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Intramolecular asymmetric olefination of binaphthyl phosphonate derivatives of 1,3-diketones

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Abstract—Intramolecular asymmetric Wittig-type reactions of some chiral binaphthyl phosphonates of 2,2-disubstituted 1,3-dicarbonyl derivatives were investigated. The base-mediated cyclization occurred with differentiation of two diastereotopic carbonyl groups to give non-racemic dihydronaphthalene derivatives with moderate to good enantiomeric excess. The degree of asymmetric induction depended upon the substrates and the best result was obtained with the indanedione derivatives having alkyl substituents in 58–73% yield with 82–88% e.e. The absolute structure of one of the products was unambiguously determined by X-ray analysis and some mechanistic consideration is also given.

1. Introduction

Since the first report by Wittig,[1] considerable refinements of the original Wittig reaction have been made. Consequently, the stereo-, regio- and chemoselectivities can be controlled to a great extent, and as such the Wittig and related reactions have become one of the most valuable organic transformations for the creation of a carbon–carbon bond, introducing a new sp^2-carbon to the carbonyl group.[2,3] It is generally recognized that reactions to carbonyl compounds occupy a central position in organic synthesis and hence in asymmetric synthesis. The Wittig-type reaction[4] between nucleophilic phosphorous-stabilized carbanions and carbonyl components is one of the most widely used synthetic tools for the construction of the carbon–carbon double bond. The transformation generally occurs at low temperature and covers a large number of carbonyl compounds. However, despite this excellent progress,[5] only a limited number of examples in which Wittig-type reactions are involved in asymmetric synthesis had been known before the last decade.

Discrimination between enantiotopic groups of symmetrical substrates such as *meso*-compounds allows the simple and direct way to synthetically useful non-racemic materials.[6] For this purpose, biocatalysts such as enzymes or yeast have been employed in one of the most convenient approaches to optically active compounds.[7] Because of a paucity of information about the structure of the substrate–enzyme complex, it is difficult to predict the absolute configuration of the major enantiomer produced in such biocatalytic processes. Therefore, promising non-enzymatic methods are still required in this field.

Substantial progress has been made recently in the development of direct syntheses of optically active olefinic compounds from achiral carbonyl compounds using Wittig-type reactions. Apart from the kinetic resolutions of racemic ketones,[8] methods for asymmetric olefination are grouped into two approaches. One is the enantiotopic face discrimination of the carbonyl compounds to dissymmetric olefins,[9,10] and the differentiation of enantiotopic carbonyl groups of *meso*-polyketones is alternative. In connection with the latter approach, we recently observed a marked degree of discrimination between the enantiotopic carbonyl or π-face, when optically active phosphonates **1** or **2** possessing an axially dissymmetric binaphthol were used as a chiral HWE agent,[11] or a Michael donor.[12] Since the Wittig-type reaction proceeds with concomitant elimination of the phosphonate, a chiral phosphonate reagent having chirality at the phosphonate moiety has an advantage of direct production of an optically active olefin, and no procedure for removal of the auxiliary group from the diastereomeric products is necessary. Additionally, unlike the chiral phosphonates bearing a

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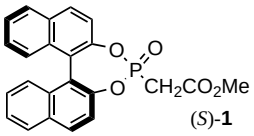
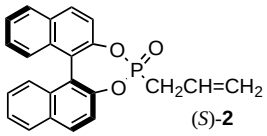
stereogenic phosphorous atom,[13] reagents of the type **1** or **2** have the advantages of easy preparation and ready availability of both enantiomers.



