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Synthesis and use in palladium-catalyzed asymmetric allylic alkylation of new planar chiral chromium complexes of 1,2-disubstituted arenes having pyridine and aryl phosphine groups

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Abstract

Optically active (1,2-disubstituted arene)chromium tricarbonyl complexes **4**–**7** having pyridine and aryl phosphorus groups were synthesized from (*o*-disubstituted benzaldehyde)tricarbonylchromium. These chromium complexes have been used as chiral ligands in the asymmetric allylic alkylation of *rac*-1,3-diphenyl-2-propenyl acetate **8** catalyzed by (η^3-allyl)palladium complex. The enantioselectivity increases as the number of electron-withdrawing substituents in the aryl phosphine increases. Significant solvent effects on the enantioselectivity were observed for **4** and **7**. By the judicious choice of the planar chiral ligand, high enantioselectivities (90% *R*, 93% *S* at 0°C) were observed.

1. Introduction

There has been great interest in asymmetric synthesis catalyzed by transition metal complexes bearing chiral P,N-ligands,[1] because an enantioselective reaction can be realized with ligands containing electronically different donor centers. The P,N-ligand represents a class of chiral auxiliaries that are easily tuned by steric and electronic modification. Of the known chiral P,N-ligands, chiral phosphinoaryldihydrooxazole ligands have been found to be particularly useful. Recently we prepared new planar chiral P,N-ligands from (arene)chromium compounds, which were derived from a commercially available (+)-(4,6-*O*-benzylidene)methyl-α-D-glucopyranoside, and these planar chiral P,N-ligands had been used in asymmetric hydroboration of styrenes.[2] The use of (arene)chromium complexes[3] and cymantrene[1f] as chiral ligands in the catalytic asymmetric allylic alkylation has been reported by other groups. It has

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been reported[4] that incorporation of electronically different phosphorus chelates can markedly enhance enantioselectivity with certain ligand frameworks. Thus, we have synthesized electronically different phosphorus P,N-chelates via the introduction of the electron-withdrawing group CF_3. Herein we report the synthesis of new planar chiral P,N-ligands **4**–**7**, bearing aryl chromium tricarbonyl, phosphines, and pyridine, and their use in the palladium-catalyzed asymmetric allylic alkylation.

2. Results and discussion

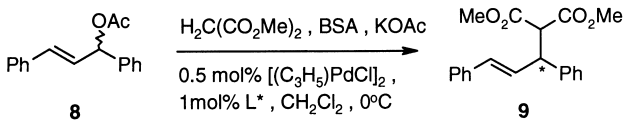
2.1. Synthesis of chiral ligands

The ligands employed in this study and their preparations are shown in Scheme 1.

The planar chiral compounds **2** were diastereoselectively synthesized from **1**.[2a] Synthesis and molecular structure of **2a** was previously prepared by us.[2a] Acid hydrolysis of **2** with 50% H_2SO_4 in THF or toluene gave **3** in 52–90% yields. Treatment of **3** with 2-lithiopyridine at −78°C led to a diastereomeric mixture of **4** and **5**. Introduction of pyridine generated a stereogenic center. Gatner et al. reported[5] the synthesis of P,N-chelate ligands based on pyridyl-substituted phosphaferrocenes by the reaction of 2-formyl-3,4-dimethylphosphaferrocene with 2-lithiopyridine. The diastereomers **4** and **5** are easily separated by chromatography. The diastereomeric ratio of **4** and **5** was slightly dependent upon the substituent in the aryl phosphine moiety. As the number of electron-withdrawing substituents increases, the relative ratio of **4** increases. We assigned the structures of **4** and **5** as shown in Scheme 1 after inspection of the ^{1}H NMR spectra of the diastereomers and the X-ray structure of **7a**.[2c] There was only one single peak from the hydroxy group in the ^{1}H NMR spectra of the diastereomers. For diastereomer **4**, there could be a hydrogen bonding between hydroxy and pyridyl groups, and the hydrogen of the hydroxy group could be seen in the ^{1}H NMR spectrum. The hydrogen of the hydroxy group of **4** appeared as a doublet due to the coupling with the benzylic hydrogen, and the benzylic proton appears as a doublet of doublet due to the coupling with the hydrogen of the hydroxy group and phosphorus. Thus, the carbon–oxygen bond is situated in the plane of the pyridine ring, with the oxygen atom *syn* to the nitrogen atom.[6] The hydrogen of the hydroxy group in **5** was not detected in the ^{1}H NMR spectrum. Thus, the benzylic proton appears as a doublet due to coupling with phosphorus only. Complex **6** or **7** was prepared by deprotonation of **4** or **5** in THF followed by addition of MeI. Thus, starting from a chromiumtricarbonyl complex of an *o*-disubstituted benzaldehyde, we have prepared chiral ligands **4**–**7**.

