A New Approach to Axially Chiral Bipyridine *N,N′*-Dioxides Bearing Aromatic Substituents and their Use for Catalytic Asymmetric Allylation of Aldehydes with Allyl(trichloro)silane

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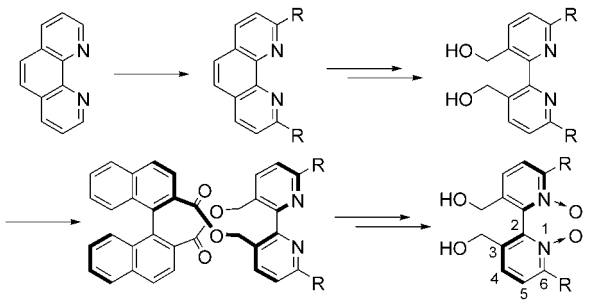
Abstract: Palladium-catalyzed cross-coupling of bipyridine *N,N′*-dioxide 6,6′-dichloride (R_{nap},R_{pyr})-**1** with the aryl Grignard reagents opened a new approach to axially chiral bipyridine *N,N′*-dioxides (*R*)-**2** bearing a variety of aryl groups at the 6 and 6′ positions. One of the *N,N′*-dioxides (*R*)-**2d** which is substituted with 3,5-dimethyl-4-methoxy groups was found to be highly catalytically active and enantioselective for the asymmetric allylation of aldehydes with allyl(trichloro)silane. The allylation took place with 0.01–0.1 mol % of (*R*)-**2d** giving homoallyl alcohols of up to 94% ee.

Keywords: allylation; asymmetric catalysis; axial chirality; bipyridine *N,N′*-dioxide; diversity-oriented strategy; Lewis bases; ligand design

Introduction

Recently, Lewis base-catalyzed asymmetric allylation of aldehydes with allyl(trichloro)silanes has been recognized to be one of the most efficient methods of obtaining homoallyl alcohols with high enantioselectivity.[1] Some chiral Lewis bases such as chiral phosphoramides and chiral formamides have been first used as the enantioselective catalysts for this asymmetric transformation.[1] Since Nakajima's report in 1998[2] that axially chiral 2,2′-bipyridine *N,N′*-dioxides are effective as catalysts for the asymmetric allylation, this class of 2,2′-bipyridine *N,N′*-dioxide derivatives has attracted considerable attention[3,4] owing to their high catalytic activity and high enantioselectivity. In our previous paper,[5] we reported a new synthetic route to axially chiral bipyridine *N,N′*-dioxides (Scheme 1), which allows us to obtain enantiomerically pure samples without optical resolution procedures. One of the bipyridine *N,N′*-dioxides which is substituted with phenyl groups at the 6 and 6′ positions is so catalytically active for the asymmetric allylation that the amount of the catalyst can be reduced to 0.01 mol % without loss of enantioselectivity. Unfortunately, however, this route has a drawback in that the 6 and 6′ substituents must be introduced at the first step of the preparation scheme, which makes it difficult to modify the bipyridine *N,N′*-dioxides at the 6 and 6′ positions. Here we report a diversity-oriented strategy for the preparation and fine-tuning of the chiral bipyridine *N,N′*-dioxide catalysts for the asymmetric allylation of aldehydes.



Scheme 1. Previous synthetic route to axially chiral bipyridine *N,N′*-dioxides.

Results and Discussion

As a versatile intermediate for the preparation of bipyridine *N,N′*-dioxides bearing a variety of aryl groups at the 6 and 6′ positions, we designed bipyridine *N,N′*-dioxide 6,6′-dichloride (R_{nap},R_{pyr})-**1**, which is expected to be readily converted into 6,6′-diarylated derivatives by transition metal-catalyzed cross-coupling reactions[6] (Scheme 2).

Treatment of cyclic diester *N,N′*-dioxides (R_{nap},R_{pyr})-**3**,[5] whose preparation has been reported previously, with phosphorus oxychloride and a large excess of sodium chloride in dimethylformamide gave a 66% yield of dichlorobipyridine (R_{nap},R_{pyr})-**4**. The high concentration of the chloride is important for this substrate, the chlorination yield being much lower (29%) in the ab-