(*S*)-**1**



(*S*)-**2**

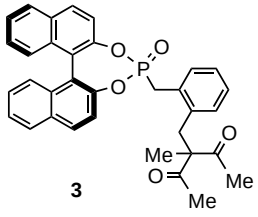
The most serious problem with the Wittig-type reactions comes from the susceptibility of steric hindrance together with enolization of the ketonic substrates under the basic conditions. Indeed, no intermolecular reaction of the hindered carbonyl compounds, such as 2,2-disubstituted cyclohexa- or cyclopenta-1,3-dione, with the anion of the reagent **1** or **2** occurred. On the other hand, it is well documented that the intramolecular process is more entropically favored than the intermolecular reaction and the creation of ring systems through intramolecular cyclization via 5- or 6-*exo*-trig processes is energetically preferred. Therefore, the intramolecular olefination might overcome some concomitant problems of the Wittig-type reaction to give a new five- or six-membered ring system having a substrated olefinic linkage.[14]

Based on the idea mentioned above, we investigated the intramolecular diastereoselective asymmetrization of symmetric 1,3-dicarbonyl systems to afford a non-racemic cyclic compound bearing a quaternary stereogenic carbon and trisubstituted olefinic bond. Comparing the enantiotopic functional group differentiation method with enzymes or Baker's yeasts,[7] only a few reports on the chemical asymmetrization with carbon–carbon bond formation have been known,[15,16] including Trost's pioneering work[16a] of intramolecular diastereotopic group discrimination as well as Hajos's annulation[15] with the aid of α-amino acids. Recently, the hydrindenone derivative, a useful building block for 1α,25-dihydroxyvitamin D3, was constructed via diastereotopic differentiation by intramolecular HWE reaction.[16b] Herein, we present our results from the intramolecular Wittig-type asymmetrization of 1,3-dicarbonyl compounds bearing axially chiral 1,1′-binaphthalene-2,2′-diol[17] as an auxiliary at the phosphorous portion.

2. Results and discussion

In order to investigate the intramolecular Wittig-type reactions, five substrates **3**–**7** were designed and prepared (Scheme 1). Thus, the *C*-alkylation of appropriate 2-alkyl-1,3-diketones **8**–**12** was first carried out with *o*-xylenedibromide **13**, which was employed as a linker arm to create a dihydronaphthalene ring. In this way, the *C*-alkylated benzylbromides **15**–**19** were uneventfully prepared by Triton-B catalyzed selective *C*-alkylation[18] of 2-alkyl-1,3-dicarbonyl compounds or, more conveniently, using a combination of lithium iodide and DBU.[19] Subsequent Arbusov reaction of the methylphosphite derivative **14** of (*S*)-(−)-1,1′-bi-2-naphthol with compounds **15**–**19** effected connective phosphorylation to give the desired substrates **3**–**7** in moderate to good yields (Scheme 2).

The reaction conditions for the cyclization of these substrates **3**–**7** by the intramolecular Wittig-type reactions was next examined using various bases and solvents. The cyclizations of **3**–**7** occurred and furnished the corresponding cyclized dihydronaphthalene derivatives **20**–**24** in moderate to good chemical yields (Scheme 3). When chelate-controlled conditions with the weakly basic DBU–LiBr system were employed, the reaction of **4** afforded the intermediate hydroxyphos-



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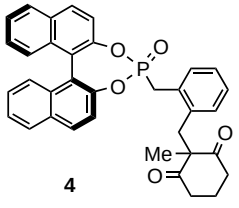

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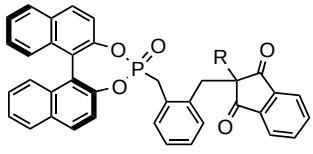
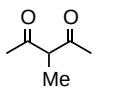


5; R = Me, **6**; R = Et, **7**; R = *i*-Pr

Scheme 1.



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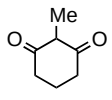

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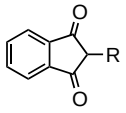
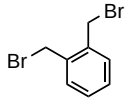


10; R = Me, **11**; R = Et, **12**; R = *i*-Pr



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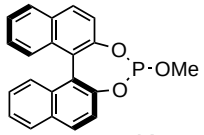

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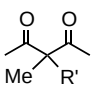

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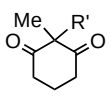