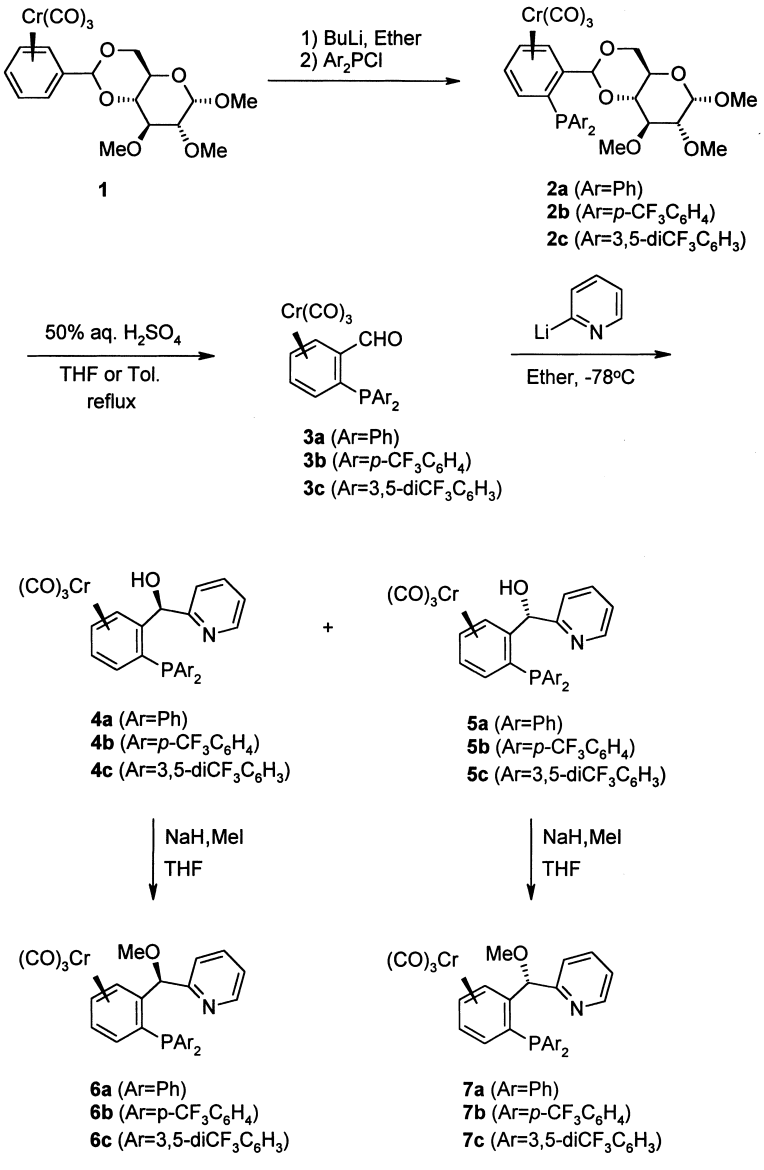
2.2. Allylic alkylation

To evaluate the effect of chiral ligand on the stereoselectivity of allylic alkylation, allylic substitution of *rac*-1,3-diphenyl-2-propenyl acetate **8** was carried out in CH_2Cl_2 at 0°C in the presence of a (η^3-allyl)palladium–ligand complex generated in situ from 0.5 mol% of bis[(η^3-allyl)palladium chloride] and 1 mol% of the appropriate ligand (Eq. 1).



