**	80	93	(*S*)-(−)
7	**7g**	4-NO_2–Ph	**9g**	83	88	(*S*)-(−)
8	**7h**	3-F–Ph	**9h**	76	94	(*S*)-(−)
9	**7i**	4-CH_3–Ph	**9i**	75	95	(*S*)-(−)
10	**7j**	3,4-DiMeO–Ph	**9j**	87	96	(*S*)-(−)
11	**7k**	2-Thiophenyl	**9k**	80	98	(*S*)-(−)
12	**7l**	2-Naphth	**9l**	88	93	(*S*)-(−)
13	**7m**	1-Naphth	**9m**	85	97	(*S*)-(−)
14	**7n**	2,6-DiCl–Ph	**9n**	82	97	(*R*)-(+)
15	**7o**	*E*-PhCH=CH_2	**9o**	92	93	(*S*)-(−)[e]
16	**7p**	PhCH–CH_2	**9p**	64	92	(*R*)-(+)
17	**7q**	*c*-C_6H_{11}	**9q**	50	92[f]	(*S*)-(−)

[a] Reaction condition: **7** (0.5 mmol), **8** (0.6 mmol), (*R*)-**1c**, (*R*)-**1b** (1 mol %) as catalyst.
[b] Isolated yield, note that some of the products are fairly volatile.
[c] ee was determined by chiral HPLC.
[d] The configuration was determined by comparing optical rotation data and HPLC retention times with literatures.
[e] Compound **9o** is levorotatory in $CHCl_3$ and dextrorotatory in Et_2O.
[f] ee was determined by formation of 3,5-dinitrobenzoate ester of **9q**.

Table 4
Asymmetric allylation of benzaldehyde with allyltrichlorosilanes catalyzed by (*R*)-**1a**, (*R*)-**1c**



10 11

Entry	Cat.	Allyltrichlorosilane	Allylic alcohol			
				Yield[a] (%)	ee[b] (%)	Config.
1[c]	(*R*)-**1a**	**10a** R^1=CH_3, R^2=R^3=H	**11a**[d]	64	94 (*anti*), 95 (*syn*)	1*S*,2*S*
2	(*R*)-**1c**	**10a** R^1=CH_3, R^2=R^3=H	**11a**	59	94 (*anti*), 95 (*syn*)	1*S*,2*S*
3[e]	(*R*)-**1a**	**10b** R^1=Ph, R^2=R^3=H	**11b**[f]	72	96	1*S*,2*R*
4	(*R*)-**1c**	**10b** R^1=Ph, R^2=R^3=H	**11b**	88	95	1*S*,2*R*
5	(*R*)-**1a**	**10c** R^1=R^2=CH_3, R^3=H	**11c**	45	94	*S*
6	(*R*)-**1c**	**10c** R^1=R^2=CH_3, R^3=H	**11c**	50	96	*S*
7	(*R*)-**1a**	**10d** R^1=R^2=H, R^3=CH_3	**11d**	19	82	*S*
8	(*R*)-**1c**	**10d** R^1=R^2=H, R^3=CH_3	**11d**	23	80	*S*

[a] Isolated yield.
[b] Determined by HPLC.
[c] *E*/*Z*=86:14.
[d] *anti*/*syn*=86:14.
[e] *E*/*Z*>99:1.
[f] *anti*/*syn*>99:1.

controlling factor based on this model is the avoidance of destabilizing 1,3-diaxial interactions in the cyclic transition state (Fig. 2). Thus, *E*-allyltrichlorosilanes **10a** and **10b** give rise to corresponding *anti* diastereomer. Obviously, it coincides with the general acceptance view on the reaction mechanism proposed by Nakajima. It was suggested that *N*-oxide functional group possess a notable electron-pair donor property, and exhibits a significant nucleophilicity toward the silicon atom in the transition state structures. This procedure involved a chair-like six-membered cyclic transition state.

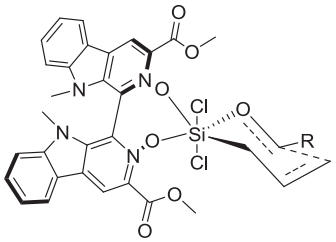


Fig. 2. The proposed transition state structure.

3. Conclusion

In conclusion, *N*,*N*′-dioxides based on the framework of biscarboline have been prepared and their potentiality as organocatalyst has been demonstrated in the addition of allyltrichlorosilanes to aldehydes. The desired alcohol products were obtained in high yields and good to excellent enantioselectivities using a broad range of aliphatic, aromatic, heteroaromatic, and unsaturated aldehydes. The preliminary structure–activity relationship study reveals that the ester group in 3,3′ position play an important role in catalyzing the reaction. Moreover, the complete diastereoselectivity verified that the allylation catalyzed by (*R*)-**1** proceeds via a six-membered chair-like transition state. In a way, this work furnishes a new dimension for design of chiral Lewis base catalyst that was not previously attentive. Further experiments to diversify the structure of the catalysts and their applications in other reactions are currently in progress.

4. Experimental section

4.1. General methods

Thin layer chromatography was performed on TLC plates (GF_{254}). Flash column chromatography was performed with silica gel (300–400 mesh). Enantiomeric excess was determined using a Waters HPLC with a 2695 pump and a 2996 diode array detector. Optical rotations were performed on an Optical Activity AA-55 polarimeter using a 10 cm cell with a Na 589 nm filter. IR spectra were obtained with an FTIR spectrometer (Bruker Tensor 27). ^{1}H NMR and ^{13}C NMR were recorded on a Bruker AV-400 or Bruker DRX-500 spectrometer. The mass spectra were measured on an API QSTAR Pulsar. All solvents for the reactions were of reagent grade and were dried and distilled before use. Compounds **2** and **5** were prepared according to our reported method, and allyltrichlorosilanes **10a**–**d** were prepared according to the literatures.[12]