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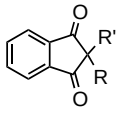
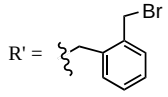
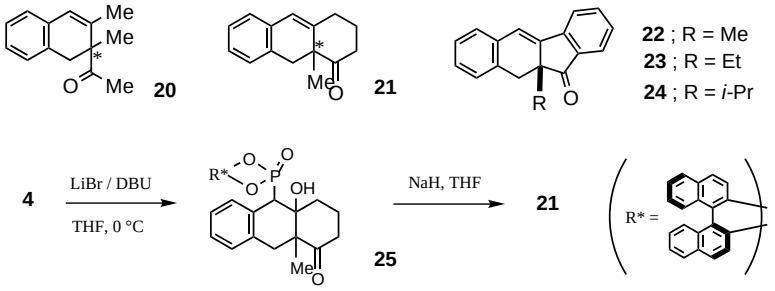


17; R = Me, **18**; R = Et, **19**; R = *i*-Pr



Scheme 2.



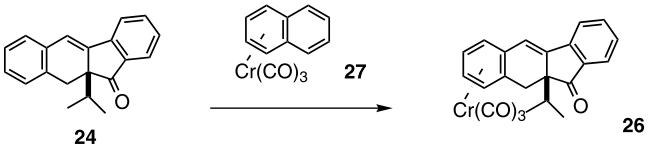
Scheme 3.

phonate **25**, which without isolation was then converted to **21** by treatment with NaH. Generally, the best results were obtained in THF with 1.2 equiv. of potassium bases such as KDA or KH in the presence of a catalytic amount of 18-crown-6. These results including the e.e.s of products are summarized in Table 1.

For the reactions of **3** and **4**, no satisfactory results with respect to both chemical and enantiomeric excesses could be obtained. On the other hand, higher e.e.s were observed with the indanedione derivatives independent of the identity of the alkyl substituents R (Scheme 4).

The absolute structures of the cyclized major enantiomers were deduced and determined by chemical transformation from the product **24** followed by X-ray crystallographic analysis of the product **26**. Thus, compound **24** was converted to its Cr-complex **26** through ligand exchange reaction with η^6-(naphthalene)-chromium tricarbonyl **27**, and crystals of the complex **26** from benzene were subjected to X-ray analysis (Fig. 1). In this way, using anomalous dispersion of the chromium atom, the absolute stereostructure of the product **24** was clearly elucidated to have an *S*-configuration at the stereogenic carbon. The stereochemistry of the other related products **22** and **23** was estimated to have the same configuration based on the above X-ray analysis as well as the mechanistic considerations mentioned below.

The observed stereostructure of the cyclized products **22**–**24** can be explained as follows. The intramolecular nucleophilic attack of the carbanion to the carbonyl occurs from the favored face opposite the substituent R (*anti*-attack). Regarding the π-face of the anion, approach to the *si*-face is sterically favored due to the chiral environment created by the optically active binaphthyl moiety. Taking two possible conformations, *s-cis* and *s-trans*, of the carbanion, as well as the approach to each carbonyl into account, four plausible transition state models (**a**)–(**d**) are considered. Among them (**a**) is the most energetically favored process lead-



Scheme 4.

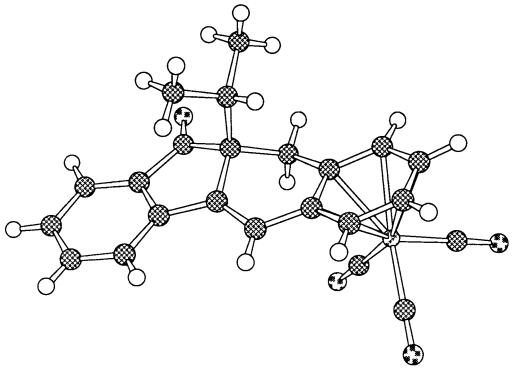


Figure 1. Crystal structure of **26**.