(1)

The nucleophile was generated from dimethyl malonate in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of KOAc. The results of the catalytic reactions are shown in Table 1.



Scheme 1.

The reactions proceeded smoothly to give high yields of **9**. Compared to other studies,[6] the reaction time was relatively short even at 0°C. The absolute configuration of the product (assigned from specific rotation determinations and comparison with literature data) was controlled by the absolute configuration at the stereogenic center of the benzylic carbon, such that the use of ligands **4** and **6** resulted in preferred formation of (*R*)-**9** while using **5** and **7** resulted in (*S*)-**9**.

The enantioselectivities observed (entries 1–3 and 7–9 in Table 1) for **4** and **6** were greater than those for **5** and **7** and varied only slightly because of the similarity of the preferred conformation of the ligands. For **4** and **6**, a more rigid transition state of the palladium complex[6–8] and a steric effect of the $Cr(CO)_3$ group would enhance the enantioselectivities. However, a less rigid transition state and a lower steric effect of the $Cr(CO)_3$ group would be expected for **5** and **7** even though the methoxy group in **7** may

Table 1
Pd-catalyzed allylic alkylation of **8**

Entry	L*	Time (h)	Yield (%)[a]	*ee* (%)[b]	Config.[c]
1	**4a**	3	87	77	*R*
2	**4b**	6	91	90	*R*
3	**4c**	6	92	84	*R*
4	**5a**	9	92	40	*S*
5	**5b**	10	80	30	*S*
6	**5c**	10	86	69	*S*
7	**6a**	7	90	64	*R*
8	**6b**	5	98	86	*R*
9	**6c**	8	95	89	*R*
10	**7a**	3	92	63	*S*
11	**7b**	5	98	72	*S*
12	**7c**	17	98	89	*S*

[a] Isolated yields.
[b] The *ee* values were determined by ^{1}H NMR using chiral shift reagent, Eu(hfc)$_3$.
[c] The absolute configuration was assigned by the sign of optical rotation.

exert some influence on the enantioselectivities. We ascribe the higher enantioselectivities to the steric effect of the methyl group in **7**. As expected, as the number of electron-withdrawing substituents in the aryl phosphine increased, the values of ee increased except in the cases of **4c** and **5b**. When we compared the ee values (entries 1, 4, 7, and 10) of the first member of each group, we expected that the highest ee value would be obtained for **4c**. However, the highest ee value (90%, entry 2 in Table 1) was obtained for **4b**. The highest values (entries 2, 9, and 12 in Table 1) for each series except **5** were almost the same (89–90% ee). Thus, the use of **5** as chiral ligands was not advisable.

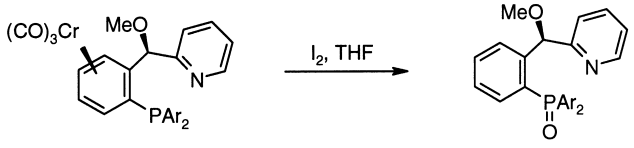
The solvent effect on the enantioselectivity with **4** or **7** as a planar chiral ligand was studied. The results are shown in Table 2. Significant solvent effects (entries 1–5 in Table 2) on the enantioselectivity were observed for **4b**: similar enantioselectivities (89–90%) were observed for toluene or methylene chloride, but a somewhat poor enantioselectivity (66%) was observed for THF. The enantioselectivities (entries 6–9 in Table 2) for the use of **7b** in toluene, CH_2Cl_2, THF, and DMF were also determined. The enantioselectivity increases as the polarity of the solvent increases. However, the best result was only 80% ee. The enantioselectivities (entries 10–12 in Table 2) for the use of **7c** as a planar chiral ligand were studied in methylene chloride and DMF. A better enantioselectivity was obtained in DMF using NaH as a base. When BSA was used as a base in the DMF solution, the reaction proceeded quite slowly presumably due to the decomposition of **7** over a long reaction time (entries 4, 9, and 11 in Table 2). In DMF, the highest ee value (93%) was obtained and the reaction time was shortened to 2 h. Of the solvents tested, methylene chloride was found to be the best solvent for **4b**, and DMF for **7c**.

