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SPANphos Ligands in Palladium-Catalyzed Asymmetric Fluorination

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The synthesis of new enantiopure wide-bite-angle diphosphanes is described as well as their use in the palladium-catalyzed asymmetric fluorination of α-cyanoacetates. Enantiomeric excesses up to 93 % were obtained when $Pd(OAc)_2$-SPANphos was used as catalyst for the fluorination of ethyl 2-cyano-2-phenylacetate with *N*-fluorobenzenesulfonimide (NFSI).

Introduction

The synthesis of enantiopure molecules bearing a fluorine atom at the stereogenic center has generated great interest, both in the field of analytical chemistry and for the synthesis of biologically active compounds. Since Togni's discovery[1] that a chiral titanium complex as a catalyst could convert β-keto esters into chiral, non-enolizable α-fluorinated β-keto esters, many examples involving chiral transition metal complexes have been published, such as complexes of nickel, copper, and palladium.[2] We recently applied chiral nitrogen-based 2,2′-spirobichroman (SPAN) derivatives as organocatalysts for the enantioselective fluorination of β-keto esters,[3] and showed that the activity can be enhanced by the addition of a nickel salt without loss of enantioselectivity. In this paper we report the use of enantiopure diphosphane SPANphos derivatives as chiral ligands for the palladium-catalyzed asymmetric fluorination of α-cyanoacetates. The fluorinated product can easily be further derivatized, either at the ester group, or through the nitrile functionality. Sodeoka first reported the use of Pd-diphosphane complexes to promote the enantioselective fluorination of both β-keto esters[4] and β-keto phosphonates[5] and, later, Kim used a similar system with BINAP as the chiral ligand to efficiently catalyze the fluorination of α-cyanoacetates[6] and α-cyanophosphonates.[6a,7]

Various racemic diphosphane SPANphos ligands have been synthesized in our group[8] but, until now, only racemic ligands were used successfully in catalysis. A dimeric Rh-SPANphos complex was the most active catalytic system for the carbonylation of methanol.[9] It was shown that, depending on the ligands borne by rhodium, SPANphos can be a *trans*-[8a] or *cis*-coordinating ligand.[8b] In the case of platinum(II) or palladium(II) complexes, only *trans*-coordinated complexes were isolated. Only a few examples of *trans*-coordinating diphosphane ligands have been used in asymmetric catalysis,[10] the TRAP ligands introduced by Ito being notable examples.[11] Recently, Ding and coworkers applied SPANbox in the Zn-catalyzed enantioselective hydroxylation of β-keto esters;[12] high enantiomeric excesses were obtained and, in this instance, neither the ligand nor the metal required *trans* coordination. We applied the same SPANbox in Ni-catalyzed fluorination, but no enantioselectivity was obtained.[3] We therefore aimed to use our enantiopure SPANphos ligands in the palladium-catalyzed asymmetric fluorination of α-cyanoacetates, which would be the first application of a *trans*-coordinating ligand for this kind of reaction. Because the reaction mechanism does not involve insertion reactions or reductive elimination reactions, which typically require *cis* coordination of the bidentate ligand in square-planar complexes, the fluorination reaction was thought to be a suitable candidate.

Results and Discussion

Racemic SPANphos ligands were synthesized according to a procedure similar to that previously reported in our laboratory,[8a] by mixing 2 equiv. of the corresponding chlorophosphane with 1 equiv. of dilithio compound. In the case of $SPAN(DBP)_2$ **2**, the enantiomers were isolated after separation by semipreparative chiral HPLC. However, this method was unsuccessful for the other diphosphanes. Racemic SPANphos derivatives were oxidized to the phosphane oxides, all of which were resolved and separated by semipreparative HPLC. Enantiopure SPANphos ligands were obtained by subsequent reduction of the oxides with MeOTf/$LiAlH_4$ (Scheme 1).[13]

For two enantiomeric phosphanes (*S*)-**4** and (*R*)-**6**, the absolute configuration was determined by X-ray diffraction. Figure 1 nicely shows the spiro character of the ligands. As usual, the POP groups in (*S*)-**4** are nearly flat and

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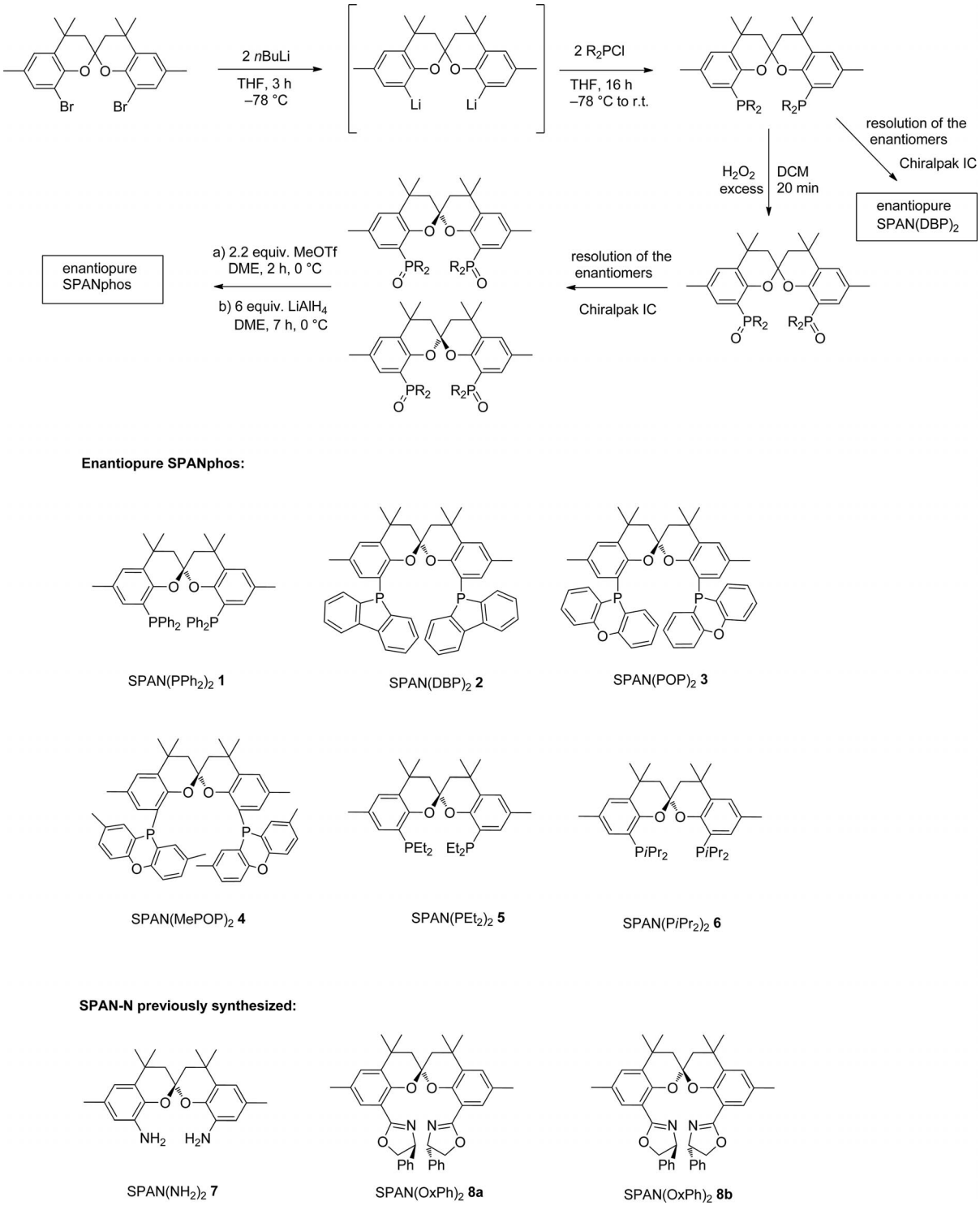