Table 1. Asymmetric intramolecular Wittig-type reactions of **3**–**7** to give **20**–**24**

Entry	Substrate	Conditions[a]	Product	Chemical yield[b]	(%) e.e.[c]
1	**3**	A	**20**	44	17
2	**4**	A	**21**	38	50
3	**4**	B	**21**	20	51
4	**4**	C	**21**[d]	16[d]	81[d]
5	**5**	A	**22**	58	88
6	**6**	A	**23**	72	82
7	**7**	A	**24**	73	86

[a] All reactions were carried out in THF. A: KDA (1.2 equiv.), 18-crown-6 (0.2 equiv.) at −78°C for 2–24 h. B: KH (1.2 equiv.) at −78°C for 2 h. C: DBU–LiBr (excess) at 0°C for 18 h.
[b] Isolated yield.
[c] Determined by HPLC with 1.0% hexane–2-PrOH on Chiralpak AD or Chiralcel OD (Daicel Chemical Inc. LTD) at the flow rate of 0.5 mL/min.
[d] After treatment with NaH.

ing to the preferential formation of **22**–**24**, since the other models impose a severe steric repulsion between some parts of the dicarbonyl substrate (Fig. 2).

3. Conclusion

In summary, we have examined the asymmetric intramolecular cyclization of a number of 1,3-dicarbonyl compounds having a chiral binaphthyl phosphonate group by Wittig-type reaction. The carbanion effectively discriminated the diastereotopic carbonyls to afford the dihydronaphthalene derivatives with satisfactory levels of e.e. This approach is applicable to the asymmetric construction of new five- or six-membered fused ring systems possessing a quaternary stereogenic carbon centre and an olefinic linkage to which the synthetic approach is difficult by other methods.

4. Experimental

4.1. General

Melting points are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were taken at 200 or 270 MHz in $CDCl_3$ with chemical shifts being reported as δ ppm from tetramethylsilane as an internal standard and couplings are expressed in hertz. Infrared (IR) spectra were measured in $CHCl_3$ solution. THF was distilled from sodium benzophenone ketyl and dichloromethane was from calcium hydride. Unless otherwise noted, all reactions were run under an argon atmosphere. All extractive organic solutions were dried over anhydrous $MgSO_4$. Flash column chromatography was carried out with silica gel 60 (spherical, 150–325 mesh), and silica gel 60 F_{254} plates (Merck) were used for preparative TLC (pTLC).

4.2. 2-Alkyl-2-(2′-bromomethyl)benzylindane-1,3-diones, 17, 18 and 19

To a stirred solution of **12** (1.5 g, 8.00 mmol) and *o*-xylenedibromide **13** (2.3 g, 8.80 mmol) in acetone (15 mL) was added dropwise a solution of benzyltrimethylammonium hydroxide (Triton B) in water (40% in water, 4.4 mL, 9.60 mmol, 1.2 equiv.) and the mixture was stirred for 12 h at room temperature. The mixture was concentrated under reduced pressure and extracted with EtOAc. The organic extracts were washed successively with water and brine, and then evaporated. Column chromatography of the residue on silica gel with hexane/EtOAc (4/1) gave **19** as crystals (2.60 g, 87%). Mp 118–119°C; colorless prisms (from $CHCl_3$/hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.82–7.68 (m, 4H), 7.16 (d, 1H, $J=7.0$ Hz), 7.00–6.87 (m, 3H), 4.70 (s, 2H), 3.43 (s, 2H), 2.41 (quintet, 1H, $J=7.0$ Hz), 1.05 (d, 6H, $J=6.9$ Hz); IR ($CHCl_3$) 2970, 1740, 1704, 1595, 1250 cm^{-1}. Anal. calcd for $C_{20}H_{19}BrO_2$: C, 64.70; H, 5.16. Found: C, 64.97; H, 5.15%.

Compounds **17** and **18** were prepared in the same way from the corresponding indanedione as described above for the preparation of **19**, in 73 and 85% yield, respectively. While, **15** and **16** were prepared by *C*-alkylation of 3-methyl-penta-2,4-dione **8** and 2-methyl-cyclo-1,3-hexadione **9** in 40 and 32% yield.