Table 2
Pd-catalyzed allylic alkylation of **8** in various solvents

Entry	L*	Solvent	Base	Time (h)	Yield (%)[a]	*ee* (%)[b]	Config.[c]
1	**4b**	toluene	BSA	18	98	89	*R*
2	**4b**	CH_2Cl_2	BSA	6	91	90	*R*
3	**4b**	THF	BSA	23	70	66	*R*
4	**4b**	DMF	BSA	19	32	80	*R*
5	**4b**	DMF	NaH		no rxn		
6	**7b**	toluene	BSA	22	49	58	*S*
7	**7b**	CH_2Cl_2	BSA	5	98	72	*S*
8	**7b**	THF	BSA	23	90	80	*S*
9	**7b**	DMF	NaH	20	43	79	*S*
10	**7c**	CH_2Cl_2	BSA	17	98	89	*S*
11	**7c**	DMF	BSA	5 days	19	91.5	*S*
12	**7c**	DMF	NaH	2	83	93	*S*

[a] Isolated yields.
[b] The *ee* values were determined by ^{1}H NMR using chiral shift reagent, Eu(hfc)$_3$.
[c] The absolute configuration was assigned by the sign of optical rotation.

In order to figure out the role of the $Cr(CO)_3$ moiety in the planar chiral ligand, demetallation of **6c** was carried out. However, treatment of **6c** with an oxidizing reagent led to the isolation of phoshine oxide **10** (Eq. 2), which was inactive in the allylic alkylation.



6c **10** (Ar=3,5-di$CF_3C_6H_3$) (2)

Thus, the coordination of the $Cr(CO)_3$ group to the arene ring is quite crucial for the stability of chiral ligands. In a recent article about the catalytic asymmetric allylic alkylation of **8**, Uemura et al. reported that the coordination of the $Cr(CO)_3$ group to the arene ring is essential for the achievement of high stereoselective asymmetric allylic alkylation.[3a]

3. Conclusion

Compounds **4**–**7** are easily accessible chiral chelating ligands in which heteroatoms can be introduced independently in consecutive synthetic steps. Such a preparation warrants great flexibility, and the

approach should allow fine tuning of the ligands with respect to both their steric and electronic properties. By appropriate electronic tuning of ligand and by using the appropriate configuration of stereogenic center present in the ligand, both enantiomers of **9** can be prepared in good enantioselectivity (90% *R*, 93% *S* at 0°C) via a catalytic asymmetric allylic alkylation reaction. Work directed towards the extension of the different ligands and further applications in homogeneous asymmetric reactions are in progress.

4. Experimental

All reactions were conducted under nitrogen using standard Schlenk type flasks. Workup procedures were done in air. THF was freshly distilled from sodium benzophenone ketyl prior to use. Most organic chemicals were purchased from Aldrich Chemical Co. and were used as received. ^{1}H NMR spectra were obtained on a Bruker-300 or Bruker AMX-500 instrument. IR spectra were recorded on a Shimadzu IR-470 spectrophotometer (spectra measured as films on NaCl by evaporation of the solvent). Elemental analyses were done at the Chemical Analytic Center, College of Engineering, Seoul National University or Inter-University Center for Natural Science Research Facilities, Seoul National University. Optical rotations were measured on a JASCO DIP360 instrument. Compounds Ar_2PCl, **1**, **2a**, **3a**, **4a**, **5a**, and **7a** were synthesized by the published procedures.[2,4a]