4.2. Preparation of biscarbolins

*4.2.1. 9,9′-Dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-3,3′-dicarboxylic acid (**3**).* To a solution of **2** (2.7 g, 5.65 mmol) in CH_3OH (40 mL) was added 1 N aqueous sodium hydroxide solution (40 mL), and the mixture was stirred at 60 °C for 5 h. The brown solution was neutralized with 3 M HCl to pH 3–4. The precipitate was collected by filtration to give **3** as a pale yellow solid, 2.5 g, yield 98%. IR (KBr) ν 3434, 2924, 1682, 1329, 1280, 743 cm^{-1}. MS-ESI, *m*/*z* 473 [M+Na]$^+$. HRMS *m*/*z* calcd for $C_{26}H_{18}N_4O_4Na$ [M+Na]$^+$ 473.1225, found 473.1230. ^{1}H NMR (400 MHz, DMSO-d_6): δ=3.47 (s, 3H×2, NCH_3), 7.42 (t, *J*=7.4 Hz, 1H×2), 7.66–7.78 (m, 2H×2), 8.58 (d, *J*=7.9 Hz, 1H×2), 9.16 (s, 1H×2). ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.6, 110.8, 117.4, 120.7, 120.8, 122.3, 129.2, 129.8, 136.3, 136.7, 139.6, 142.6, 166.8.

*4.2.2. Diethyl 9H,9′H-1,1′-bipyrido[3,4-b]indole-3,3′-dicarboxylate (**4a**). General procedure for the preparation of **4**:* To EtOH (25 mL) cooled to −15 °C was added dropwise $SOCl_2$ (0.95 g, 8 mmol). After stirring for 15 min, **3** (0.6 g, 1.33 mmol) was added followed by reflux at 60 °C for 12 h. The reaction mixture was condensed under reduced pressure to give **4a** as white solid, 0.65 g, yield 96%. IR (KBr) ν 3440, 1703, 1620, 1328, 1260, 1038, 744 cm^{-1}. MS-ESI, *m*/*z* 507 [M+H]$^+$. HRMS *m*/*z* calcd for $C_{30}H_{26}N_4O_4Na$ [M+Na]$^+$ 529.1857, found 529.1853. ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.45 (t, *J*=7.0 Hz, 3H×2), 3.51 (s, 3H×2, NCH_3), 4.50 (m, 2H×2), 7.40 (t, *J*=7.5 Hz, 1H×2), 7.47 (d, *J*=8.2 Hz, 1H×2), 7.66 (t, *J*=7.6 Hz, 1H×2), 8.30 (d, *J*=7.8 Hz, 1H×2), 9.01 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 32.9, 61.5, 110.0, 117.8, 120.8, 121.3, 121.7, 129.1, 130.6, 136.2, 137.6, 139.9, 142.9, 165.9.

*4.2.3. Diisopropyl 9H,9′H-1,1′-bipyrido[3,4-b]indole-3,3′-dicarboxylate (**4b**).* Following the general procedure, **4b** was obtained as a white solid, yield 97%. IR (KBr) ν 3428, 1722, 1699, 1257, 1104, 1039, 741 cm^{-1}. MS-ESI, *m*/*z* 535 [M+H]$^+$. HRMS *m*/*z* calcd for $C_{32}H_{31}N_4O_4$ [M+H]$^+$ 535.2345, found 535.2349. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (d, *J*=6.2 Hz, 6H×2), 3.57 (s, 3H×2, NCH_3), 5.37 (m, 1H×2), 7.40 (t, *J*=7.5 Hz, 1H×2), 7.48 (d, *J*=8.3 Hz, 1H×2), 7.66 (t, *J*=7.5 Hz, 1H×2), 8.30 (d, *J*=7.9 Hz, 1H×2), 9.00 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 33.2, 68.9, 110.1, 117.4, 120.6, 121.3, 121.6, 129.0, 130.5, 136.4, 137.5, 140.1, 143.0, 165.3.

*4.2.4. Dibutyl 9,9′-dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-3,3′-dicarboxylate (**4c**).* Following the general procedure, **4b** was obtained as white solid, yield 97%. IR (KBr) ν 3436, 2956, 1707, 1260, 736 cm^{-1}. MS-ESI, *m*/*z* 585 [M+Na]$^+$. HRMS *m*/*z* calcd for $C_{34}H_{34}N_4O_4Na$ [M+Na]$^+$ 585.2477, found 585.2474. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, *J*=7.4 Hz, 3H×2), 1.45–1.53 (m, 2H×2), 1.79–1.85 (m, 2H×2), 3.55 (s, 3H×2, NCH_3), 4.42–4.53 (m, 2H×2), 7.41 (t, *J*=7.5 Hz, 1H×2), 7.48 (d, *J*=8.3 Hz, 1H×2), 7.67 (t, *J*=7.4 Hz, 1H×2), 8.31 (d, *J*=7.8 Hz, 1H×2), 9.01 (s, 1H×2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.2, 30.9, 33.0, 65.3, 110.0, 117.6, 120.8, 121.3, 121.7, 129.1, 130.6, 136.2, 137.6, 140.0, 143.0, 165.9.

*4.2.5. Diisopentyl 9,9′-dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-3,3′-dicarboxylate (**4d**).* Following the general procedure, **4d** was obtained as white solid, yield 98%. IR (KBr) ν 3435, 2956, 1707, 1260, 1110, 737 cm^{-1}. MS-ESI, *m*/*z* 613 [M+Na]$^+$. HRMS *m*/*z* calcd for $C_{36}H_{38}N_4O_4Na$ [M+Na]$^+$ 613.2790, found 613.2790. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (d, *J*=6.4 Hz, 6H×2), 1.73–1.75 (m, 2H×2), 1.78–1.83 (m, 1H×2), 3.57 (s, 3H×2, NCH_3), 4.42–4.54 (m, 2H×2), 7.41 (t, *J*=7.5 Hz, 1H×2), 7.48 (d, *J*=8.3 Hz, 1H×2), 7.67 (t, *J*=7.5 Hz, 1H×2), 8.31 (d, *J*=7.8 Hz, 1H×2), 8.98 (s, 1H×2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.5, 25.2, 33.0, 37.5, 64.2, 110.0, 117.6, 120.8, 121.3, 121.7, 129.1, 130.6, 136.2, 137.6, 140.0, 143.0, 165.9.