Compound **15**: Colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35–7.45 (m, 1H), 7.20–7.30 (m, 2H), 7.05 (m, 2H), 4.54 (s, 2H), 3.40 (s, 2H), 2.16 (s, 6H), 1.36 (s, 3H); IR ($CHCl_3$) 2960, 2945, 1726, 1697, 1460, 1360, 1250 cm^{-1}; anal. MS (*m*/z) 298, 296, 255, 253, 234, 209, 191, 173, 159, 138, 131 (100%), 117, 104, 91, 78, 59.

Compound **16**: Mp 99–100°C; colorless prisms (from AcOEt/hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.14–

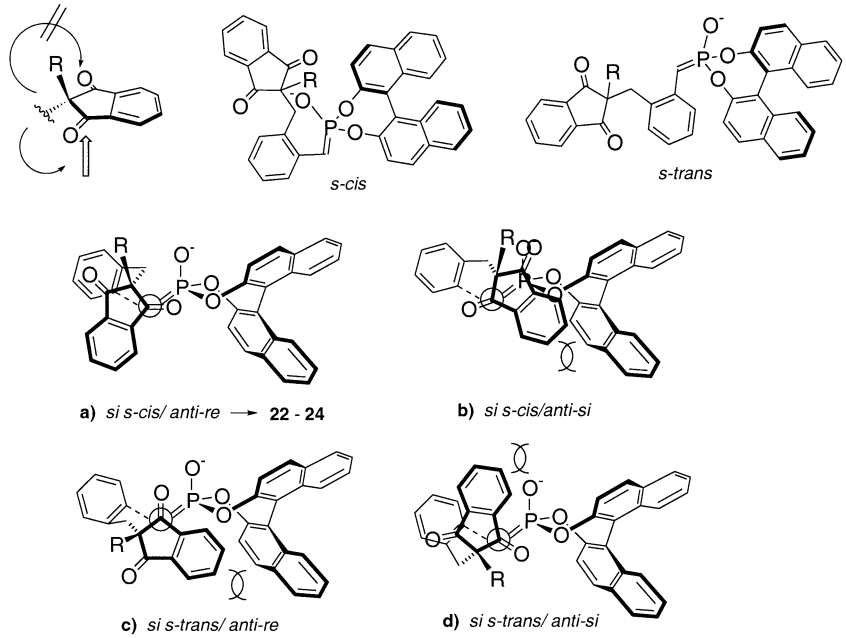


Figure 2. Possible mechanism of the intramolecular cyclization of anions of **5**–**7**.

7.37 (m, 3H), 6.94–7.03 (m, 1H), 4.60 (s, 2H), 3.33 (s, 2H), 2.53–2.73 (m, 2H), 2.30–2.46 (m, 2H), 1.61–1.95 (m, 2H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 23.3, 32.1, 37.7, 39.0, 49.4, 64.9, 127.6, 128.9, 130.1, 130.3, 131.1, 131.3, 211.9. IR ($CHCl_3$) 3030, 3015, 2960, 1725, 1693, 1605, 1230, 1215, 780 cm^{-1}; MS (m/z) 310, 308, 293, 267, 265, 246.

Compound **17**: Mp 99–100°C; colorless prisms (from AcOEt/hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.89–7.74 (m, 4H), 7.21 (m, 1H), 7.02–6.97 (m, 3H), 4.68 (s, 2H), 3.38 (s, 2H), 1.48 (s, 3H); IR ($CHCl_3$) 3020, 1740, 1710, 1598, 1378, 1258 cm^{-1}. Anal. calcd for $C_{18}H_{15}BrO_2$: C, 62.99; H, 4.40. Found: C, 63.36; H, 4.30%.

Compound **18**: Mp 93–94°C; colorless prisms (from AcOEt/hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.87–7.72 (m, 4H), 7.20 (brd, 1H, J=6.5 Hz), 7.04–6.93 (m, 3H), 4.67 (s, 2H), 3.35 (s, 2H), 2.08 (q, 2H, J=7.4 Hz), 0.78 (t, 3H, J=7.6 Hz); IR ($CHCl_3$) 3010, 1740, 1705, 1595, 1462, 1360, 1255 cm^{-1}. Anal. calcd for $C_{19}H_{17}BrO_2$: C, 63.88; H, 4.80. Found: C, 64.08; H, 4.77%.