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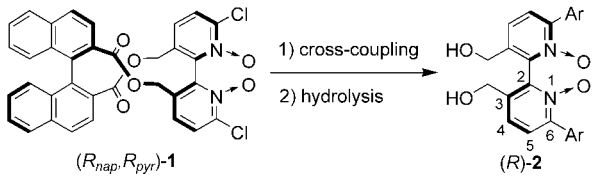
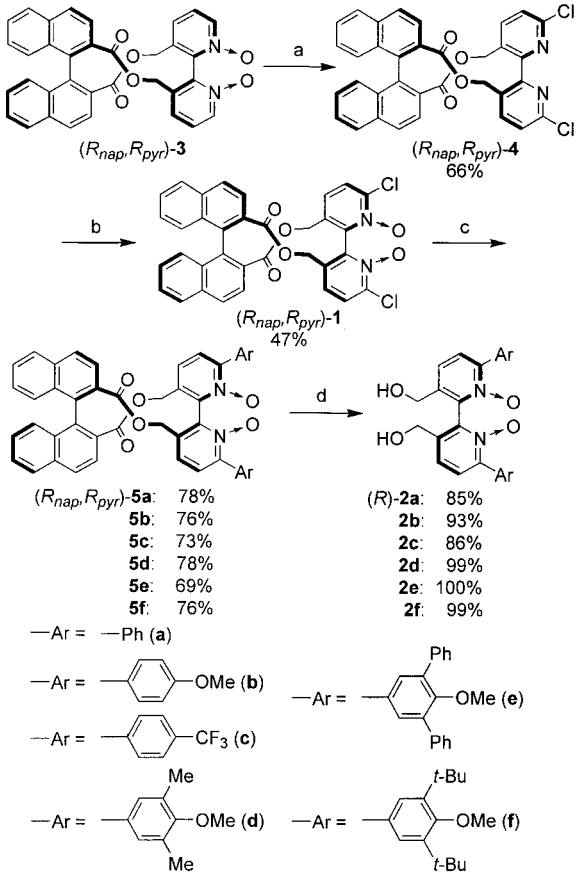


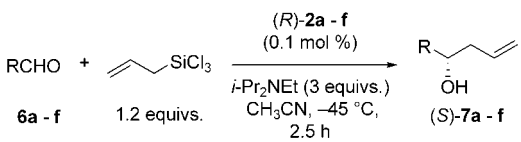
Scheme 2. New approach to axially chiral bipyridine *N,N′*-dioxides (*R*)-**2** bearing various aromatic substituents at the 6 and 6′ positions.

sence of sodium chloride.[7] Bipyridine dichloride **4** was subjected to the oxidation with urea/hydrogen peroxide adduct and trifluoroacetic anhydride.[8] Unfortunately, the oxidation was very slow for this electron-deficient pyridine to give only 21% of the dichlorobipyridine *N,N′*-dioxide **1**. The oxidation of recovered substrate **4** and its monoxide two more times gave a 47% combined yield of the dioxide **1**. The cross-coupling of dichloride (R_{nap},R_{pyr})-**1** with aryl Grignard reagents (3.0 equivs.) proceeded in the presence of $PdCl_2$(dppf)[9] (5 mol %) in tetrahydrofuran at −15 °C to give high yields of the 6,6′-diarylated-2,2′-bipyridine *N,N′*-dioxides (R_{nap},R_{pyr})-**5a–f**, where the aryl groups are phenyl (**a**), 4-methoxyphenyl (**b**), 4-trifluoromethylphenyl (**c**), 3,5-dimethyl-4-methoxyphenyl (**d**), 3,5-diphenyl-4-methoxyphenyl (**e**), and 3,5-di(*tert*-butyl)-4-methoxyphenyl (**f**). It is noteworthy that the dichloride **1** undergoes the palladium-catalyzed cross-coupling under mild conditions. The electron-withdrawing character of the pyridine *N*-oxide, which accelerates the oxidative addition to a palladium(0), is probably responsible for the high reactivity toward the cross-coupling.[10,11] Alkaline hydrolysis of cyclic diester (R_{nap},R_{pyr})-**5** gave high yields of the bipyridine *N,N′*-dioxide diols (*R*)-**2** which are substituted with the aryl groups at the 6 and 6′ positions. The chiral auxiliary, (*R*)-1,1′-binaphthalene-2,2′-dicarboxylic acid, was recovered quantitatively.