Scheme 1. Ligand structures and synthesis.

the dihydropyran groups have an envelope conformation in both (*S*)-**4** and (*R*)-**6**. Distances and angles show normal values (see the Supporting Information).

We were also able to isolate single crystals of the *trans*-chelated dichloropalladium complex **A** with racemic SPANphos **1** after mixing 1 equiv. of [Pd(cod)Cl_2] with phosphane **1** (Figure 2).

Complex **A** exhibits a large bite angle of the phosphane on the palladium atom (P1–Pd–P2: 175.46°) (see the Supporting Information), which is 4° larger than that reported for the $PtCl_2$-SPANphos complex **1**.[8a]

We first screened several palladium precursors in the presence of enantiopure SPANphos **1** under previously reported reaction conditions (5 mol-% catalyst, NFSI as

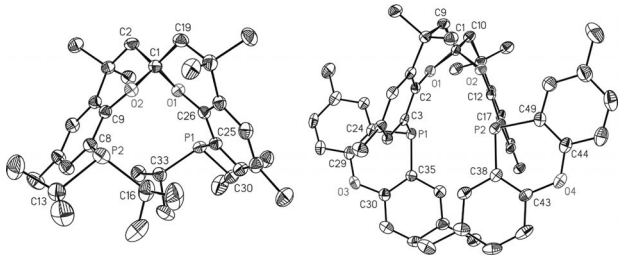


Figure 1. ORTEP plots (40%) of complex (*R*)-**6** (left) and (*S*)-**4** (right). Hydrogen atoms have been omitted for clarity.

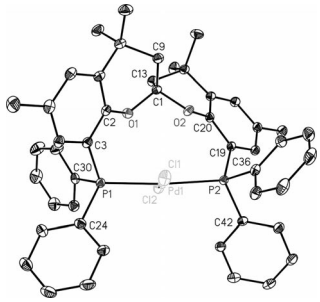
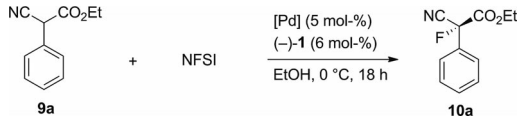


Figure 2. ORTEP plot of complex **A**. Hydrogen atoms have been omitted for clarity.

fluorine donor)[6] except that ethanol was used instead of methanol because of the lack of solubility of **1** in methanol (Table 1).

Table 1. Palladium precursor screening.

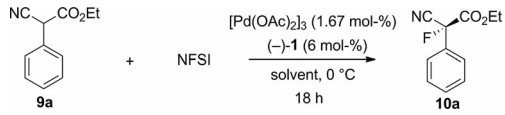


[Pd]	Conv.[a] (yield[b]) [%]	*ee* [%][c]
$[Pd(OAc)_2]_3$	100 (97)	93
$Pd(dba)_2$	100 (95)	67
$Pd(acac)_2$	100 (95)	74
$[Pd(allyl)Cl]_2$	100 (98)	86
$[Pd(4\text{-}CNPh)(Br)\{P(o\text{Tol})_3\}_2]$	31 (n.d.)	32

[a] Determined by ^{1}H NMR analysis of the crude product. [b] Isolated yield. [c] Determined by chiral-phase HPLC analysis of purified **10a**.

After 18 h at 0 °C, palladium acetate trimer provided **10a** with an excellent 93%*ee* with full conversion, thus, this palladium precursor was used for further studies. The system **1**/$Pd(OAc)_2$ could be used to efficiently catalyze the reaction in almost any solvent, affording fluorinated cyanoacetate **10a** with full conversion and enantiomeric excesses of more than 70%. Worse results were obtained in methanol, which may be due to the low solubility of SPANphos **1** ligand in this solvent. Complex **A** is not reported in the table because of its insolubility in polar solvents such as alcohols. There is no clear correlation with polarity or protic character of the solvent, and ethers gave only modest results (Table 2).

Table 2. Solvent screening.



Solvent	Conv.[a] (yield[b]) [%]	*ee* [%][c]
EtOH	100 (97)	93
MeOH	85 (75)	47
*i*PrOH	100 (92)	88
DME	100 (88)	72
THF	100 (95)	67
Toluene	100 (95)	83
CH_2Cl_2	100 (91)	82
MeCN	100 (92)	91

[a] Determined by ^{1}H NMR analysis on the crude product. [b] Isolated yield. [c] Determined by chiral-phase HPLC analysis of purified **10a**.

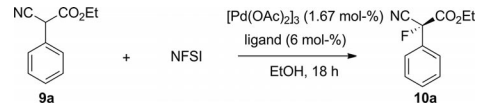
Several of our enantiopure SPAN ligands as well as commercially available (*R*)-BINAP were then tested (Table 3). In each case, the reaction was performed both at 0 °C and at room temperature for 18 h, leading to good conversion. Except in the case of SPANbox **8b**, enantiomeric excesses were higher at 0 °C than at room temperature. SPANphos **1** was the best ligand in the series and provided higher enantioselectivities than BINAP. The orientation of the substituents on the phosphorus atom had a dramatic effect on the enantioselectivity; this was clearly demonstrated in the case of ligand **2**, which provided only racemic products. Steric hindrance also had an influence, as shown by the difference in the enantiomeric excess observed with SPANphos **3** and **4**. Previously, we reported that SPANamine **7** gave a high enantiomeric excess for this reaction when used with Ni salts,[3] but in this catalytic system SPAN nitrogen-based derivatives did not lead to appreciable *ee* values.