4.3. Synthesis of phosphonates 3–7

A solution of (*S*)-(−)-1,1′-bi-2-naphthol (750 mg, 2.60 mmol) and diisopropylethylamine (740 mg, 5.70 mmol, 2.2 equiv.) in CH_2Cl_2 (30 mL) was stirred at 0°C for 15 min and dichloromethylphosphite (380 mg, 2.90 mmol, 1.2 equiv.) was added. The mixture was stirred for 1.5 h at room temperature, and concentrated at ambient temperature to afford crude **14**, which was used in the next reaction without purification.

A mixture of crude **14**, **19** (1.20 g, 3.30 mmol, 1.3 equiv.), hydroquinone (10.0 mg) and dichlorobenzene (2.0 mL) was heated at 160°C under an argon atmosphere with stirring for 24 h. The reaction mixture was diluted with CH_2Cl_2 (70 mL) and the resulting solution was washed with water and brine and then dried. Evaporation under reduced pressure gave the oily residue, which was subjected to column chromatography on silica gel with hexane/EtOAc (1/1). Compound **7** was obtained as an amorphous solid (660 mg, 41%). The absence of racemization was confirmed by the HPLC analysis of the sample obtained in this way.

Compound **7**: amorphous; $[\alpha]_D^{18}$ +235.0 (c 1.30, $CHCl_3$, >99% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.17–6.80 (m, 20H), 3.69 (dd, 1H, J=45.7, 15.4 Hz), 3.59 (dd, 1H, J=48.4, 15.3 Hz), 3.05 (dd, 2H, J=42.8, 14.3 Hz), 1.73 (m, 1H), 0.54 (t, 6H, J=6.5 Hz); IR ($CHCl_3$) 3015, 1738, 1730, 1592, 1509, 1228 cm^{-1}; MS (m/z) 622 (M$^+$); HRMS (m/z) calcd for $C_{40}H_{31}O_5P$ (M$^+$) 622.1909. Found: 622.1901.

Compounds **3**, **4**, **5** and **6** were afforded from **15**, **16**, **17** and **18**, respectively, without racemization via treatment with **14** in a similar manner to that described above for the preparation of **7**.

Compound **3**: Mp 185–186°C (from AcOEt/hexane); white crystals; $[\alpha]_D^{18}$ −6.14 (c 0.53, $CHCl_3$, >99% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.90–8.10 (m, 4H), 7.04–7.60 (m, 10H), 6.94–7.04 (m, 2H), 3.52 (d, 2H, J=21.5 Hz), 3.19 (dd, 2H, J=33.0, 15.0 Hz), 1.90 (s, 3H), 1.88 (s, 3H), 1.15 (s, 3H); IR ($CHCl_3$) 3020, 1741, 1708, 1592, 1280, 1220 cm^{-1}; MS (m/z) 549 (M$^+$+1), 530, 507, 463, 435, 391, 307, 154. Anal. calcd for $C_{34}H_{29}O_5P$: C, 74.44; H, 5.33. Found: C, 74.06; H, 5.13%.

Compound **4**: Mp 215–216°C (from Et_2O/hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.90–8.15 (m, 16H), 3.51–3.61 (d, 2H, J=20.8 Hz), 3.16 (dd, 2H, J=24.6, 14.3 Hz), 2.42–2.60 (m, 2H), 2.16–2.36 (m, 2H), 1.45–1.83 (m, 2H), 0.97 (s, 3H); IR ($CHCl_3$) 3060, 3015, 1721, 1692, 1621, 1590, 1511, 1465, 1280, 1221 cm^{-1}; MS (m/z) 561 (M$^+$+1), 560 (M$^+$), 544, 532, 517, 286, 268 (100%), 239, 55. Anal. calcd for $C_{35}H_{29}O_5P$ (560): C, 74.99; H, 5.18. Found; C, 74.79; H, 5.10%.