*4.2.6. (9,9′-Dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-3,3′-diyl) bis(methylene)bis(3,3-dimethylbutanoate) (**6a**).* To a stirring solution of **5** (0.5 g, 1.19 mmol) in CH_2Cl_2 was added Et_3N (0.3 g, 2.96 mmol) followed by *tert*-butylacetyl chloride (0.38 g, 2.84 mmol) and DMAP (5 mol %). The reaction mixture was stirred at rt for 12 h, washed with water, and dried over anhydrous Na_2SO_4. The solvents were then evaporated under reduced pressure. The residue was purified by chromatography (silica gel) eluting with petroleum ether/EtOAc/CH_2Cl_2=4:0.5:1 to give **6a** as a white solid, 0.65 g, yield 89%. IR (KBr) ν 3434, 2954, 1728, 1468, 1245, 1129, 1041, 743 cm^{-1}. MS-ESI, *m*/*z* 619 [M+H]$^+$. HRMS *m*/*z* calcd for $C_{38}H_{43}N_4O_4$ [M+H]$^+$ 619.3284, found 619.3268. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 9H×2), 2.33 (s, 2H×2), 3.30 (s, 3H×2, NCH_3), 5.47 (s, 2H×2, ArCH_2), 7.34 (t, *J*=7.4 Hz, 1H×2), 7.40 (d, *J*=8.0 Hz, 1H×2), 7.62 (t, *J*=7.4 Hz, 1H×2), 8.23–8.24 (m, 2H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.7, 30.8, 31.9, 47.9, 67.3, 109.6, 113.9, 119.9, 120.9, 121.7, 128.8, 130.9, 135.5, 140.0, 142.9, 143.8, 172.1.

*4.2.7. 3,3′-Bis(methoxymethyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido [3,4-b]indole (**6b**). General procedure for the preparation of **6b**,**c**:* NaH (80% oil dispersion, 0.13 g, 4.3 mmol) was suspended in anhydrous DMF (20 mL) under a N_2 atmosphere at 0 °C. Compound **5**

(0.6 g, 1.4 mmol) was added following by CH_3I (0.8 g, 5.68 mmol) and the mixture was stirred at rt for 12 h, and then poured into ice-water (60 mL). The mixture extracted with EtOAc, the organic phase was washed with water and dried over anhydrous Na_2SO_4. The solvents were evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (Petroleum ether/EtOAc=2:1) to give **6b** as a white solid, 0.54 g, yield 85%. IR (KBr) ν 3442, 2927, 2867, 2826, 1621, 1470, 1374, 1242, 1107, 1039, 743 cm^{-1}. MS-ESI, *m/z* 451 $[M+H]^+$. HRMS *m/z* calcd for $C_{28}H_{27}N_4O_2$ $[M+H]^+$ 451.2134, found 451.2141. ^1H NMR (400 MHz, $CDCl_3$) δ 3.25 (s, 3H×2, NCH_3), 3.57 (s, 3H×2, OCH_3), 4.86 (d, *J*=3.5 Hz, 2H×2, ArCH_2), 7.32 (t, *J*=7.9 Hz, 1H×2), 7.37 (d, *J*=8.3 Hz, 1H×2), 7.60 (t, *J*=7.3 Hz, 1H×2), 8.24 (d, *J*=7.9 Hz, 1H××2), 8.27 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.8, 58.7, 75.9, 109.5, 112.6, 119.8, 120.9, 121.7, 128.6, 130.9, 135.4, 139.8, 142.9, 146.2.

*4.2.8. 3,3′-Bis(benzyloxymethyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido [3,4-b]indole (**6c**).* Following the general procedure, further purified by column chromatography on silica gel (petroleum ether/EtOAc/CH_2Cl_2=4:0.5:1) to give **6c** as a white solid, yield 80%. IR (KBr) ν 3442, 3028, 2854, 1621, 1465, 1241, 739 cm^{-1}. MS-ESI, *m/z* 603 $[M+H]^+$. HRMS *m/z* calcd for $C_{40}H_{35}N_4O_2$ $[M+H]^+$ 603.2760, found 603.2749. ^1H NMR (400 MHz, $CDCl_3$) δ 3.24 (s, 3H×2, NCH_3), 4.76 (s, 2H×2, OCH_2Ph), 4.97 (s, 2H×2, ArCH_2), 7.30–7.39 (m, 5H×2), 7.45 (t, *J*=7.5 Hz, 2H×2), 7.60 (t, *J*=7.7 Hz, 1H×2), 8.23 (d, *J*=7.9 Hz, 1H×2), 8.33 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.8, 72.8, 73.6, 109.5, 112.7, 119.7, 121.0, 121.8, 127.7, 127.9, 128.4, 128.6, 131.0, 135.4, 138.2, 139.8, 142.9, 146.4.

4.3. General procedure for (*R*)-1

m-CPBA (3 mmol) was added portion-wise to a stirred solution of 1,1′-biscarboline (1 mmol) in CH_2Cl_2 (50 mL) at 0 °C, and stirred at rt for 24 h. Then the mixture was poured into saturated aqueous $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by chromatography (silica gel) eluting with CH_2Cl_2/CH_3OH=80:1 to give the corresponding compounds.