4.1. Synthesis of *2*

A typical procedure for **2**. To the solution of **1** (1.5 g, 3.4 mmol) in 40 mL of Et_2O at −78°C was added *n*-BuLi (1.6 mL, 2.5 M in hexane). The resulting solution was stirred for 1 h at −78°C and treated with $ClP(4\text{-}CF_3C_6H_4)_2$ (1.22 g, 3.4 mmol) at −78°C. After stirring for an additional 15 min at −78°C, the solution was allowed to warm to room temperature (rt) and stirred for 3 h. After quenching with aq. NH_4Cl and Et_2O, the organic layer was separated, dried over anhydrous $MgSO_4$, concentrated, and chromatographed on a silica gel column eluting with hexane and Et_2O (v/v, 3:2) to yield a yellow solid **2b** (2.1 g, 80%). Mp 197–199°C; IR νCO 1968, 1900 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.67–7.26 (m, 8H), 6.04 (d, 5.4 Hz, 1H), 5.64 (m, 2H), 5.05 (t, 5.9 Hz, 1H), 4.95 (d, 6.0 Hz, 1H), 4.78 (d, 3.0 Hz, 1H), 4.28 (dd, 9.7, 4.0 Hz, 1H), 3.70 (m, 3H), 3.42 (s, 6H), 3.29 (t, 9.1 Hz, 1H), 3.16 (dd, 8.8, 3.1 Hz, 1H), 2.65 (s, 3H) ppm. Anal. calcd for $C_{33}H_{29}CrF_6O_9P$: C, 51.71; H, 3.81. Found: C, 51.66; H, 3.73. $[\alpha]_D^{17}$ 264 (c 0.27, CH_2Cl_2).

2c: Yield: 97%; mp 102–105°C; IR νCO 1976, 1903 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.97 (s, 1H), 7.89 (m, 3H), 7.64 (d, 5.8 Hz, 2H), 5.99 (d, 4.7 Hz, 1H), 5.73 (t, 6.2 Hz, 1H), 5.67 (m, 1H), 5.10 (t, 6.6 Hz, 1H), 4.87 (d, 6.6 Hz, 1H), 4.80 (d, 3.5 Hz, 1H), 4.33 (m, 2H), 3.76 (m, 2 H), 3.45 (s, 3H), 3.42 (s, 3H), 3.30 (t, 9.1 Hz, 1H), 3.18 (dd, 9.0, 3.3 Hz, 1H), 2.59 (s, 3 H) ppm. Anal. calcd for $C_{35}H_{27}CrF_{12}O_9P$: C, 46.58; H, 3.02. Found: C, 46.50; H, 2.89. $[\alpha]_D^{19}$ 215 (c 0.23, CH_2Cl_2).

4.2. Synthesis of *3*

A typical procedure for **3**. A solution of **2b** (2.1 g, 2.7 mmol) in 30 mL of toluene was added 2mL of 50% aq. H_2SO_4. The solution was heated at reflux for 4 h, allowed to cool to rt, and extracted with $Et_2O/NaHCO_3$. The organic layer was separated, dried over anhydrous $MgSO_4$, and chromatographed on a silica gel column eluting with Et_2O:hexane (1:4). Removal of the solvent gave a red solid **3b** in 73% yield (1.10 g). Mp 150°C (dec.); IR νCO 1974, 1905 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 9.85 (d, 4.7 Hz, 1H), 7.67 (m, 4H), 7.48 (m, 4H), 6.00 (d, 5.4 Hz, 1H), 5.57 (t, 6.3 Hz, 1H), 5.47 (t, 5.1 Hz, 1H), 4.51 (d, 6.4

Hz, 1H) ppm. Anal. calcd for $C_{24}H_{13}CrF_6O_4P$: C, 51.26; H, 2.33. Found: C, 51.35; H, 2.16. $[\alpha]_D^{16}$ 240 (c 0.11, CH_2Cl_2).