Subsequently, we studied the effect of the ester substituent of the α-cyanoacetate (Table 4). Replacement of the ethyl group of the ester by a methyl group led to slightly lower enantioselectivity, but when the bulkier *tert*-butyl ester was used both activity and enantioselectivity dropped considerably. The latter substrate gave the best enantioselectivities in Kim's system.[6]

To study the substrate scope of the new catalysts, we synthesized several ethyl 2-arylcyanoacetates and carried out their fluorination under the previously optimized conditions (Scheme 2).

Apart from substrate **9a**, the highest enantioselectivities were obtained using electron-donating *para*-substituted substrates such as **9g** and **9i**. In contrast, with electron-withdrawing substituents the enantiomeric excess dropped to 45%, as was the case for substrate **9h**. The activity of the catalytic system also decreased when *ortho*-halogenated substrates were used, such as **9d** and **9e**. Most likely this is a steric effect, because the naphthyl derivative **9f** also gave a low *ee*. In the latter molecules the enolate intermediate cannot be planar, and this may influence the enantioselectivity.

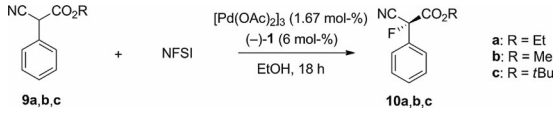
Table 3. Substrate screening.



Chiral ligand	*T* [°C]	Conv.[a] (yield[b]) [%]	*ee* [%][c]
1	r.t.	100 (97)	78
	0	100 (97)	93
	–20	100 (94)	91
2	r.t.	100 (93)	0
	0	95 (89)	0
3	r.t.	100 (91)	12
	0	95 (85)	12
4	r.t.	82 (76)	36
	0	75 (68)	51
5	r.t.	100 (89)	22
	0	100 (79)	29
6	r.t.	100 (94)	14
	0	100 (92)	38
7	r.t.	98 (90)	4
	0	80 (78)	8
8a	r.t.	100 (95)	6
	0	92 (86)	8
8b	r.t.	100 (88)	38
	0	95 (90)	10
(*R*)-Binap	r.t.	100 (94)	72
	0	100 (94)	78

[a] Determined by ^{1}H NMR analysis of the crude product. [b] Isolated yield. [c] Determined by chiral-phase HPLC analysis of purified **10a**.

Table 4. Influence of the ester group.

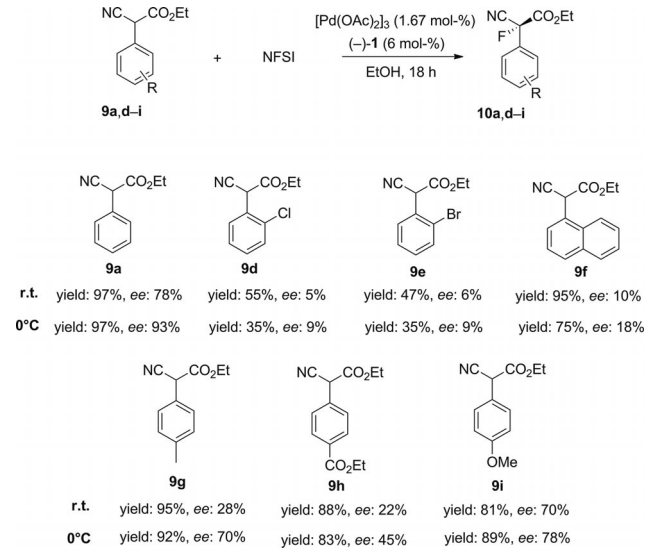


Substrate	*T* [°C]	Conv.[a] (yield[b]) [%]	*ee* [%][c]
9a	r.t.	100 (97)	78
	0	100 (97)	93
9b	r.t.	100 (95)	74
	0	100 (89)	80
9c	r.t.	72 (59)	10
	0	41 (35)	11

[a] Determined by ^{1}H NMR analysis of the crude product. [b] Isolated yield. [c] Determined by chiral-phase HPLC analysis of purified **10a**–**c**.

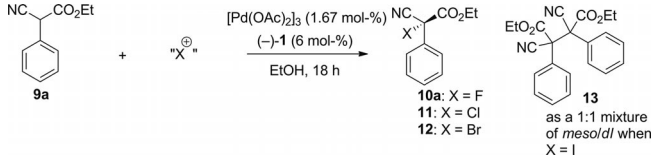
Our catalytic system was also tested with other halides donors such as *N*-halosuccinimides in an attempt to obtain enantioenriched α-chloro-, -bromo- and -iodocyanoacetates (Table 5). When the reaction was performed with *N*-chlorosuccinimide at 0 °C, substrate **9a** was fully converted into the chlorinated product **11** with low enantioselectivity, whereas only racemic **12** was obtained when *N*-bromosuccinimide was used in the reaction. No traces of the expected iodinated product was isolated after reaction with *N*-iodosuccinimide; substrate **9a** was fully converted into its dimeric adduct (*meso*/*dl*) **13**, presumably through a radical mechanism.

As regards the mechanism, we envisage that a palladium enolate is formed during the catalytic cycle, which then reacts with NFSI to release the fluorinated cyanoacetate and regenerate the catalyst (Scheme 3). We did not attempt to characterize the intermediates, but they may well be *trans* complexes, because this is the preferred structure of SPANphos complexes in the absence of other *cis* enforcing ligands.[8] The P–P distance in the free ligands are 4.979(4) and 6.184(3) Å for **4** and **6**, respectively. The free ligands have a clear C_2-symmetric twist, but apparently this pronounced asymmetry is not always effective in the complex or in the catalytic reaction. The reason may be that even in **4**, which has a distance close to that required for a *trans* complex, considerable rotation of the phosphorus lone pairs is needed to enable the formation of a *trans* complex. A crystal structure was obtained for only one ligand and $PdCl_2$, rather than the acetate (see Figure 2 and the Supporting Information). The crystal structure of the parent SPANphos **1** and $PdCl_2$ show a clear C_2 symmetry with two axial and two equatorial phenyl groups. This is also the best performing ligand and, thus, we suggest that a *trans* complex may be the active species.