The axially chiral bipyridine *N,N′*-dioxide diols (*R*)-**2** obtained here were examined for their catalytic activity and enantioselectivity in the asymmetric allylation of aldehydes **6** with allyl(trichloro)silane (Scheme 4). All of the bipyridine *N,N′*-dioxides (*R*)-**2** were highly active for the allylation, catalyzing the reaction at −45 °C with 0.1 mol % loading. Table 1 summarizes the results obtained for the asymmetric allylation of 4-methoxybenzaldehyde (**6a**) and 4-trifluoromethylbenzaldehyde (**6b**), where the reaction was stopped after reaction period of 2.5 h to compare the catalytic activity. Remarkable points are as follows: 1) Aldehyde **6a** which is substituted with a methoxy group is always more reactive toward the present allylation than aldehyde **6b** which is substituted with a trifluoromethyl group, and the enantioselectivity is always higher for **6a** than for **6b** irrespective of the aryl substituents on the bipyridine *N,N′*-dioxide catalysts. 2) The electron-donating or -withdrawing character of the *para*-substituent on the *N,N′*-dioxide



Scheme 3. Preparation of axially chiral bipyridine *N,N′*-dioxides (*R*)-**2**; a) $POCl_3$ (3 equivs.), NaCl (20 equivs.), DMF, 60 °C, 2 h; b) $H_2NCONH_2 \cdot H_2O_2$ (3.1 equivs.), $(CF_3CO)_2O$ (3 equivs.), CH_3CN/CH_2Cl_2, 0 °C to rt, 3 h, (×3); c) ArMgBr (3 equivs.), $PdCl_2$(dppf) (5 mol %), THF, −15 °C, 1 h; d) 6 N NaOH, MeOH.



Scheme 4. Asymmetric allylation of aldehydes with allyl(trichloro)silane; R = 4-$MeOC_6H_4$ (**6a**), 4-$CF_3C_6H_4$ (**6b**), Ph (**6c**), 2-MeC_6H_4 (**6d**), 2-furyl (**6e**), (*E*)-PhCH=CH (**6f**).

catalysts does not strongly affect the enantioselectivity, but it affects the catalytic activity. The electron-rich *N,N′*-dioxide **2b** is more catalytically active than the electron-poor **2c**. 3) Introduction of methyl or phenyl groups at the 3 and 5 positions on the phenyl group of *N,N′*-dioxides increased the enantioselectivity for the allylation of **6b**.

Bipyridine *N,N′*-dioxide **2d**, which contains both 4-methoxy group and 3,5-dimethyl groups on the phenyl ring, showed higher catalytic activity and higher enantioselectivity for the asymmetric allylation of some oth-

Table 1. Asymmetric allylation of aldehydes **6a** and **6b** with allyl(trichloro)silane catalyzed by 0.1 mol % of (*R*)-**2a–f**.[a]

Entry	Catalyst (Ar-)	Aldehyde	Conversion[b] [%]	Yield[c] [%]	% ee[d]
1[e]	(*R*)-**2a** (Ph-)	**6a**	100	96	94
2[e]	(*R*)-**2a** (Ph-)	**6b**	91	83	56
3	(*R*)-**2b** (4-$MeOC_6H_4$-)	**6a**	100	96	91
4	(*R*)-**2b** (4-$MeOC_6H_4$-)	**6b**	97	84	53
5	(*R*)-**2c** (4-$CF_3C_6H_4$-)	**6a**	93	78	91
6	(*R*)-**2c** (4-$CF_3C_6H_4$-)	**6b**	76	66	52
7	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)	**6a**	100	98	94
8	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)	**6b**	97	90	75
9	(*R*)-**2e** (3,5-Ph_2-4-$MeOC_6H_2$-)	**6a**	94	89	91
10	(*R*)-**2e** (3,5-Ph_2-4-$MeOC_6H_2$-)	**6b**	91	87	77
11	(*R*)-**2f** (3,5-*t*-Bu_2-4-$MeOC_6H_2$-)	**6a**	100	96	89
12	(*R*)-**2f** (3,5-*t*-Bu_2-4-$MeOC_6H_2$-)	**6b**	88	79	61

[a] The allylation was carried out with (*R*)-**2a–f** (0.1 mol %), allyl(trichloro)silane (1.2 equivs.), and diisopropylethylamine (3.0 equivs.) in 1.0 M acetonitrile solution at $-45\,^{\circ}C$ for 2.5 h.
[b] Conversion was determined by NMR analysis (**7**/(**6**+**7**)).
[c] Yield of isolated product
[d] Determined by GLC analysis with CP-Chirasil-Dex for **7a**, **7b**.
[e] Reported in Ref.[5b]

Table 2. Asymmetric allylation of aldehydes **6c–f** with allyl(trichloro)silane catalyzed by 0.1 mol % of (*R*)-**2a** or (*R*)-**2d**.[a]