3c: Yield: 73%; mp 57–60°C; IR νCO 1982, 1918 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.61 (d, 3.1 Hz, 1H), 7.97 (d, 8,9 Hz, 2H), 7.80 (d, 6.8 Hz, 2H), 7.73 (d, 6.0 Hz, 2H), 5.93 (d, 4.1 Hz, 1H), 5.55 (m, 2H), 4.42 (d, 5.6 Hz, 1H) ppm. Anal. calcd for $C_{26}H_{11}CrF_{12}O_4P$: C, 44.72; H, 1.59. Found: C, 44.72; H, 1.55. $[\alpha]_D^{18}$ 480 (c 0.11, CH_2Cl_2).

4.3. Synthesis of *4* and *5*

A typical procedure for **4** and **5**. *n*-BuLi (0.22 mL, 2.5 M in hexane) was added to a solution of 2-bromopyridine (0.06 mL, 0.67 mmol) in 10 mL of Et_2O at −78°C. After the solution was stirred for 30 min, a solution of **3b** (1.10 g, 2.33 mmol) in 10 mL of Et_2O was transferred via cannula to the solution. After the solution had been stirred at −78°C for 30 min, it was allowed to warm to rt and quenched with $NaHCO_3/Et_2O$. The organic layer was dried over $MgSO_4$ and chromatographed on a silica gel column eluting with Et_2O:hexane (1:3). The first eluant was **4b** (0.49 g) and the second eluant **5b** (0.42 g). The overall yield was 73% and the dr (**4b**:**5b**) was 53:47.

4b: A yellow solid; mp 100°C (dec.); IR νCO 1963, 1888 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.57 (d, 4.6 Hz, 1H), 7.80 (t, 6.2 Hz, 1H), 7.58 (m, 9H), 7.32 (m, 1H), 6.33 (dd, 7.2, 6.5 Hz, 1H), 5.36 (t, 6.3 Hz, 1H), 5.23 (t, 6.2 Hz, 1H), 4.99 (d, 7.2 Hz, 1H), 4.77 (d, 6.3 Hz, 1H), 4.53 (m, 1H) ppm. Anal. calcd for $C_{29}H_{18}CrF_6NO_4P$: C, 54.30; H, 2.83; N, 2.18. Found: C, 54.49; H, 2.73; N, 2.25. $[\alpha]_D^{18}$ 260 (c 0.15, CH_2Cl_2).

5b: A yellow solid; mp 100°C (dec.); IR νCO 1960, 1885 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.09 (d, 4.1 Hz, 1H), 7.64 (d, 7.8 Hz, 2H), 7.49 (t, 7.5 Hz, 2H), 7.41 (d, 7.8 Hz, 2H), 7.25 (m, 2H), 7.13 (t, 7.2 Hz, 3H), 6.89 (dd, 7.3, 4.6 Hz, 1H), 6.60 (d, 6.0 Hz, 1H), 5.73 (m, 2H), 5.13 (t, 6.0 Hz, 1H), 4.87 (d, 6.2 Hz, 1H) ppm. Anal. calcd for $C_{29}H_{18}CrF_6NO_4P$: C, 54.30; H, 2.83; N, 2.18. Found: C, 54.42; H, 2.62; N, 2.44. $[\alpha]_D^{18}$ 370 (c 0.15, CH_2Cl_2).

4c: A yellow solid; yield: 37%; mp 130°C (dec.); IR νCO 1963, 1888 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.60 (d, 4.6 Hz, 1H), 7.89 (m, 7H), 7.59 (d, 7.8 Hz, 1H), 7.34 (m, 1H), 6.31 (dd, 7.6, 5.8 Hz, 1H), 5.42 (t, 6.4 Hz, 1H), 5.23 (t, 6.4 Hz, 1H), 5.11 (d, 7.6 Hz, 1H), 4.71 (d, 6.3 Hz, 1H), 4.42 (m, 1H) ppm. Anal. calcd for $C_{31}H_{16}CrF_{12}NO_4P$: C, 47.89; H, 2.07; N, 1.80. Found: C, 47.63; H, 1.77; N, 1.97. $[\alpha]_D^{20}$ 280 (c 0.10, CH_2Cl_2).