Compound **5**: Amorphous; $[\alpha]_D^{18}$ +317 (c 2.2, $CHCl_3$, >99% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.14–6.89 (m, 20H), 3.60 (d, 2H, J=20.6 Hz), 3.09 (dd, 3H, J=48.8, 14.4 Hz), 1.05 (s, 3H); IR ($CHCl_3$) 3020, 1741, 1708, 1592, 1280, 1220 cm^{-1}; MS (m/z) 594 (M$^+$); HRMS (m/z) calcd for $C_{38}H_{27}O_5P$ (M$^+$) 594.1596. Found: 594.1573.

Compound **6**: Amorphous; $[\alpha]_D^{18}$ +223 (c 1.4, $CHCl_3$, >99% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.16–6.84 (m, 20H), 3.60 (dd, 2H, J=19.9, 5.94 Hz), 3.02 (dd, 3H, J=49.1, 14.3 Hz), 1.50 (m, 2H), 0.45 (t, 3H, J=7.5 Hz); IR ($CHCl_3$) 3015, 1740, 1706, 1621, 1592, 1230 cm^{-1}; MS (m/z) 608 (M$^+$); HRMS (m/z) calcd for $C_{39}H_{29}O_5P$ (M$^+$) 608.1752. Found: 608.1744.

4.4. Asymmetric cyclization to afford 20–24

The preparation of compounds **20**–**24** was carried out by the cyclization described in Table 1. A representative example is as follows: a solution of **7** (768 mg, 1.23 mmol) and 18-crown-6 (70.1 mg, 0.27 mmol, 0.2 equiv.) in THF (18 mL) was treated with KDA (6.2 mL, 0.24 M in THF, 1.48 mmol, 1.2 equiv.) at −78°C under argon and the resulting mixture was stirred for 24 h at the same temperature. The mixture was quenched by addition of a sat. NH_4Cl solution and extracted with EtOAc. The organic extract was washed with water and brine, and then evaporated. The residue was purified by preparative TLC (hexane/EtOAc, 5/1) to give **24** (18.3 mg, 64%). The sample was analyzed by HPLC on a chiral stationary phase.

Compound **24**: Mp 64°C; colorless needle (from Et_2O); $[\alpha]_D^{16}$ +184 (c 0.44, $CHCl_3$, >99% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.68 (brt, 1H, J=7.6 Hz), 7.44 (brt, 1H, J=7.1 Hz), 7.24 (m, 4H), 7.00 (s, 1H), 3.34 (d, 1H, J=15.8 Hz), 2.80 (d, 1H, J=15.8 Hz), 1.95 (m, 1H), 1.01 (d, 3H, J=7.0 Hz), 0.54 (d, 3H, J=7.0 Hz); IR ($CHCl_3$) 3015, 2965, 1703, 1600, 1470, 1215 cm^{-1}. Anal. calcd for $C_{20}H_{18}O$: C, 87.59; H, 6.57. Found: C, 87.57; H, 6.79%.

Compound **20**: Colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.95–7.20 (m, 4H), 6.37 (m, 1H), 2.97 (dd, 2H, $J=89.4$, 15.7 Hz), 2.11 (s, 3H), 1.87 (d, 3H, $J=1.5$ Hz), 1.23 (s, 3H). MS (m/z) 201, 200 (M^+), 175, 169, 142, 115, 91, 77. HRMS (m/z) calcd for $C_{14}H_{16}O$ (M^+) 200.1201. Found: 200.1197.

Compound **21**: Colorless oil; $[\alpha]_D^{18}$ +45.8 (c 0.6, $CHCl_3$, 51% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.10–7.25 (m, 3H), 6.98–7.06 (m, 1H), 6.27 (m, 1H), 2.98 (dd, 2H, $J=29.0$, 16.0 Hz), 2.45–2.70 (m, 4H), 1.60–1.85 (m, 2H), 1.16 (s, 3H) IR ($CHCl_3$) 2950, 2880, 1708, 1642, 1488, 1455, 910 cm^{-1}.