Entry	Aldehyde	Catalyst (Ar-)	Yield[b] [%]	% ee[c]
1	Ph (**6c**)	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)	96	91
2[d]	Ph (**6c**)	(*R*)-**2a** (Ph-)	95	84
3	Ph (**6c**)	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)[e]	84	91
4	2-MeC_6H_4 (**6d**)	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)	99	90
5	2-MeC_6H_4 (**6d**)	(*R*)-**2a** (Ph-)	93	85
6	2-furyl (**6e**)	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)	94	71
7	2-furyl (**6e**)	(*R*)-**2a** (Ph-)	93	63
8	(*E*)-PhCH=CH (**6f**)	(*R*)-**2d** (3,5-Me_2-4-$MeOC_6H_2$-)	95	72
9[d]	(*E*)-PhCH=CH (**6f**)	(*R*)-**2a** (Ph-)	95	60

[a] The allylation was carried out with (*R*)-**2a** or (*R*)-**2d** (0.1 mol %), allyl(trichloro)silane (1.2 equivs.), and diisopropylethylamine (3.0 equivs.) in 1.0 M acetonitrile solution at $-45\,^{\circ}C$ for 2.5 h.
[b] Yield of isolated product.
[c] Determined by HPLC analysis with Chiralcel OD-H for **7c**, **7f**, by HPLC analysis with Chiralpak AD for **7d**, and GLC analysis with CP-Chirasil-Dex for **7e**.
[d] Reported in Ref.[5b]
[e] 0.01 mol % of (*R*)-**2d** was used, and the reaction time was 24 h.

er aldehydes. The results are summarized in Table 2, which also contains the data obtained with the standard phenyl-substituted bipyridine *N,N′*-dioxide **2a** for comparison. Although the enantioselectivity is still not satisfactory, it was improved by about 10% by use of (*R*)-**2d** in the reaction of benzaldehyde (**6c**) (entries 1 and 2), an aldehyde substituted at the *ortho* position **6d** (entries 4 and 5), a heteroaryl aldehyde **6e** (entries 6 and 7), and an alkenyl aldehyde **6f** (entries 8 and 9). The high catalytic activity of **2d** is highlighted in entry 3 where 0.01 mol % of (*R*)-**2d** catalyzes the asymmetric allylation of benzaldehyde (**6c**) to give an 84% yield of the corresponding homoallyl alcohol (*S*)-**7c** without loss of the enantioselectivity (91% ee).

Conclusion

We have developed a new preparative method for axially chiral bipyridine *N,N′*-dioxides where various aryl substituents can be introduced at the 6 and 6′ positions by the palladium-catalyzed cross-coupling of the key dichloride (R_{nap},R_{pyr})-**1**. Those containing a 4-methoxy group on the phenyl groups at the 6 and 6′ positions were found to be more catalytically active than others for the asymmetric allylation of aldehydes with allyl(trichloro)silane. Highest enantioselectivity in the asymmetric allylation was observed with the bipyridine *N,N′*-dioxide (*R*)-**2d**, which is substituted with the 4-methoxy-3,5-dimethylphenyl group.

Experimental Section

General Procedures

All moisture sensitive manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5. Chemical shifts are reported in δ ppm referenced to an internal tetramethylsilane standard for ^{1}H NMR and chloroform-*d* (δ = 77.0 ppm) for ^{13}C NMR.

Materials and Reagents

Cyclic diester *N,N′*-dioxide (R_{nap},R_{pyr})-**3**,[5] $PdCl_2$(dppf),[9] 4-methoxy-3,5-di(*tert*-butyl)phenyl bromide,[12] and 4-methoxy-3,5-diphenylphenyl bromide,[12] were prepared according to the reported procedures.

Preparation of Bipyridine *N,N′*-Dioxide Dichloride (R_{nap},R_{pyr})-1

Dichloro cyclic diester (R_{nap},R_{pyr})-4: A mixture of cyclic diester *N,N′*-dioxide (R_{nap},R_{pyr})-**3** (200 mg, 0.361 mmol), sodium chloride (421 mg, 7.20 mmol), dimethylformamide (1.8 mL), and phosphorus oxychloride (0.10 mL, 1.1 mmol) was stirred at 60 °C for 2 h. The mixture was quenched with water and extracted with chloroform three times. The combined extracts were washed with saturated aqueous sodium bicarbonate and aqueous sodium chloride. The organic layer was dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was chromatographed on alumina (benzene/ethyl acetate = 20/1) to give (R_{nap},R_{pyr})-**4**; yield: 141 mg (66%); $[\alpha]_D^{20}$: +439 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 4.75 (d, *J* = 12.2 Hz, 2H), 5.60 (d, *J* = 12.2 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.88 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 63.5, 123.6, 125.1, 127.0, 127.4, 127.6, 127.8, 127.9, 127.9, 129.6, 132.8, 134.4, 138.6, 141.6, 150.1, 155.6, 166.4; anal. calcd, for $C_{34}H_{20}Cl_2N_2O_4$: C 69.05, H 3.41; found: C 69.15, H 3.70.