*4.3.1. 3,3′-Bis(ethoxycarbonyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido [3,4-b]indole-2,2′-dioxide ((R)-**1b**).* Following the general procedure above, **1b** (yield, 52%) was isolated as pale yellow solid from the reaction of **4a**. Racemic **1b** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, CH_2Cl_2/THF/EtOH=70:10:20) and both enantiomers (*R*)-(+)-**1b** and (*S*)-(−)-**1b** were obtained. $[\alpha]_D$ +637 (*c* 0.16, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3439, 2927, 1735, 1392, 1239, 1008, 747 cm^{-1}. MS-ESI, *m/z* 539 $[M+H]^+$. HRMS *m/z* calcd for $C_{30}H_{27}N_4O_6$ $[M+H]^+$ 539.1930, found 539.1936. ^1H NMR (500 MHz, $CDCl_3$) δ 1.44 (t, *J*=7.1 Hz, 3H×2), 3.44 (s, 3H×2, NCH_3), 4.48 (q, *J*=6.7 Hz, 2H×2), 7.34–7.37 (m, 2H×2), 7.56 (t, *J*=7.4 Hz, 1H×2), 8.07 (d, *J*=7.8 Hz, 1H×2), 8.48 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 29.3, 62.3, 109.8, 118.7, 120.1, 120.8, 121.3, 121.6, 126.1, 128.3, 133.9, 139.4, 143.6, 162.5.

*4.3.2. 3,3′-Bis(isopropoxycarbonyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-2,2′-dioxide ((R)-**1c**).* Following the general procedure above, **1c** (yield, 58%) was isolated as pale yellow solid from the reaction of **4b**. Racemic **1c** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, CH_2Cl_2/2-propanol=78:22) and both enantiomers (*R*)-(+)-**1c** and (*S*)-(−)-**1c** were obtained. $[\alpha]_D$ +705 (*c* 0.18, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3435, 2929, 1729, 1596, 1390, 1239, 1096, 1006, 746 cm^{-1}. MS-ESI, *m/z* 567 $[M+H]^+$. HRMS *m/z* calcd for $C_{32}H_{31}N_4O_6$ $[M+H]^+$ 567.2243, found 567.2255. ^1H NMR (400 MHz, $CDCl_3$) δ 1.42 (d, *J*=6.3 Hz, 3H×2), 1.43 (d, *J*=6.3 Hz, 3H×2), 3.45 (s, 3H×2, NCH_3), 5.33 (m, 1H×2), 7.34–7.38 (m, 2H×2), 7.56 (t, *J*=8.0 Hz, 1H×2), 8.08 (d, *J*=7.5 Hz, 1H×2), 8.40 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 21.8, 29.3, 70.3, 109.8, 118.3, 120.0, 120.8, 121.1, 121.5, 125.9, 128.3, 134.2, 139.1, 143.4, 161.9.

*4.3.3. 3,3′-Bis(butoxycarbonyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido [3,4-b]indole-2,2′-dioxide ((R)-**1d**).* Following the general procedure above, **1d** (yield, 41%) was isolated as pale yellow solid from the reaction of **4c**. Racemic **1d** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, CH_2Cl_2/THF/CH_3OH=75:23:2) and both enantiomers (*R*)-(+)-**1d** and (*S*)-(−)-**1d** were obtained. $[\alpha]_D$ +560.4 (*c* 0.20, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3434, 2956, 1732, 1394, 1243, 747 cm^{-1}. MS-ESI, *m/z* 617 $[M+Na]^+$. HRMS *m/z* calcd for $C_{34}H_{34}N_4O_6Na$ $[M+Na]^+$ 617.2376, found 617.2370. ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, *J*=7.4 Hz, 3H×2), 1.42–1.51 (m, 2H×2), 1.75–1.82 (m, 2H×2), 3.44 (s, 3H×2, NCH_3), 4.40–4.43 (m, 2H×2), 7.34–7.37 (m, 2H×2), 7.56 (t, *J*=7.7 Hz, 1H×2), 8.08 (d, *J*=7.9 Hz, 1H×2), 8.46 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 19.1, 29.3, 30.5, 66.2, 109.8, 118.7, 120.1, 120.8, 121.1, 121.6, 126.0, 128.3, 133.7, 139.2, 143.5, 162.5.

*4.3.4. 3,3′-Bis(isopentyloxycarbonyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-2,2′-dioxide ((R)-**1e**).* Following the general procedure above, **1e** (yield, 42%) was isolated as pale yellow solid from the reaction of **4d**. Racemic **1e** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, CH_2Cl_2/THF/CH_3OH=75:23:2) and both enantiomers (*R*)-(+)-**1e** and (*S*)-(−)-**1e** were obtained. $[\alpha]_D$ +657.2 (*c* 0.21, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3436, 2955, 1732, 1394, 1247, 748 cm^{-1}. MS-ESI, *m/z* 623 $[M+H]^+$. HRMS *m/z* calcd for $C_{36}H_{39}N_4O_6$ $[M+H]^+$ 623.2869, found 623.2865. ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, *J*=6.4 Hz, 6H×2), 1.68–1.82 (m, 3H×2), 3.45 (s, 3H×2, NCH_3), 4.43–4.46 (m, 2H×2), 7.34–7.38 (m, 2H×2), 7.56 (t, *J*=7.7 Hz, 1H×2), 8.08 (d, *J*=7.9 Hz, 1H×2), 8.45 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5, 25.1, 29.3, 37.2, 65.1, 109.9, 118.7, 120.0, 120.9, 121.2, 121.6, 126.0, 128.3, 133.7, 139.3, 143.5, 162.6.

*4.3.5. 3,3′-Bis((3,3-dimethylbutoxy)methyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-2,2′-dioxide ((R)-**1i**).* Following the general procedure above, **1i** (yield, 89%) was isolated as pale yellow solid from the reaction of **6a**. Racemic **1i** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, CH_2Cl_2/CH_3OH=70:30) and both enantiomers (*R*)-(+)-**1i** and (*S*)-(−)-**1i** were obtained. $[\alpha]_D$ +329 (*c* 0.21, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3436, 2954, 1735, 1605, 1396, 1335, 1241, 1127, 1006, 746 cm^{-1}. MS-ESI, *m/z* 651 $[M+H]^+$. HRMS *m/z* calcd for $C_{38}H_{43}N_4O_6$ $[M+H]^+$ 651.3182, found 6351.3181. ^1H NMR (500 MHz, $CDCl_3$) δ 1.11 (s, 9H×2), 2.41 (s, 2H×2), 3.29 (s, 3H×2, NCH_3), 5.48 (d, *J*=14.8 Hz, 1H×2, ArCH_2), 5.68 (d, *J*=14.8 Hz, 1H×2, ArCH_2), 7.34 (m, 2H×2), 7.54 (t, *J*=7.7 Hz, 1H×2), 8.09 (d, *J*=7.7 Hz, 1H×2), 8.20 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.3, 29.7, 30.9, 47.8, 60.6, 109.5, 115.7, 120.8, 121.0, 121.0, 125.4, 128.0, 133.0, 137.7, 138.3, 143.3, 171.8.