5c: A yellow solid; yield: 26%; mp 140°C (dec.); IR νCO 1968, 1896 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.13 (s, 1H), 7.89 (m, 4H), 7.55 (d, 6.3 Hz, 2H), 7.47 (m, 2H), 6.94 (m, 1H), 6.67 (m, 1H), 5.78 (t, 6.4 Hz, 1H), 5.68 (m, 1H), 5.17 (t, 6.0 Hz, 1H), 4.93 (d, 6.6 Hz, 1H), 2.89 (br s, 1H) ppm. Anal. calcd for $C_{31}H_{16}CrF_{12}NO_4P$: C, 47.89; H, 2.07; N, 1.80. Found: C, 48.15; H, 2.03; N, 1.77. $[\alpha]_D^{19}$ 305 (c 0.12, CH_2Cl_2).

4.4. Synthesis of *6* and *7*

A typical procedure for **6** and **7**. NaH (10 mg, 60% oil) was added to a solution of **4b** (0.10 g, 0.16 mmol) in 5 mL of THF. After the solution was stirred at rt for 15 min, MeI (0.05 mL, 0.80 mmol) was added to the solution. The resulting solution was stirred for 2 h, quenched with $NaHCO_3/Et_2O$, and chromatographed on a silica gel column eluting with Et_2O:hexane (1:2). Removal of the solvent gave a yellow solid **6b** in 53% yield (56 mg).

6a: A yellow solid; yield: 58%; mp 110°C (dec.); IR νCO 1958, 1891 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.74 (d, 4.5 Hz, 1H), 7.78 (t, 9.0 Hz, 1H), 7.60 (d, 9.0 Hz, 1H), 7.41 (m, 10H), 7.30 (m, 1H), 5.92 (d, 6.6

Hz, 1H), 5.27 (t, 6.5 Hz, 1H), 5.18 (t, 6.3 Hz, 1H), 4.92 (m, 1H), 4.72 (d, 6.2 Hz, 1H), 2.89 (s, 3H) ppm. Anal. calcd for $C_{28}H_{22}CrNO_4P$: C, 64.74; H, 4.27; N, 2.70. Found: C, 64.75; H, 4.49; N, 2.80. $[\alpha]_D^{20}$ 270 (c 0.11, CH_2Cl_2).

6b: A yellow solid; mp 120°C (dec.); IR νCO 1963, 1887 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.77 (d, 4.4 Hz, 1H), 7.81 (t, 7.6 Hz, 1H), 7.59 (m, 9H), 7.34 (dd, 6.7, 4.9 Hz, 1H), 5.89 (d, 5.8 Hz, 1H), 5.35 (t, 6.4 Hz, 1H), 5.17 (t, 6.2 Hz, 1H), 4.74 (d, 6.3 Hz, 1H), 4.67 (m, 1H), 2.95 (s, 3H) ppm. Anal. calcd for $C_{30}H_{20}CrF_6NO_4P$: C, 54.97; H, 3.08; N, 2.14. Found: C, 55.18; H, 2.94; N, 2.17. $[\alpha]_D^{18}$ 200 (c 0.13, CH_2Cl_2).

7b: A yellow solid; yield: 63%; mp 85°C (dec.); IR νCO 1965, 1885 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.05 (d, 4.8 Hz, 1H), 7.62 (d, 7.8 Hz, 2H), 7.44 (t, 7.6 Hz, 2H), 7.25 (m, 4H), 6.95 (t, 7.1 Hz, 2H), 6.79 (m, 1H), 5.99 (d, 5.7 Hz, 1H), 5.88 (m, 1H), 5.75 (t, 6.3 Hz, 1H), 5.08 (t, 6.4 Hz, 1H), 4.75 (m, 1H), 3.49 (s, 3H) ppm. Anal. calcd for $C_{30}H_{20}CrF_6NO_4P$: C, 54.97; H, 3.08; N, 2.14. Found: C, 55.13; H, 2.94; N, 2.33. $[\alpha]_D^{20}$ 315 (c 0.17, CH_2Cl_2).