Dichloro cyclic diester *N,N′*-dioxide (R_{nap},R_{pyr})-1: A suspension of dichloro cyclic diester (R_{nap},R_{pyr})-**4** (3.02 g, 5.11 mmol) and urea-hydrogen peroxide adduct (1.49 g, 15.8 mmol) in dichloromethane (5.1 mL) and acetonitrile (5.1 mL) was cooled to 0 °C. Trifluoroacetic anhydride (2.2 mL, 15 mmol) was slowly added and the reaction mixture was stirred at 0 °C for 1 h and at room temperature for additional 2 h. The reaction was quenched by the addition of an aqueous solution of sodium sulfite and stirred for 15 minutes, followed by dilution with chloroform. The organic layer was separated and washed with saturated aqueous sodium bicarbonate, and aqueous sodium chloride. It was dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was chromatographed on silica gel (acetone/hexane = 1/1) to give (R_{nap},R_{pyr})-**1**; yield: 665 mg (21%). The recovered substrate and the monoxide were subjected to the oxidation two more times to give (R_{nap},R_{pyr})-**1**; combined yield: 1.48 g (47%); $[\alpha]_D^{20}$: +797 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 4.95 (d, *J* = 12.7 Hz, 2H), 5.07 (d, *J* = 12.7 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.90 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 63.2, 125.1, 126.4, 126.7, 127.1, 127.3, 127.3, 127.9, 128.0, 132.7, 134.5, 135.3, 138.7, 142.2, 142.8, 166.2; anal. calcd. for $C_{34}H_{20}Cl_2N_2O_6$: C 65.50, H 3.23; found: C 65.35, H 3.38.

General Procedure for the Palladium-Catalyzed Cross-Coupling Reaction of (R_{nap},R_{pyr})-1

To a solution of (R_{nap},R_{pyr})-**1** (100 mg, 0.160 mmol) and $PdCl_2$(dppf) (5.87 mg, 8.02 μmol) in tetrahydrofuran (1.6 mL) was added dropwise a Grignard reagent (THF solution, 0.48 mmol) at −15 °C. The reaction mixture was stirred at −15 °C for 1 h, before aqueous ammonium chloride was added. The mixture was extracted with chloroform three times. The combined organic layer was washed with saturated aqueous sodium bicarbonate and aqueous sodium chloride, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was chromatographed on silica gel (acetone/hexane = 1/1) to give (R_{nap},R_{pyr})-**5**. The yields are listed in Scheme 3.

Cyclic diester *N,N′*-dioxide (Ar = phenyl) (R_{nap},R_{pyr})-5a: The analytical and spectral data for (*R*)-**5a** have been reported.[5]

Cyclic diester *N,N′*-dioxide (Ar = 4-methoxyphenyl) (R_{nap},R_{pyr})-5b: $[\alpha]_D^{20}$: +794 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 3.85 (s, 6H), 4.94 (d, *J* = 12.5 Hz, 2H), 5.22 (d, *J* = 12.5 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 4H), 7.17 (t, *J* = 7.4 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 7.90 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 55.4, 63.9, 113.7, 124.7, 125.4, 126.3, 126.6, 127.0, 127.5, 127.7, 127.8, 127.9, 131.0, 132.8, 134.5, 134.8, 138.8, 143.0, 149.0, 160.7, 166.4.

Cyclic diester *N,N′*-dioxide (Ar = 4-trifluoromethylphenyl) (R_{nap},R_{pyr})-5c: $[\alpha]_D^{20}$: +712 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 4.91 (d, *J* = 12.5 Hz, 2H), 5.30 (d, *J* = 12.5 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.1 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 4H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.3 Hz, 4H); ^{13}C NMR ($CDCl_3$): δ = 63.5, 123.8 (q, $J_{C\text{-}F}$ = 272.5 Hz), 125.2 (q, $J_{C\text{-}F}$ = 3.6 Hz), 125.3, 127.0 (q, $J_{C\text{-}F}$ = 18.6 Hz), 127.4, 127.9, 127.9, 128.0, 129.8, 131.2, 131.4, 131.7, 132.8, 134.6, 135.8, 136.4, 139.1, 142.8, 148.0, 166.2.