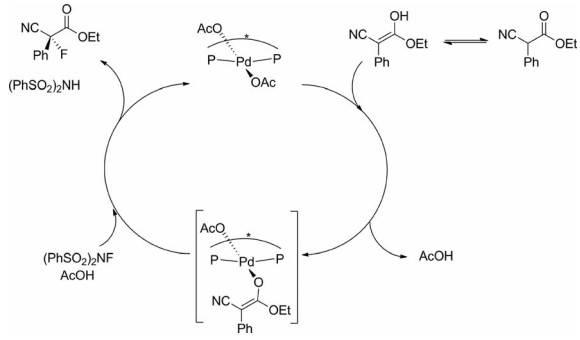
Scheme 2. Substrate screening.

Table 5. Effect of the halide donor.



Halide donor (X)	Conv.[a] (yield[b]) [%]	*ee* [%][c]
NFSI (F)	100 (97)	93
N-Chlorosuccinimide (Cl)	100 (91)	32
N-Bromosuccinimide (Br)	100 (90)	0
N-Iodosuccinimide (I)	100 (85)[d]	n.d.

[a] Determined by ^{1}H NMR analysis of the crude product. [b] Isolated yield. [c] Determined by chiral-phase HPLC analysis of purified **10a**. [d] Fully converted into **13** as a 1:1 *meso*/*dl* mixture.



Scheme 3. Tentatively proposed mechanism.

Conclusions

We have developed an efficient synthesis of several enantiopure *P*-aryl- and *P*-alkylphosphanes that are efficient chiral ligands for the palladium-catalyzed fluorination of α-cyanoacetates. It is the first example of the application of *trans*-chelating ligands for this kind of reaction, and the behavior of SPANphos-Pd complexes seems to differ from the previously reported complexes by Sodeoka and Kim, which are *cis*-coordinated. Studies are ongoing in our laboratory to ensure faster, direct syntheses of enantiopure SPANphos derivatives[14] and to discover new applications for these ligands.

Experimental Section

General: Unless otherwise specified, materials were obtained from commercial suppliers and were used without further purification. All reactions were carried out using standard Schlenk techniques for the synthesis of the ligands or in 5 mL sealed screw vials for the catalysis, under dry argon. Glassware was dried with a heat gun under vacuum prior to use. All solvents were dried using a Solvent Purification System (SPS) or using standard procedures. Methyl trifluoromethanesulfonate (98%; Aldrich) was transferred and kept in a Schlenk vessel under argon. Dimethoxyethane (DME; anhydrous, 99.5%; Sigma–Aldrich), was stored over activated 4 Å molecular sieves and was degassed by bubbling dry argon for 30 min. Chlorodiphenylphosphane was purchased from Fluka and distilled under an inert gas prior to use. Chlorodiethylphosphane (min. 95%) and chlorodiisopropylphosphane (min. 98% from Strem) were stored in a glove box and were used as received. 8,8′-Dibromo-4,4,4′,4′,6,6′-hexamethyl-2,2′-spirobi[chroman],[8a] 2,8-dimethyl-10-chlorophenoxaphosphane,[15] 10-chlorophenoxaphosphane,[16] and 9-chlorodibenzo[*bd*]phosphole[17] were prepared according to literature procedures. SPANphos **1** can also be purchased from Strem. ^{1}H, ^{13}C, ^{31}P and ^{19}F NMR were recorded in $CDCl_3$ with a Bruker Avance 400 Ultrashield NMR spectrometer (400.1 MHz for ^{1}H, 100.6 MHz for ^{13}C, 162.0 MHz for ^{31}P, and 377.0 MHz for ^{19}F). Chemical shifts (δ) for ^{1}H and ^{13}C NMR signals were referenced to internal solvent resonances and are reported relative to TMS in units of ppm; chemical shifts for ^{31}P and ^{19}F NMR signals are reported using 85% phosphoric acid and $CFCl_3$, respectively, as external standards in ^{1}H-decoupling mode. Optical rotations were measured with a Jasco-1030 polarimeter. Chromatographic analyses (resolution of ligands, load studies, enantiomeric excesses) were performed with an HPLC Agilent 1100 apparatus, using a Daicel Chiralpak IC column (250 mm length, 4.6 mm diameter, 5 μm particle size, 1 mL/min, λ = 254 nm). Chiral separation of the SpanPhos enantiomers was performed with semi-preparative Waters HPLC equipment (4.7 mL/min) equipped with a Daicel Chiralpak IC column (250 mm length, 10 mm diameter, 5 μm particle size). HRMS data were recorded at the High-Resolution Mass Spectrometry Unit of the ICIQ (Tarragona, Spain) with Waters LCT Premier liquid chromatography equipment coupled with a time-of-flight mass spectrometer and using a positive electrospray ionization method. Elemental analyses were performed at the Unidade de Análise Elemental of the Universidade de Santiago de Compostela (Spain).

X-ray Data: Single crystals suitable for X-ray analysis were grown by slow diffusion of *n*-hexane into a CH_2Cl_2 solution of enantiopure (*S*)-**4** or enantiopure (*R*)-**6** at room temp. Crystal structure determination for (*S*)-**4** was carried out with an Apex DUO Kappa 4-axis goniometer equipped with an APPEX 2 4K CCD area detector, a Microfocus Source E025 IuS using Mo-K_α radiation, Quazar MX multilayer Optics as monochromator, and an Oxford Cryosystems low temperature device Cryostream 700 plus (T = –173 °C). Crystal structure determination for (*R*)-**6** and complex **A** were carried out with a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector, an FR591 rotating anode with Mo-K_α radiation, and Montel mirrors as monochromator. Full-sphere data collection was used with ω and ϕ scans. Programs used: Data collection APEX-2,[18] data reduction Bruker Saint[19] V/.60A and absorption correction SADABS.[20]

Structure Solution and Refinement: Crystal structure solution was achieved by using direct methods as implemented in SHELXTL[21] and visualized using the program XP. Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F^2 using all measured intensities was carried out using the program SHELXTL. All non-hydrogen atoms were refined by including anisotropic displacement parameters.

Crystal Data

Sample (*S*)-4 at 100 K: $C_{51}H_{50}O_4P_2{\cdot}0.22C_6H_{14}$; M_r = 808.00 g mol^{-1}; rhombohedral; *R*3; a = 36.379(4) Å, b = 36.379(4) Å, c = 9.7332(10) Å; V = 11155.4(19) Å^3; Z = 9; $\rho_{calcd.}$ = 1.082 Mg/m^3; R_1 = 0.0618 (all 0.0977), $wR2$ = 0.1258 (all 0.1443), for 7077 reflections with $I > 2\sigma(I)$ (for 9848 reflections [R_{int} = 0.0528] with a total measured of 15327 reflections), goodness-of-fit on F^2 = 1.028, Flack parameter (std) = –0.03(1), largest diff. peak (hole) = 0.299 (–0.233) e Å^{-3}. The asymmetric unit of (*S*)-**4** is made up of the main molecule and a highly disordered *n*-hexane molecule. The *n*-hexane molecule is located in a crystal channel, and only 22% of its presence could be localized.