Compound **22**: 58% yield, mp 114–116°C; colorless needle (from Et_2O); $[\alpha]_D^{18}$ +100.9 (c 0.59, $CHCl_3$, 88% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.91 (m, 2H), 7.73 (brt, 1H, $J=5.9$ Hz), 7.50 (brt, 1H, $J=6.4$ Hz), 7.31 (m, 4H), 7.03 (s, 1H), 3.07 (d, 1H, $J=15.5$ Hz), 2.89 (d, 1H, $J=15.3$ Hz), 1.14 (s, 3H); IR ($CHCl_3$) 3018, 2970, 1712, 1603, 1216 cm^{-1}; MS (m/z) 246 (M^+); HRMS (m/z) calcd for $C_{18}H_{14}O$ (M^+) 246.1044. Found: 246.1050. Anal. calcd for $C_{18}H_{14}O$: C, 87.78; H, 5.73. Found: C, 87.50; H, 5.66%.

Compound **23**: 72% yield, mp 64–65°C; colorless needle (from Et_2O); $[\alpha]_D^{20}$ +82.7 (c 1.3, $CHCl_3$, 82% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.83 (d, 2H, $J=8.4$ Hz), 7.69 (brt, 1H, $J=8.3$ Hz), 7.45 (brt, 1H, $J=8.1$ Hz), 7.25 (m, 4H), 7.00 (s, 1H), 3.14 (d, 1H, $J=15.5$ Hz), 2.85 (d, 1H, $J=15.8$ Hz), 1.58 (s, 2H), 0.67 (t, 3H, $J=7.5$ Hz); IR ($CHCl_3$) 3015, 2986, 1708, 1600, 1470, 1217 cm^{-1}. Anal. calcd for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.27; H, 6.42%.

Cr-complex **26**. The cyclized compound **24** mentioned above was first purified to give an enantiomerically pure sample by preparative HPLC with a Chiralcel OD preparative column. A mixture of purified **24** (75 mg, 0.27 mmol, 100% e.e.), complex **27** (106 mg, 0.40 mmol, 1.5 equiv.) and Et_2O/THF mixture (1/10, 5.5 mL) was heated at 90°C under an argon atmosphere in a sealed tube for 40 h. After cooling the mixture was filtered and the filtrate was concentrated to give a residue, which was subjected to p-TLC on silica gel with the solvent system of Et_2O/hexane (1/5) to afford **26** as crystals (23.7 mg, 21%).

Compound **26**: mp 171–178°C (decomp.); reddish prisms (from benzene); $[\alpha]_D^{16}$ −1791 (c 0.35, $CHCl_3$, ~100% e.e.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.80 (m, 3H), 7.52 (t, 1H, $J=6.6$ Hz), 6.64 (s, 1H), 5.57 (d, 1H, $J=6.0$ Hz), 5.44 (d, 2H, $J=3.4$ Hz), 5.25 (dd, 1H, $J=6.5$, 3.7 Hz), 3.13 (d, 1H, $J=15.9$ Hz), 2.91 (d, 1H, $J=15.8$ Hz), 1.96 (m, 1H), 1.00 (d, 3H, $J=6.9$ Hz), 0.59 (d, 3H, $J=7.0$ Hz); IR ($CHCl_3$) 1967, 1897, 1713, 1600, 1470 cm^{-1}. Anal. calcd for $C_{23}H_{18}CrO_4$: C, 67.32; H, 4.42. Found: C, 66.97; H, 4.45%. Crystallized as orthorhombic, space group $P2_12_12_1$ with $a=14.280$ (1), $b=18.265$ (2), $c=7.507$ (2) Å, $V=1957.9$ (5) Å^3, $Z=4$, $D_{calcd}=1.392$ g/cm^3. The structure was refined to $R=0.055$, $Rw=0.075$, goodness of fit = 1.51. The structure elucidated was supported by comparison with the R factor of *ent*-**26** ($R=0.109$), and furthermore, by the Flack parameter[20] of **26** ($X=-0.0079$). Crystallographic data for the structure **26** have been deposited with Cambridge Crystallographic Data Centre (deposition number CCDC 183967).

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