6c: A yellow solid; yield: 61%; mp 70°C (dec.); IR νCO 1965, 1890 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.78 (d, 4.8 Hz, 1H), 7.88 (m, 7H), 7.57 (d, 7.8 Hz, 1H), 7.37 (m, 1H), 5.89 (d, 5.3 Hz, 1H), 5.41 (t, 6.5 Hz, 1H), 5.20 (t, 6.4 Hz, 1H), 4.72 (d, 6.1 Hz, 1H), 4.62 (m, 1H), 3.04 (s, 3H) ppm. Anal. calcd for $C_{32}H_{18}CrF_{12}NO_4P$: C, 48.56; H, 2.29; N, 1.77. Found: C, 48.58; H, 2.08; N, 1.92. $[\alpha]_D^{20}$ 340 (c 0.11, CH_2Cl_2).

7c: A yellow solid; yield: 54%; mp 56°C (dec.); IR νCO 1965, 1900 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.93 (s, 1H), 7.90 (d, 4.3 Hz, 1H), 7.78 (m, 3H), 7.43 (t, 7.6 Hz, 1H), 7.32 (m, 3H), 6.84 (dd, 4.9, 7.5 Hz, 1H), 6.03 (d, 5.9 Hz, 1H), 5.80 (m, 2H), 5.11 (m, 1H), 4.76 (d, 1H), 3.55 (s, 3H) ppm. Anal. calcd for $C_{32}H_{18}CrF_{12}NO_4P$: C, 48.56; H, 2.29; N, 1.77. Found: C, 48.24; H, 2.09; N, 1.90. $[\alpha]_D^{22}$ 240 (c 0.16, CH_2Cl_2).

4.5. Demetalation

Excess iodine was added to the solution of **6c** in 10 mL THF. The resulting solution was stirred at rt for 2 h. After the solution was quenched with aq. $Na_2S_2O_3$, diethyl ether (50 mL) and aq. $NaHCO_3$ (20 mL) were added. The ethereal layer was collected and chromatographed on a silica gel column eluting with hexane and ethyl acetate (v/v, 10:1). Removal of the solvent gave a white solid (**10**) (140 mg, 67%). ^1H NMR ($CDCl_3$): δ 8.28 (d, 4.3 Hz, 1H), 8.12 (m, 3H), 8.03 (m, 3H), 7.66 (m, 2H), 7.56 (m, 1H), 7.42 (d, 8.0 Hz, 1H), 7.34 (m, 1H), 7.00 (m, 2H), 6.41 (s, 1H), 3.23 (s, 3H) ppm. Anal. calcd for $C_{29}H_{18}F_{12}NO_2P$: C, 51.88; H, 2.70; N, 2.09. Found: C, 51.74; H, 2.44; N, 2.24.

*4.6. General procedure for palladium-catalyzed allylic alkylation of **8***

The palladium complex $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (1 mol% Pd) was added to the solution of ligand (1 mol%) and **8** (110 mg, 0.52 mmol) in 5 mL of CH_2Cl_2. The solution was stirred at rt for 10 min and cooled to 0°C. Dimethyl malonate (0.09 mL, 1.5 equiv.) and BSA (0.19 mL, 1.5 equiv.) were added followed by KOAc (2 mg). The reaction mixture was stirred at 0°C for an appropriate reaction time and then was diluted with Et_2O and washed with saturated aqueous NH_4Cl. After drying ($MgSO_4$), chromatographic workup of the residue resulted in pure **9** (56–98% yield). The enantiomeric excess was measured by ^1H NMR spectroscopy using Eu(hfc)$_3$ as a chiral shift reagent. The absolute configuration was determined by polarimetric measurements.

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