Sample (*R*)-6 at 297 K: $C_{35}H_{54}O_2P_2$; M_r = 568.72 g mol^{-1}; monoclinic; $P2_1$; a = 10.394(2) Å, b = 11.113(3) Å, c = 15.355(3) Å; β = 104.042(5)°, V = 1720.5(7) Å^3; Z = 2; $\rho_{calcd.}$ = 1.098 Mg/m^3; R_1 = 0.0514 (all 0.0741), $wR2$ = 0.1295 (all 0.1463), for 8156 reflections with $I > 2\sigma(I)$ (for 10550 reflections [R_{int} = 0.0597] with a total measured of 36718 reflections), goodness-of-fit on F^2 = 1.050, Flack parameter (std) = –0.11(07), largest diff. peak (hole) = 0.554 (–0.314) e Å^{-3}.

Complex A at 100 K: $C_{47}H_{46}Cl_2O_2P_2Pd$; M_r = 882.08 g mol^{-1}; orthorombic; $Pna2_1$; a = 17.2250(9) Å, b = 13.0500(8) Å, c = 17.5240(9) Å; V = 3939.2(4) Å^3; Z = 4; $\rho_{calcd.}$ = 1.487 Mg/m^3; R_1 = 0.0356 (all 0.0432), $wR2$ = 0.0868 (all 0.0933), for 16770 reflections with $I > 2\sigma(I)$ (for 15006 reflections [R_{int} = 0.0315] with a total measured of 36850 reflections), goodness-of-fit on F^2 = 1.044, Flack parameter (std) = –0.015(14), largest diff. peak (hole) = 1.250 (–0.774) e Å^{-3}.

CCDC-892611 [for (*S*)-**4**], -892612 [for (*R*)-**4**] and -892613 (for **A**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Ligand Synthesis and Resolution

(+)- and (–)-4,4,4′,4′,6,6′-Hexamethyl-2,2′-spirobi[chroman]-8,8′-diylbis(diphenylphosphane) [(+)-1 and (–)-1]: A solution of 8,8′-dibromo-4,4,4′,4′,6,6′-hexamethyl-2,2′-spirobi[chroman] (2 g, 4.1 mmol) in THF (40 mL) was cooled to –78 °C. *n*BuLi (2.5 M in hexanes, 3.7 mL, 9.3 mmol) was then added dropwise, and the solution was stirred at –78 °C for 3 h. Chlorodiphenylphosphane (1.97 g, 8.9 mmol) in THF (15 mL) was added, and the solution was warmed slowly to room temperature over 16 h. The reaction was quenched with degassed water and then extracted with dichloromethane. The combined organic layers were dried with magnesium sulfate, and the solvents were evaporated. The crude product was washed with methanol (3 × 10 mL) and finally dried in vacuo to afford the racemic SPANphos **1** as a white powder (2.34 g, 3.32 mmol, 82% yield).

Synthesis of the Racemic Bis(phosphane oxide) *rac*-1-Oxd: Racemic **1** (2 g, 2.84 mmol) was dissolved in CH_2Cl_2 (100 mL), and hydrogen peroxide (30 wt.-% in water, 3.3 mL) was then carefully added at room temp. The mixture was vigorously stirred at room temperature for 20 min, and water (20 mL) was added. The organic phase was separated using ammonium chloride salt, further washed with another portion of water (20 mL), and finally dried with magnesium sulfate. The solvent was removed in vacuo to afford the bis(phosphane oxide) as a white powder (1.88 g, 2.56 mmol, 90% yield).

***rac*-1-Oxd:** ^{31}P NMR ($CDCl_3$, 25 °C): δ = 32.7 (s) ppm. HPLC (CH_2Cl_2/*i*PrOH, 90:10): t_R = 5.9 [(+)-enantiomer], 7.5 [(–)-enantiomer] min. $[\alpha]_D^{29}$ = –36.9 (*c* = 0.56, CH_2Cl_2).

Reduction of (–)-1-Oxd To Give (+)-1: To (–)-**1**-Oxd (464 mg, 0.63 mmol) dissolved in DME (8 mL) was added, dropwise, methyl triflate (0.160 mL, 1.4 mmol) at room temperature, and the solution was stirred for 2 h. The solution was then cooled to 0 °C, and $LiAlH_4$ (146 mg, 3.8 mmol) was added in one portion. The mixture was stirred at 0 °C for 7 h, quenched with water, and the solvent was removed in vacuo. The residue was taken up in chloroform (10 mL), filtered through a pad of basic alumina, and the solvent was removed in vacuo. The solid was washed with MeOH and dried in vacuo to afford enantiopure (+)-**1** as a white powder. If necessary the product could be further purified by filtration through a pad of silica using chlorinated solvents. Yield: 382 mg (0.54 mmol, 86%). $[\alpha]_D^{27}$ = +70.8 (*c* = 0.94, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 25 °C): δ = 1.14 (s, 6 H, CH_3), 1.41 (s, $^5J_{H,P}$ = 1.1 Hz, 6 H, CH_3), 1.81 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 1.88 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 1.99 (s, 6 H, CH_3), 6.05 (ddd, $^4J_{H,H}$ = 2.1, $^4J_{H,H}$ = 0.5, $^3J_{H,P}$ = 4.7 Hz, 2 ArH, CH), 6.84 (dd, $^4J_{H,H}$ = 2.1, $^4J_{H,H}$ = 0.5 Hz, 2 ArH, CH), 6.94–6.98 (m, 7 ArH, CH), 7.00–7.06 (m, 7 ArH, CH), 7.14–7.19 (m, 6 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 21.1 (s, CH_3), 30.3 (d, $^4J_{C,P}$ = 1.5 Hz, C_q), 32.2 (d, $^4J_{C,P}$ = 10.3 Hz, CH_3), 33.8 (s, CH_3), 47.2 (s, CH_2), 98.1 (s, C_q), 123.9 (d, $J_{C,P}$ = 13.2 Hz, C_q), 128.0–128.2 (3 × d, CH_{Ar}), 128.4 (s, CH_{Ar}), 130.3 (s, C_q), 130.6 (d, $J_{C,P}$ = 2.5 Hz, C_q), 132.3 (s, CH_{Ar}), 133.8 (d, $J_{C,P}$ = 19.1 Hz, CH_{Ar}), 134.0 (d, $J_{C,P}$ = 20.5 Hz, CH_{Ar}), 137.1 (d, $J_{C,P}$ = 11.6 Hz, C_q), 138.1 (d, $J_{C,P}$ = 11.8 Hz, C_q), 150.8 (d, $J_{C,P}$ = 17.2 Hz, C_q) ppm. ^{31}P NMR ($CDCl_3$, 25 °C): δ = –12.6 (s) ppm. HRMS (ESI): calcd. for $C_{47}H_{47}O_2P_2$ [M + H^+] 705.3051; found 705.3023. $C_{47}H_{46}O_2P_2$ (704.83): calcd. C 80.09, H 6.58; found C 79.82, H 6.62.