Cyclic diester *N,N′*-dioxide (Ar = 3,5-dimethyl-4-methoxyphenyl) (R_{nap},R_{pyr})-5d: $[\alpha]_D^{20}$: +756 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 2.37 (s, 12H), 3.78 (s, 6H), 4.95 (d, *J* = 12.5 Hz, 2H), 5.20 (d, *J* = 12.5 Hz, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.58 (s, 4H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 16.2, 59.6, 63.8, 125.4, 126.5, 126.6, 127.0, 127.4, 127.7, 127.7, 127.8, 127.8, 127.9, 130.0, 130.9, 132.8, 134.5, 135.0, 138.8, 143.0, 149.2, 158.2, 166.4.

Cyclic diester *N,N′*-dioxide (Ar = 3,5-diphenyl-4-methoxyphenyl) (R_{nap},R_{pyr})-5e: $[\alpha]_D^{20}$: +554 (*c* 0.502, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 3.22 (s, 6H), 4.95 (d, *J* = 12.5 Hz, 2H), 5.24 (d, *J* = 12.5 Hz, 2H), 6.87 (d, 8.7 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 4H), 7.45 (t, *J* = 7.4 Hz, 8H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* =

7.7 Hz, 2H), 7.66 (d, $J=8.4$ Hz, 8H), 7.69 (d, $J=8.6$ Hz, 2H), 7.88 (d, $J=8.6$ Hz, 2H), 7.89 (d, $J=8.0$ Hz, 2H), 7.92 (s, 4H); ^{13}C NMR ($CDCl_3$): $\delta=60.5$, 63.6, 125.3, 126.7, 126.9, 127.0, 127.3, 127.4, 127.6, 127.8, 127.9, 128.0, 128.2, 129.3, 131.6, 132.8, 134.5, 135.1, 135.6, 138.0, 138.7, 143.0, 148.8, 156.1, 166.3.

Cyclic diester *N,N′*-dioxide [Ar = 3,5-di(*tert*-butyl)-4-methoxyphenyl] (R_{nap},R_{pyr})-5f: $[\alpha]_D^{20}$: +632 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=1.50$ (s, 36H), 3.77 (s, 6H), 4.94 (d, $J=12.4$ Hz, 2H), 5.24 (d, $J=12.4$ Hz, 2H), 6.86 (d, $J=8.2$ Hz, 2H), 6.88 (d, $J=8.7$ Hz, 2H), 7.21 (t, $J=7.6$ Hz, 2H), 7.36 (d, $J=8.2$ Hz, 2H), 7.51 (t, $J=7.6$ Hz, 2H), 7.70 (d, $J=8.6$ Hz, 2H), 7.78 (s, 4H), 7.91 (d, $J=8.6$ Hz, 2H), 7.92 (d, $J=8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta=32.1$, 36.0, 64.0, 64.4, 125.4, 126.8, 126.8, 126.9, 127.1, 127.5, 127.8, 127.9, 128.0, 128.1, 132.9, 134.5, 134.6, 138.7, 143.2, 143.6, 150.1, 160.8, 166.5.

General Procedure for the Hydrolysis of (R_{nap},R_{pyr})-5a–c

To a suspension of (R_{nap},S_{pyr})-**5a–c** (0.11 mmol) in methanol (6 mL) was added 6 N aqueous sodium hydroxide (1 mL). After stirring at room temperature for 34 h, methanol was removed from the reaction mixture to give a white precipitate. It was filtered, and the filter cake was washed with 15% aqueous sodium hydroxide to give (*R*)-3,3′-bis(hydroxymethyl)-6,6′-disubstituted-2,2′-bipyridine *N,N′*-dioxides [(*R*)-**2a–c**]. The yields are listed in Scheme 3.

(*R*)-3,3′-Bis(hydroxymethyl)-6,6′-diphenyl-2,2′-bipyridine *N,N′*-dioxide [(*R*)-2a]: The analytical and spectral data for (*R*)-**2a** have been reported.[5]

(*R*)-3,3′-Bis(hydroxymethyl)-6,6′-bis(4-methoxyphenyl)-2,2′-bipyridine *N,N′*-dioxide [(*R*)-2b]: $[\alpha]_D^{20}$: −151 (*c* 0.25, $CHCl_3$/MeOH = 1/1); ^{1}H NMR ($CDCl_3$): $\delta=3.86$ (s, 6H), 4.29 (d, $J=11.9$ Hz, 2H), 4.39 (t, $J=11.0$ Hz, 2H), 4.96 (d, $J=9.7$ Hz, 2H), 6.98 (d, $J=8.7$ Hz, 4H), 7.62 (s, 4H), 7.81 (d, $J=8.7$ Hz, 4H); ^{13}C NMR ($CDCl_3$): $\delta=55.4$, 63.1, 113.7, 124.1, 127.8, 129.1, 131.2, 138.5, 142.7, 149.6, 160.9; HRMS(FAB): calcd. for $C_{26}H_{25}N_2O_6$ [M^+ + H]: 461.1713; found: 461.1712.