*4.3.6. 3,3′-Bis(methoxymethyl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido [3,4-b]indole-2,2′-dioxide ((R)-**1j**).* Following the general procedure above, **1j** (yield, 86%) was isolated as pale yellow solid from the reaction of **6b**. Racemic **1j** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, THF/CH_3OH=50:50) and both enantiomers (*R*)-(+)-**1j** and (*S*)-(−)-**1j** were obtained. $[\alpha]_D$ +235 (*c* 0.26, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3441, 2927, 1604, 1472, 1394, 1194, 1113, 1006, 749 cm^{-1}. MS-ESI, *m/z* 483 $[M+H]^+$. HRMS *m/z* calcd for $C_{28}H_{27}N_4O_4$ $[M+H]^+$ 483.2032, found 483.2028. ^1H NMR (400 MHz, $CDCl_3$) δ 3.25 (s, 3H×2, NCH_3), 3.67 (s, 3H×2, OCH_3), 4.89 (d, *J*=15.6 Hz, 1H×2, ArCH_2), 4.96 (d, *J*=15.5 Hz, 1H×2, ArCH_2), 7.32 (m 2H×2), 7.53 (t, *J*=7.8 Hz, 1H×2), 8.12 (d, *J*=7.8 Hz, 1H×2), 8.29 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.4, 59.5, 69.2, 109.4, 114.2, 120.8, 120.9, 121.1, 121.4, 125.2, 127.9, 137.2, 140.6, 143.3.

*4.3.7. 3,3′-Bis(2-hydroxypropan-2-yl)-9,9′-dimethyl-9H,9′H-1,1′-bipyrido[3,4-b]indole-2,2′-dioxide ((R)-**1k**).* Following the general

procedure above, **1k** (yield, 84%) was isolated as pale yellow solid from the reaction of **6c**. Racemic **1i** was resolved by HPLC on a Chiralpak-IC column (250×10 mm, THF/CH_3OH=80:20) and both enantiomers (*R*)-(+)-**1k** and (*S*)-(−)-**1k** were obtained. $[\alpha]_D$ +160 (*c* 0.25, $CHCl_3$). Mp >300 °C. IR (KBr) ν 3440, 1605, 1471, 1393, 1239, 1196, 1097, 1004, 746 cm^{-1}. MS-ESI, *m*/*z* 635 $[M+H]^+$. HRMS *m*/*z* calcd for $C_{40}H_{35}N_4O_4$ $[M+H]^+$ 635.2658, found 635.2668. ^1H NMR (400 MHz, $CDCl_3$) δ 3.23 (s, 3H×2, NCH_3), 4.83 (s, 2H×2, OCH_2Ph), 5.00 (d, *J*=15.8 Hz, 1H×2, ArCH_2), 5.04 (d, *J*=15.7 Hz, 1H×2, ArCH_2), 7.29–7.36 (m, 3H×2), 7.41 (t, *J*=7.5 Hz, 2H×2), 7.51 (m, 3H×2), 8.11 (d, *J*=7.7 Hz, 1H×2), 8.35 (s, 1H×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ=29.5, 67.0, 73.8, 109.4, 114.4, 120.8, 121.0, 121.1, 121.5, 125.1, 127.9, 128.0, 128.0, 128.6, 137.2, 137.7, 140.8, 143.3.

4.4. General procedure for reaction of allyltrichlorosilanes with aldehydes

Allyltrichlorosilane **8** or **10** (0.6 mmol) was added to a solution of the catalyst (*R*)-**1** (1 mol %), diisopropylethylamine (1.5 mmol), and aldehyde **7** (0.5 mmol) in anhydrous CH_2Cl_2 (2 mL) under nitrogen at −80 °C. The mixture was stirred at the same temperature for 16 h and then quenched with aqueous saturated $NaHCO_3$ (1 mL). The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with saturated NaCl, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc) to give alcohols **9** or **11**.

*4.4.1. (S)-1-Phenylbut-3-en-1-ol (**9a**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.09 (br s, 1H), 2.45–2.56 (m, 2H), 4.74 (dd, *J*=7.3, 5.5 Hz, 1H), 5.13–5.19 (m, 2H), 5.76–5.86 (m, 1H), 7.28–7.36 (m, 5H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=95:5, 0.6 mL/min), t_R (minor)=13.2 min (*R*); t_R (major)=15.4 min (*S*), ee=95%. $[\alpha]_D$ −66.1 (*c* 0.86, $CHCl_3$). The reported value for the *S*-enantiomer (92% ee) is $[\alpha]_D$ −61.2 (*c* 1.05, $CHCl_3$).[7a]

*4.4.2. (S)-1-(4-Methoxyphenyl)but-3-en-1-ol (**9b**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.04 (br s, 1H), 2.50 (t, *J*=6.8 Hz, 2H), 3.80 (s, 3H), 4.68 (t, *J*=6.4 Hz, 1H), 5.11–5.18 (m, 2H), 5.76–5.83 (m, 1H), 6.88 (d, *J*=8.6 Hz, 2H), 7.28 (d, *J*=8.6 Hz, 2H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=95:5, 0.6 mL/min), t_R (minor)=17.9 min (*R*); t_R (major)=19.6 min (*S*), ee=99%. $[\alpha]_D$ −59.1 (*c* 0.80, $CHCl_3$). The reported value for the *S*-enantiomer (92% ee) is $[\alpha]_D$ −48.0 (*c* 1.0, $CHCl_3$).[7a]