(+)- and (–)-4,4,4′,4′,6,6′-Hexamethyl-2,2′-spirobi[chroman]-8,8′-diylbis(9-dibenzo[*bd*]phosphole) [(+)-2 and (–)-2]: *rac*-**2** was synthesized using the same procedure used for *rac*-**1** and was obtained as a white solid. Yield 1.18 g (1.68 mmol, 42%). HPLC resolution of *rac*-**2** (hexane/CH_2Cl_2, 85:15): t_R = 4.9 [(–)-enantiomer], 6.0 [(+)-enantiomer] min.

(–)-2: $[\alpha]_D^{28}$ = –106.6 (*c* = 0.76, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 25 °C): δ = 1.41 (s, 6 H, CH_3), 1.99 (d, $^5J_{H,P}$ = 1.4 Hz, 6 H, CH_3), 2.0 (s, 6 H, CH_3), 2.29 (d, $^2J_{H,H}$ = 14.3 Hz, 2 H, CH_2), 2.45 (d, $^2J_{H,H}$ = 14.3 Hz, 2 H, CH_2), 5.88 (dd, $^3J_{H,H}$ = 7.4, $^3J_{H,P}$ = 4.5 Hz, 2 ArH, CH), 6.04 (ddt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 0.9 Hz, $^4J_{H,P}$ = 2.8 Hz, 2 ArH, CH), 6.19 (dd, $^4J_{H,H}$ = 1.9 Hz, $^3J_{H,P}$ = 4.6 Hz, 2 ArH, CH), 6.95 (dt, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.0 Hz, 2 ArH, CH), 7.12 (d, $^4J_{H,H}$ = 1.9 Hz, 2 ArH, CH), 7.33 (ddt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.0 Hz, $^4J_{H,P}$ = 2.9 Hz, 2 ArH, CH), 7.46 (dt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.0 Hz, 2 ArH, CH), 7.70 (d, $^3J_{H,H}$ = 7.8 Hz, 2 ArH, CH), 7.73 (dd, $^3J_{H,H}$ = 7.4 Hz, $^3J_{H,P}$ = 4.4 Hz, 2 ArH, CH), 7.90 (d, $^3J_{H,H}$ = 7.7 Hz, 2 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 27 °C): δ = 20.8 (s, CH_3), 30.8 (d, $^4J_{C,P}$ = 2.2 Hz, C_q), 32.9 (d, $^4J_{C,P}$ = 13.2 Hz, CH_3), 34.0 (s, CH_3), 47.5 (s, CH_2), 98.8 (s, C_q), 120.6 (s, CH_{Ar}), 121.4 (s, CH_{Ar}), 124.0 (d, $J_{C,P}$ = 21.9 Hz, C_q), 126.9 (d, $^3J_{C,P}$ = 7.4 Hz, CH_{Ar}), 127.3 (d, $^3J_{C,P}$ = 6.6 Hz, CH_{Ar}), 127.6 (s, CH_{Ar}), 128.5 (s, CH_{Ar}), 129.6 (s, CH_{Ar}), 130.1 (d, $^2J_{C,P}$ = 3.3 Hz, CH_{Ar}), 130.7 (d, $^2J_{C,P}$ = 21.1 Hz, CH_{Ar}), 131.1 (d, $^2J_{C,P}$ = 21.9 Hz, CH_{Ar}), 131.4 (s, C_q), 131.8 (d, $J_{C,P}$ = 3.0 Hz, C_q), 142.3–142.4 (2 × d, C_q), 142.9 (d, $J_{C,P}$ = 6.6 Hz, C_q), 144.9 (d, $J_{C,P}$ = 3.7 Hz, C_q), 152.0 (d, $J_{C,P}$ = 19.8 Hz, C_q) ppm. ^{31}P NMR ($CDCl_3$, 25 °C): δ = –22.1 (s) ppm. HRMS (ESI): calcd. for $C_{47}H_{42}O_2P_2Na$ [M + Na^+] 723.2558; found 723.2571. $C_{47}H_{42}O_2P_2{\cdot}(CH_2Cl_2)_{0.25}$ (700.80): calcd. C 78.60, H 5.95; found C 78.21, H 6.55 (determined on the crystalline dichloromethane solvates formed when a solution of amorphous **2** in dichloromethane was left to slowly concentrate at room temperature).

(+)- and (–)-4,4,4′,4′,6,6′-Hexamethyl-2,2′-spirobi[chroman]-8,8′-diylbis(10-phenoxaphosphane) [(+)-3 and (–)-3]: *rac*-**3** was synthesized using the same procedure used for *rac*-**1** and was obtained as a white solid. Yield 1.84 g (2.5 mmol, 65%).

***rac*-3-Oxd:** ^{31}P NMR ($CDCl_3$, 25 °C): δ = 1.3 (s) ppm. HPLC resolution of *rac*-**3**-Oxd (CH_2Cl_2/*i*PrOH = 84:16): t_R = 6.5 [(–)-enantiomer], 8.1 [(+)-enantiomer] min. $[\alpha]_D^{29}$ = +44.1 (*c* = 0.49, CH_2Cl_2).