(*R*)-3,3′-Bis(hydroxymethyl)-6,6′-bis(4-trifluoromethylphenyl)-2,2′-bipyridine *N,N′*-dioxide [(*R*)-2c]: $[\alpha]_D^{20}$: −21.7 (*c* 0.25, $CHCl_3$/MeOH = 1/1); ^{1}H NMR ($CDCl_3$): $\delta=4.33$ (d, $J=11.5$ Hz, 2H), 4.44 (m, 4H), 7.65 (d, $J=8.1$ Hz, 2H), 7.69 (d, $J=8.1$ Hz, 2H), 7.74 (d, $J=8.1$ Hz, 4H), 7.93 (d, $J=8.1$ Hz, 4H); ^{13}C NMR ($CDCl_3$): $\delta=60.9$, 123.8 (q, $J_{C\text{-}F}=274$ Hz), 125.3 (q, $J_{C\text{-}F}=4.1$ Hz), 127.8, 128.1, 130.1, 131.8 (q, $J_{C\text{-}F}=32.1$ Hz), 135.4, 141.0, 141.1, 147.6; HRMS(FAB): calcd. for $C_{26}H_{19}F_6N_2O_4$ [M^+ + H]: 537.1249; found: 537.1254.

General Procedure for the Hydrolysis of (R_{nap},R_{pyr})-5d–f

To a solution of (R_{nap},R_{pyr})-**5d–f** (0.100 mmol) in methanol (20 mL) and tetrahydrofuran (5 mL) was added 6 N aqueous sodium hydroxide (5 mL), and the mixture was stirred at 40 °C for 79 h. After removal of methanol, the aqueous layer was extracted with chloroform three times. The combined organic layer was washed with aqueous sodium chloride, dried over anhydrous sodium sulfate, and evaporated to give (*R*)-3,3′-bis(hydroxymethyl)-6,6′-disubstituted-2,2′-bipyridine *N,N′*-dioxides [(*R*)-**2d–f**]. The yields are listed in Scheme 3.

(*R*)-3,3′-Bis(hydroxymethyl)-6,6′-bis(3,5-dimethyl-4-methoxyphenyl)-2,2′-bipyridine *N,N′*-dioxide [(*R*)-2d]: $[\alpha]_D^{20}$: +157 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=2.31$ (s, 12H), 3.76 (s, 6H), 4.27 (d, $J=12.2$ Hz, 2H), 4.33 (br, 2H), 4.87 (br, 2H), 7.48 (s, 4H), 7.57 (d, $J=8.3$ Hz, 2H), 7.59 (d, $J=8.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta=16.2$, 59.7, 62.4, 127.3, 127.9, 128.4, 130.1, 130.9, 138.8, 142.2, 149.4, 158.3; HRMS (FAB): calcd. for $C_{30}H_{33}N_2O_6$ [M^+ + H]: 517.2339; found: 517.2344.

(*R*)-3,3′-Bis(hydroxymethyl)-6,6′-bis(3,5-diphenyl-4-methoxyphenyl)-2,2′-bipyridine *N,N′*-dioxide [(*R*)-2e]: $[\alpha]_D^{20}$: +33.4 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=3.21$ (s, 6H), 4.32 (d, $J=12.2$ Hz, 2H), 4.39 (br, 2H), 4,74 (br, 2H), 7.35 (t, $J=7.4$ Hz, 4H), 7.42 (t, $J=7.6$ Hz, 8H), 7.61 (d, $J=7.1$ Hz, 8H), 7.63 (d, $J=8.2$ Hz, 2H), 7.69 (d, $J=8.2$ Hz, 2H), 7.82 (s, 4H); ^{13}C NMR ($CDCl_3$): $\delta=60.5$, 62.3, 127.4, 127.5, 127.9, 128.2, 128.3, 129.2, 131.6, 135.6, 137.9, 139.1, 142.1, 148.9, 156.2; HRMS (FAB): calcd. for $C_{50}H_{41}N_2O_6$ [M^+ + H]: 765.2965; found: 765.2961.