*4.4.3. (S)-1-(3-Methoxyphenyl)but-3-en-1-ol (**9c**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.09 (d, *J*=3.0 Hz, 1H), 2.52 (m, 2H), 3.82 (s, 3H), 4.71 (m, 1H), 5.13–5.19 (m, 2H), 5.76–5.86 (m, 1H), 6.82 (ddd, *J*=8.0, 2.4, 0.8 Hz, 1H), 6.93 (m, 2H), 7.26 (dd, *J*=9.1, 7.1 Hz, 1H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=95:5, 0.6 mL/min), t_R (minor)=22.7 min (*R*); t_R (major)=24.3 min (*S*), ee=97%. $[\alpha]_D$ −55.1 (*c* 0.80, $CHCl_3$). The reported value for the *R*-enantiomer (97% ee) is $[\alpha]_D$ +53.8 (*c* 0.9, benzene).[13]

*4.4.4. (S)-1-(3-Chlorophenyl)but-3-en-1-ol (**9d**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.17 (s, 1H), 2.41–2.55 (m, 2H), 4.71 (m, 1H), 5.15–5.20 (m, 2H), 5.73–5.84 (m, 1H), 7.21–7.30 (m, 3H), 7.37 (s, 1H). Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=98:2, 0.7 mL/min), t_R (major)=14.6 min (*S*); t_R (minor)=18.7 min (*R*), ee=95%. $[\alpha]_D$ −54.9 (*c* 0.95, $CHCl_3$).[11]

*4.4.5. (S)-1-(4-Chlorophenyl)but-3-en-1-ol (**9e**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.13 (d, *J*=2.7 Hz, 1H), 2.41–2.54 (m, 2H), 4.71 (m, 1H), 5.14–5.18 (m, 2H), 5.74–5.81 (m, 1H), 7.26–7.33 (m, 4H). Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=95:5, 0.5 mL/min), t_R (major)=13.8 min (*S*); t_R (minor)=14.7 min (*R*), ee=97%. $[\alpha]_D$ −68.6 (*c* 0.87, $CHCl_3$). The reported value for the *S*-enantiomer (89% ee) is $[\alpha]_D$ −60.6 (*c* 1.5, $CHCl_3$)[7a] and for *R*-enantiomer (99% ee) is $[\alpha]_D$ +63.3 (*c* 1.14, $CHCl_3$).[13]

*4.4.6. (S)-1-(3-Nitrophenyl)but-3-en-1-ol (**9f**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.33 (d, *J*=3.1 Hz, 1H), 2.43–2.52 (m, 1H), 2.53–2.62 (m, 1H), 4.87 (m, 1H), 5.18–5.22 (m, 2H), 5.75–5.85 (m, 1H), 7.53 (t, *J*=7.9 Hz, 1H), 7.71 (d, *J*=7.6 Hz, 1H), 8.14 (d, *J*=8.0 Hz, 1H), 8.25 (s, 1H).[14] Enantiomeric excess was determined by HPLC with a chiralpak-IC column (hexane/2-propanol=90:10, 1.6 mL/min), t_R (major)=23.9 min (*S*); t_R (minor)=24.9 min (*R*), ee=93%. $[\alpha]_D$ −51.9 (*c* 0.83, $CHCl_3$).

*4.4.7. (S)-1-(4-Nitrophenyl)but-3-en-1-ol (**9g**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.30 (d, *J*=3.2 Hz, 1H), 2.44–2.49 (m, 1H), 2.54–2.60 (m, 1H), 4.87 (m, 1H), 5.17–5.22 (m, 2H), 5.76–5.80 (m, 1H), 7.53 (d, *J*=10.7 Hz, 2H), 8.22 (d, *J*=10.4 Hz, 2H). Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=90:10, 0.8 mL/min), t_R (major)=15.6 min (*S*); t_R (minor)=17.3 min (*R*), ee=87%. $[\alpha]_D$ −51.2 (*c* 0.70, $CHCl_3$). The reported value for the *S*-enantiomer (65% ee) is $[\alpha]_D$ −33.2 (*c* 0.50, $CHCl_3$)[9d] and for *R*-enantiomer (98% ee) is $[\alpha]_D$ +65.8 (*c* 1.07, $CHCl_3$).

*4.4.8. (S)-1-(3-Fluorophenyl)but-3-en-1-ol (**9h**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.13 (d, *J*=3.0 Hz, 1H), 2.45–2.56 (m, 2H), 4.75 (m, 1H), 5.16–5.21 (m, 2H), 5.76–5.82 (m, 1H), 6.95–6.99 (m, 1H), 7.08–7.14 (m, 2H), 7.30–7.34 (m, 1H).[15] Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=98:2, 0.8 mL/min), t_R (major)=12.6 min (*S*); t_R (minor)=18.5 min (*R*), ee=94%. $[\alpha]_D$ −50.2 (*c* 0.75, $CHCl_3$).

*4.4.9. (S)-1-p-Tolylbut-3-en-1-ol (**9i**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.05 (d, *J*=2.6 Hz, 1H), 2.36 (s, 3H), 2.49–2.53 (m, 2H), 4.72 (m, 1H), 5.14–5.19 (m, 2H), 5.77–5.87 (m, 1H), 7.18 (d, *J*=7.9 Hz, 2H), 7.26 (d, *J*=7.9 Hz, 2H). Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=95:5, 0.7 mL/min), t_R (major)=9.6 min (*S*); t_R (minor)=10.9 min (*R*), ee=95%. $[\alpha]_D$ −55.7 (*c* 0.90, $CHCl_3$). The reported value for the *S*-enantiomer (89% ee) is $[\alpha]_D$ −43.4 (*c* 1.1, $CHCl_3$)[6b] and for *R*-enantiomer (98% ee) is $[\alpha]_D$ +55.7 (*c* 0.98, $CHCl_3$).[13]