Reduction of (+)-3-Oxd To Give (+)-3: Using (+)-**3**-Oxd (310 mg, 0.41 mmol) dissolved in DME (4 mL) and applying the same reduction procedure used for (–)-**1**-Oxd afforded (+)-**3** as a white solid. Yield 250 mg (0.34 mmol, 84%). $[\alpha]_D^{28}$ = +111.6 (*c* = 0.16, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 25 °C): δ = 1.37 (s, 6 H, CH_3), 2.00 (d, $^5J_{H,P}$ = 0.9 Hz, 6 H, CH_3), 2.09 (s, 6 H, CH_3), 2.19 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 2.36 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 5.66 (ddd, $^3J_{H,H}$ = 7.6 Hz, $^4J_{H,H}$ = 1.6 Hz, $^3J_{H,P}$ = 9.9 Hz, 2 ArH, CH), 5.84 (ddt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.1 Hz, $^4J_{H,P}$ = 1.2 Hz, 2 ArH, CH), 6.61 (ddd, $^4J_{H,H}$ = 2.2 Hz, $^4J_{H,H}$ = 0.6 Hz, $^3J_{H,P}$ = 3.9 Hz, 2 ArH, CH), 6.79 (ddd, $^3J_{H,H}$ = 8.3 Hz, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,H}$ = 1.7 Hz, 2 ArH, CH), 6.87 (ddd, $^3J_{H,H}$ = 8.2 Hz, $^4J_{H,H}$ = 1.1 Hz, $^4J_{H,P}$ = 1.0 Hz, 2 ArH, CH), 7.01 (ddt, $^3J_{H,H}$ = 7.3 Hz, $^4J_{H,H}$ = 1.2 Hz, $^4J_{H,P}$ = 1.1 Hz, 2 ArH, CH), 7.12 (ddd, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = 1.1 Hz, $^4J_{H,P}$ = 1.0 Hz, 2 ArH, CH), 7.12 (dd, $^4J_{H,H}$ = 2.3 Hz, $^4J_{H,H}$ = 0.6 Hz, 2 ArH, CH), 7.29 (ddd, $^3J_{H,H}$ = 8.3 Hz, $^3J_{H,H}$ = 7.3 Hz, $^4J_{H,H}$ = 1.7 Hz, 2 ArH, CH), 7.33 (ddd, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.7 Hz, $^3J_{H,P}$ = 9.7 Hz, 2 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 27 °C): δ = 20.8 (s, CH_3), 30.6 (d, $^4J_{C,P}$ = 1.5 Hz, C_q), 32.7 (d, $^4J_{C,P}$ = 13.8 Hz, CH_3), 34.2 (s, CH_3), 47.2 (s, CH_2), 98.4 (s, C_q), 116.5 (s, CH_{Ar}), 117.5 (s, CH_{Ar}), 117.9 (d, $J_{C,P}$ = 8.9 Hz, C_q), 118.4 (d, $J_{C,P}$ = 5.9 Hz, C_q), 123.1–123.3 (2 × d, CH_{Ar}), 128.2 (d, $J_{C,P}$ =

28.8 Hz, C_q), 129.3 (s, CH_{Ar}), 129.6 (s, CH_{Ar}), 130.2 (s, CH_{Ar}), 131.1 (s, C_q), 131.6 (d, $J_{C,P}$ = 2.9 Hz, C_q), 133.6 (d, $^2J_{C,P}$ = 4.2 Hz, CH_{Ar}), 134.2 (d, $^2J_{C,P}$ = 32.6 Hz, CH_{Ar}), 134.9 (d, $^2J_{C,P}$ = 34.0 Hz, CH_{Ar}), 150.8 (d, $J_{C,P}$ = 22.0 Hz, C_q), 153.4 (s, C_q), 155.2 (d, $J_{C,P}$ = 1.5 Hz, C_q) ppm. ^{31}P NMR ($CDCl_3$, 25 °C): δ = 68.2 (s) ppm. HRMS (ESI): calcd. for $C_{47}H_{42}O_4P_2Na$ [M + Na^+] 755.2456; found 755.2464. $C_{47}H_{42}O_4P_2$ (732.79): calcd. C 77.04, H 5.78; found C 76.69, H 6.44.

(+)- and (–)-4,4,4′,4′,6,6′-Hexamethyl-2,2′-spirobi[chroman]-8,8′-diylbis(2,8-dimethyl-10-phenoxaphosphane) [(+)-4 and (–)-4]: *rac*-**4** was synthesized using the same procedure used for *rac*-**1** and was obtained as a white powder (2.25 g, 2.85 mmol, 71% yield). Racemic bis(phosphane oxide) *rac*-**4**-Oxd was synthesized using the same procedure used for *rac*-**1**-Oxd and was obtained as a white powder (1.81 g, 2.2 mmol, 87% yield).

***rac*-4-Oxd:** ^{31}P NMR ($CDCl_3$, 25 °C): δ = 0.2 (s) ppm. HPLC resolution of *rac*-**4**-Oxd (CH_2Cl_2/*i*PrOH, 85:15): t_R = 5.7 [(+)-enantiomer], 8.9 [(–)-enantiomer] min. $[\alpha]_D^{29}$ = –58.4 (*c* = 0.48, CH_2Cl_2).

Reduction of (–)-4-Oxd To Give (–)/(*S*)-4: Using (–)-**4**-Oxd (524 mg, 0.64 mmol) dissolved in DME (4 mL) and applying the same reduction procedure used for (–)-**1**-Oxd afforded enantiopure (–)/(*S*)-**4** as a white powder. Yield 417 mg (0.53 mmol, 83%). $[\alpha]_D^{29}$ = –162.5 (*c* = 0.10, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 25 °C): δ = 1.37 (s, 6 H, CH_3), 1.41 (s, 6 H, CH_3), 2.00 (d, $^5J_{H,P}$ = 0.9 Hz, 6 H, CH_3), 2.09 (s, 6 H, CH_3), 2.20 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 2.23 (s, 6 H, CH_3), 2.36 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 5.87 (dd, $^4J_{H,H}$ = 1.9 Hz, $^3J_{H,P}$ = 10.7 Hz, 2 ArH, CH), 6.71 (ddd, $^4J_{H,H}$ = 2.1 Hz, $^4J_{H,H}$ = 0.6 Hz, $^3J_{H,P}$ = 3.8 Hz, 2 ArH, CH), 6.85 (dd, $^3J_{H,H}$ = 8.5 Hz, $^4J_{H,H}$ = 2.0 Hz, 2 ArH, CH), 6.91 (d, $^3J_{H,H}$ = 8.3 Hz, 2 ArH, CH), 6.95 (d, $^3J_{H,H}$ = 8.3 Hz, 2 ArH, CH), 7.01 (dd, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = 2.0 Hz, 2 ArH, CH), 7.10 (dd, $^4J_{H,H}$ = 1.9 Hz, $^3J_{H,P}$ = 10.5 Hz, 2 ArH, CH), 7.10–7.12 (m, 2 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 19.6 (s, CH_3), 20.6 (s, CH_3), 20.9 (s, CH_3), 31.0 (d, $^4J_{C,P}$ = 1.2 Hz, C_q), 32.9 (d, $^4J_{C,P}$ = 13.3 Hz, CH_3), 34.3 (s, CH_3), 47.4 (s, CH_2), 98.8 (s, C_q), 116.8 (s, CH_{Ar}), 117.1 (s, CH_{Ar}), 118.0 (d, $J_{C,P}$ = 5.9 Hz, C_q), 119.3 (d, $J_{C,P}$ = 7.2 Hz, C_q), 128.6 (d, $J_{C,P}$ = 28.6 Hz, C_q), 129.1 (s, CH_{Ar}), 130.7 (s, CH_{Ar}), 130.7 (s, C_q), 130.8 (s, CH_{Ar}), 132.2 (d, $J_{C,P}$ = 10.8 Hz, C_q), 132.5 (d, $J_{C,P}$ = 3.5 Hz, C_q), 132.9 (d, $J_{C,P}$ = 11.2 Hz, C_q), 133.8 (d, $^2J_{C,P}$ = 4.7 Hz, CH_{Ar}), 134.7 (d, $^2J_{C,P}$ = 34.5 Hz, CH_{Ar}), 135.0 (d, $^2J_{C,P}$ = 35.9 Hz, CH_{Ar}), 150.7 (d, $J_{C,P}$ = 22.7 Hz, C_q), 152.7 (s, C_q), 152.8 (s, C_q) ppm. ^{31}P NMR ($CDCl_3$, 25 °C): δ = –68.4 (s) ppm. HRMS (ESI): calcd. for $C_{51}H_{51}O_4P_2$ [M + H^+], 789.3263; found 789.3284. $C_{51}H_{50}O_4P_2{\cdot}(CH_2Cl_2)_{1.25}$ (893.26): calcd. C 70.11, H 5.91; found C 70.18, H 6.13 (determined on the crystalline dichloromethane solvates formed when a solution of amorphous **4** in dichloromethane was left to slowly evaporate at room temperature).