(*R*)-3,3′-Bis(hydroxymethyl)-6,6′-bis(3,5-di(*tert*-butyl)-4-methoxyphenyl)-2,2′-bipyridine *N,N′*-dioxide [(*R*)-2f]: $[\alpha]_D^{20}$: +112 (*c* 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=1.44$ (s, 36H), 3.74 (s, 6H), 4.30 (d, $J=11.9$ Hz, 2H), 4.41 (d, $J=11.9$ Hz, 2H), 7.61 (d, $J=8.3$ Hz, 2H), 7.64 (d, $J=8.3$ Hz, 2H), 7.69 (s, 4H); ^{13}C NMR ($CDCl_3$): $\delta=32.0$, 35.9, 62.8, 64.3, 126.1, 128.1, 128.1, 128.8, 138.4, 142.6, 143.5, 150.4, 161.0; HRMS(FAB): calcd. for $C_{42}H_{57}N_2O_6$ [M^+ + H]: 685.4217; found: 685.4221.

General Procedure for the Asymmetric Allylation Catalyzed by (*R*)-2:

To a solution of a given catalyst (*R*)-**2** (0.001 mmol, 0.1 mol %), aldehyde **6** (1.00 mmol) and diisopropylethylamine (0.52 mL, 3.0 mmol) in acetonitrile (1 mL) was added dropwise allyl(trichloro)silane (0.17 mL, 1.2 mmol) at −45 °C. The reaction mixture was stirred at −45 °C for 2.5 h, before 1 mL of 3 N sodium hydroxide was added. The mixture was stirred at room temperature for additional 10 min, and then extracted with diethyl ether three times. The combined organic layer was washed with aqueous sodium chloride, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash column chromatography (ethyl acetate/hexane = 1/5) to give the corresponding homoallyl alcohol [(*S*)-**7**]. The yields and ees are listed in Tables 1 and 2.

(*S*)-1-(2-Methylphenyl)-3-buten-1-ol [(*S*)-7d]:[13] $[\alpha]_D^{20}$: −46.8 (*c* 1.26, EtOH); 90% ee by HPLC analysis: t_R (*R*)-(+), 15.8 min; (*S*)-(−), 18.1 min (Daicel Chiralpak AD, hexane/2-propanol = 19/1, 0.50 mL/min); ref.[13] for (*R*)-**7d** of 65% ee: $[\alpha]_D$: +30.4 (EtOH); ^{1}H NMR ($CDCl_3$): $\delta=1.95$ (br, 1H), 2.36 (s, 3H), 2.46 (m, 2H), 4.98 (m, 1H), 5.15 (ddt, $J=10.2$, 1.9, 1.1 Hz, 1H), 5.18 (ddt, $J=17.3$, 1.9, 1.6 Hz, 1H), 5.85 (dddd, $J=17.3$, 10.2, 7.7, 6.5 Hz, 1H), 7.12 (d, $J=7.4$ Hz, 1H), 7.17 (t, $J=7.4$ Hz, 1H), 7.23 (t, $J=7.7$ Hz, 1H), 7.48 (d, $J=7.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta=19.0$, 42.6, 69.6, 118.2, 125.1, 126.2, 127.2, 130.3, 134.3, 134.7, 141.9.

(*S*)-1-(2-Furyl)-3-buten-1-ol [(*S*)-7e]:[14] $[\alpha]_D^{20}$: −28.7 (*c* 1.60, $CHCl_3$); 71% ee by GLC analysis: t_R (*S*)-(−) 12.3 min; (*R*)-(+), 13.1 min (CP-Chirasil-Dex CB, column temperature 95 °C); Ref.[14] for (*R*)-**7e** of 83% ee: $[\alpha]_D^{29}$: +24.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=2.08$ (br, 1H), 2.63 (m, 2H), 4.75 (br, 1H), 5.12 (ddt, $J=10.2$, 1.8, 1.1 Hz, 1H), 5.14 (ddt, $J=17.1$, 1.8, 1.5 Hz, 1H), 5.81 (ddt, $J=17.1$, 10.2, 7.1 Hz, 1H), 6.25 (m,

1H), 6.33 (dd, $J = 3.3, 1.8$ Hz, 1H), 7.37 (dd, $J = 1.8, 0.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 40.0$, 66.9, 106.0, 110.1, 118.3, 133.7, 141.9, 156.0.

(*S*)-1-(4-Methoxyphenyl)-3-buten-1-ol [(*S*)-7a], (*S*)-1-(4-Trifluoromethylphenyl)-3-buten-1-ol [(*S*)-7b], (*S*)-1-Phenyl-3-buten-1-ol [(*S*)-7c], (*S*)-1-Phenyl-1,5-hexadien-3-ol [(*S*)-7f]: The analytical and spectral data for alcohols, (*S*)-**7a**, **7b**, **7c**, and **7f** have been reported.[5]

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