*4.4.10. (S)-1-(3,4-Dimethoxyphenyl)but-3-en-1-ol (**9j**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.10 (d, *J*=2.3 Hz, 1H), 2.49–2.52 (m, 2H), 3.88 (s, 3H), 3.90 (s, 3H), 4.69 (m, 1H), 5.13–5.19 (m, 2H), 5.76–5.86 (m, 1H), 6.83 (d, *J*=8.3 Hz, 1H), 6.88 (dd, *J*=8.3, 1.6 Hz, 1H), 6.93 (d, *J*=1.6 Hz, 1H). Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=90:10, 0.7 mL/min), t_R (major)=18.5 min (*S*); t_R (minor)=22.0 min (*R*), ee=96%. $[\alpha]_D$ −41.3 (*c* 0.80, $CHCl_3$). The reported value for the *S*-enantiomer (96% ee) is $[\alpha]_D$ −37.8 (*c* 1.9, benzene).[9b]

*4.4.11. (S)-1-(Thiophen-2-yl)but-3-en-1-ol (**9k**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.26 (d, *J*=3.9 Hz, 1H), 2.60–2.64 (m, 2H), 5.00 (m, 1H), 5.16–5.23 (m, 2H), 5.79–5.87 (m, 1H), 6.98 (m, 2H), 7.25 (m, 1H). Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=90:10, 0.8 mL/min), t_R (major)=12.7 min (*S*); t_R (minor)=13.9 min (*R*), ee=98%. $[\alpha]_D$ −25.3 (*c* 0.78, $CHCl_3$). The reported value for the *S*-enantiomer (83% ee) is $[\alpha]_D$ −19.0 (*c* 1.0, $CHCl_3$)[7a] and for *S*-enantiomer (96% ee) is $[\alpha]_D$ −12.3 (*c* 1.07, $CHCl_3$).[13]

*4.4.12. (S)-1-(Naphthalen-2-yl)but-3-en-1-ol (**9l**).* ^1H NMR (400 MHz, $CDCl_3$) δ 2.24 (br s, 1H), 2.57–2.66 (m, 2H), 4.92 (m, 1H), 5.15–5.23 (2H, m), 5.79–5.90 (1H, m), 7.48–7.51 (3H, m), 7.82–7.86 (4H, m).

Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=95:5, 0.8 mL/min), t_R (major)=17.3 min (*S*); t_R (minor)=19.6 min (*R*), ee=93%. $[\alpha]_D$ −61.2 (*c* 0.91, $CHCl_3$). The reported value for the *S*-enantiomer (90% ee) is $[\alpha]_D$ −55.0 (*c* 1.16, $CHCl_3$).[9d]

*4.4.13. (S)-1-(Naphthalen-1-yl)but-3-en-1-ol (**9m**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (br s, 1H), 2.55–2.63 (m, 1H), 2.73–2.78 (m, 1H), 5.16–5.24 (m, 2H), 5.19 (m, 1H), 5.88–5.94 (m, 1H), 7.46–7.52 (m, 3H), 7.66 (d, *J*=7.2 Hz, 1H), 7.78 (d, *J*=8.1 Hz, 1H), 7.87 (d, *J*=7.5 Hz, 1H), 8.06 (d, *J*=8.1 Hz, 1H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=90:10, 0.8 mL/min), t_R (major)=10.0 min (*S*); t_R (minor)=16.2 min (*R*), ee=97%. $[\alpha]_D$ −105.1 (*c* 0.79, $CHCl_3$). The reported value for the *S*-enantiomer (81% ee) is $[\alpha]_D$ −84.1 (*c* 1.0, $CHCl_3$)[6b] and for *R*-enantiomer (98% ee) is $[\alpha]_D$ +98.6 (*c* 1.06, benzene).[13]

4.4.14. (R)-1-(2,6-Dichlorophenyl)but-3-en-1-ol (9n). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65–2.71 (m, 1H), 2.82–2.87 (m, 1H), 2.89 (d, *J*=9.8 Hz, 1H), 5.08–5.15 (m, 2H), 5.50 (m, 1H), 5.81–5.86 (m, 1H), 7.13 (t, *J*=7.9 Hz, 1H), 7.29 (d, *J*=7.9 Hz, 2H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=98:2, 0.7 mL/min), t_R (major)=11.4 min (*R*); t_R (minor)=12.6 min (*S*), ee=97%. $[\alpha]_D$ +9.1 (*c* 0.88, benzene). The reported value for the *S*-enantiomer (84% ee) is $[\alpha]_D$ −59.4 (*c* 0.5, CH_2Cl_2).[16]

*4.4.15. (S)-(E)-1-Phenylhexa-1,5-dien-3-ol (**9o**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 (s, 1H), 2.37–2.47 (m, 2H), 4.36 (m, 1H), 5.16–5.22 (m, 2H), 5.83–5.90 (m, 1H), 6.25 (dd, *J*=15.9, 6.3 Hz, 1H), 6.61 (d, *J*=15.9 Hz, 1H), 7.24 (d, *J*=7.4 Hz, 1H), 7.32 (t, *J*=7.6 Hz, 2H), 7.26 (d, *J*=7.4 Hz, 2H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=90:10, 0.7 mL/min), t_R (minor)=9.3 min (*R*); t_R (major)=13.5 min (*S*), ee=93%. $[\alpha]_D$ −30.6 (*c* 0.95, $CHCl_3$) and $[\alpha]_D$ +11.2 (*c* 0.86, Et_2O). The reported value for the *S*-enantiomer (83% ee) is $[\alpha]_D$ −36.9 (*c* 1.06, $CHCl_3$) and $[\alpha]_D$ +10.3 (*c* 1.31, Et_2O),[6b] for *R*-enantiomer (96% ee) is $[\alpha]_D$ −9.8 (*c* 1.12, Et_2O).[13]

*4.4.16. (R)-1-Phenylhex-5-en-3-ol (**9p**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66 (d, *J*=5.2 Hz, 1H), 1.78–1.82 (m, 2H), 2.15–2.22 (m, 1H), 2.28–2.34 (m, 1H), 2.66–2.73 (m, 1H), 2.78–2.86 (m, 1H), 3.68 (m, 1H), 5.13–5.17 (m, 2H), 5.77–5.86 (m, 1H), 7.18–7.22 (m, 3H), 7.27–7.31 (m, 2H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=95:5, 0.8 mL/min), t_R (minor)=10.2 min (*S*); t_R (major)=14.9 min (*R*), ee=92%. $[\alpha]_D$ +12.1 (*c* 0.98, $CHCl_3$). The reported value for the *R*-enantiomer (49% ee) is $[\alpha]_D$ +1.8 (*c* 0.9, $CHCl_3$)[6b] and for *S*-enantiomer (87% ee) is $[\alpha]_D$ −25.4 (*c* 1.0, benzene).[13]

*4.4.17. (S)-1-Cyclohexylbut-3-en-1-ol (**9q**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02–1.32 (m, 5H), 1.58 (d, *J*=3.9 Hz, 1H), 1.67–1.89 (m, 6H), 2.05–2.15 (m, 1H), 2.30–2.38 (m, 1H), 3.39 (m, 1H), 5.11–5.17 (m, 2H), 5.78–5.89 (m, 1H). Enantiomeric excess was determined by formation of 3,5-dinitrobenzoate ester of the title compound followed by HPLC with a chiralcel OD-H column (hexane/ethanol=95:5, 0.8 mL/min), t_R (minor)=12.5 min (*R*); t_R (major)=13.5 min (*S*), ee=97%. $[\alpha]_D$ −11.8 (*c* 1.18, EtOH). The reported value for the *R*-enantiomer (73% ee) is $[\alpha]_D$ +5.3 (*c* 1.0, EtOH).[13]

*4.4.18. (1S,2S)-2-Methyl-1-phenylbut-3-en-1-ol (**11a**).* ^{1}H NMR (400 MHz, $CDCl_3$) *anti-isomer* δ 0.86 (d, *J*=6.8 Hz, 3H), 2.23 (br s, 1H), 2.43–2.52 (m, 1H), 4.34 (d, *J*=7.9 Hz, 1H), 5.17–5.22 (m, 2H), 5.76–5.85 (m, 1H), 7.25–7.38 (m, 5H). *syn-Isomer* δ 1.00 (d, *J*=6.8 Hz, 3H), 2.06 (br s, 1H), 2.55–2.60 (m, 1H), 4.60 (d, *J*=7.9 Hz, 1H), 5.02–5.06 (m, 2H), 5.71–5.76 (m, 1H), 7.25–7.38 (m, 5H). Enantiomeric excess was determined by HPLC with a chiralpak-IC column (hexane/2-propanol=97:3, 2.0 mL/min), t_R (minor)=13.7 min ((1*R*,2*S*), *syn*), t_R (major)=14.8 min ((1*S*,2*R*), *syn*); t_R (minor)=15.6 min ((1*R*,2*R*), *anti*), t_R (major)=16.9 min ((1*S*,2*S*), *anti*), ee=94%:95% (*anti*/*syn*, 86:14). $[\alpha]_D$ −82.1 (*c* 1.42, $CHCl_3$) mixture of *anti* and *syn*. The reported value for the (1*R*,2*R*)-enantiomer (46% ee) is $[\alpha]_D$ +44.7 (*c* 0.75, $CHCl_3$) pure *anti*.[12]

*4.4.19. (1S,2R)-1,2-Diphenylbut-3-en-1-ol (**11b**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (br s, 1H), 3.56 (t, *J*=8.4 Hz, 1H), 4.84 (d, *J*=7.8 Hz, 1H), 5.20–5.28 (m, 2H), 6.23–6.30 (m, 1H), 7.04–7.23 (m, 10H).[17] Enantiomeric excess was determined by HPLC with a chiralcel OB-H column (hexane/2-propanol=95:5, 1.0 mL/min), t_R (major)=9.3 min (1*S*,2*R*); t_R (minor)=10.3 min (1*S*,2*S*), ee=96%. $[\alpha]_D$ −11.1 (*c* 0.93, $CHCl_3$).

*4.4.20. (S)-2,2-Dimethyl-1-phenylbut-3-en-1-ol (**11c**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 3H), 1.01 (s, 3H), 2.05 (s, 1H), 4.43 (s, 1H), 5.09 (d, *J*=17.5 Hz, 1H), 5.14 (d, *J*=10.8 Hz, 1H), 5.92 (dd, *J*=17.5, 10.8 Hz, 1H), 7.26–7.31 (m, 5H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=95:5, 0.6 mL/min), t_R (major)=11.0 min (*S*); t_R (minor)=14.8 min (*R*), ee=96%. $[\alpha]_D$ −42.6 (*c* 0.47, $CHCl_3$). The reported value for the *R*-enantiomer (66% ee) is $[\alpha]_D$ +22 (*c* 0.8, benzene).[12]

*4.4.21. (S)-3-Methyl-1-phenylbut-3-en-1-ol (**11d**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.81 (s, 3H), 2.15 (d, *J*=1.7 Hz, 1H), 2.43 (d, *J*=7.0 Hz, 2H), 4.82 (t, *J*=6.8 Hz, 1H), 4.87 (d, *J*=1.2 Hz, 1H), 4.93 (d, *J*=1.4 Hz, 1H), 7.28–7.40 (m, 5H). Enantiomeric excess was determined by HPLC with a chiralcel OD-H column (hexane/2-propanol=97:3, 0.6 mL/min), t_R (major)=15.6 min (*S*); t_R (minor)=17.3 min (*R*), ee=82%. $[\alpha]_D$ −44.4 (*c* 0.18, $CHCl_3$). The reported value for the *R*-enantiomer (66% ee) is $[\alpha]_D$ +51.8 (*c* 0.58, benzene).[12]

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