(+)- and (–)-4,4,4′,4′,6,6′-Hexamethyl-2,2′-spirobi[chroman]-8,8′-diylbis(diethylphosphane) [(+)-5 and (–)-5]: *rac*-**5** was synthesized using the same procedure used for *rac*-**1** and obtained as a white solid. Yield 1.41 g (2.75 mmol, 68%).

***rac*-5-Oxd:** ^{31}P NMR ($CDCl_3$, 27 °C): δ = 45.0 (s) ppm. HPLC resolution of *rac*-**5**-Oxd (CH_2Cl_2/Hexane/*i*PrOH, 65:20:15): t_R = 10.9 [(–)-enantiomer], 12.0 [(+)-enantiomer] min. $[\alpha]_D^{25}$ = +45.2 (*c* = 0.70, CH_2Cl_2).

Reduction of (+)-5-Oxd To Give (+)-5: Using (+)-**5**-Oxd (240 mg, 0.44 mmol) dissolved in DME (18 mL) and applying the same reduction procedure used for (–)-**1**-Oxd afforded (+)-**5** as a white solid. Yield 90 mg (0.18 mmol, 40%). $[\alpha]_D^{27}$ = +77.6 (*c* = 0.025, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 27 °C): δ = 0.50–0.71 (m, 10 H, CH_2/CH_3), 1.01 (dt, $^3J_{H,H}$ = 7.7 Hz, $^3J_{H,P}$ = 15.5 Hz, 6 H, CH_3), 1.32 (s, 6 H, CH_3), 1.47–1.63 (m, 4 H, CH_2), 1.79 (s, 6 H, CH_3), 2.05 (d, $^2J_{H,H}$ = 14.2 Hz, 2 H, CH_2), 2.18 (d, $^2J_{H,H}$ = 14.2 Hz, 2 H, CH_2), 2.26 (s, 6 H, CH_3), 6.71–6.74 (m, 2 ArH, CH), 7.07–7.10 (m, 2 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 27 °C): δ = 9.9 (d, $^2J_{C,P}$ = 11.7 Hz, CH_3), 10.3 (d, $^2J_{C,P}$ = 16.8 Hz, CH_3), 16.0 (d, $^1J_{C,P}$ = 11.8 Hz, CH_2), 19.3 (d, $^1J_{C,P}$ = 12.7 Hz, CH_2), 21.1 (s, CH_3), 30.5 (d, $^4J_{C,P}$ = 1.5 Hz, C_q), 32.8 (d, $^4J_{C,P}$ = 12.0 Hz, CH_3), 34.1 (s, CH_3), 47.1 (s, CH_2), 97.9 (s, C_q), 126.3 (d, $J_{C,P}$ = 18.2 Hz, C_q), 127.8 (s, CH), 128.2 (s, CH), 130.4 (s, C_q), 131.2 (d, $J_{C,P}$ = 2.6 Hz, C_q), 150.7 (d, $J_{C,P}$ = 15.4 Hz, C_q) ppm. ^{31}P NMR ($CDCl_3$, 27 °C): δ = –26.5 (s) ppm. HRMS (ESI): calcd. for $C_{31}H_{46}O_2P_2Na$ [M + Na^+] 535.2871; found 535.2858. $C_{31}H_{46}O_2P_2{\cdot}(CH_2Cl_2)_{1.00}$ (596.25): calcd. C 64.32, H 8.10; found C 64.16, H 8.01 (determined on the crystalline dichloromethane solvates formed when a solution of amorphous **5** in dichloromethane was left to slowly evaporate at room temperature).

(+)- and (–)-4,4,4′,4′,6,6′-Hexamethyl-2,2′-spirobi[chroman]-8,8′-diylbis(diisopropylphosphane) [(+)-6 and (–)-6]: *rac*-**6** was synthesized using the same procedure used for *rac*-**1** and was obtained as a white solid. Yield 1.45 g (2.55 mmol, 63%).

***rac*-6-Oxd:** ^{31}P NMR ($CDCl_3$, 25 °C): δ = 54.2 (s) ppm. HPLC resolution of *rac*-**6**-Oxd (THF/Hexane/*i*PrOH, 92:5:3): t_R = 6.1 [(+)-enantiomer] min {$[\alpha]_D^{27}$ = +3.4 (*c* = 0.74, CH_2Cl_2)]}; (–)-enantiomer t_R = 7.3 min.

Reduction of (+)-6-Oxd To Give (–)/(*R*)-6: Using (+)-**6**-Oxd (284 mg, 0.47 mmol) dissolved in DME (20 mL) and applying the same reduction procedure used for (–)-**1**-Oxd afforded (–)/(*R*)-**6** as a white solid. Yield 99 mg (0.17 mmol, 37%). $[\alpha]_D^{27}$ = –116.0 (*c* = 0.090, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 27 °C): δ = 0.59 (dd, $^3J_{H,H}$ = 7.1 Hz, $^3J_{H,P}$ = 8.5 Hz, 6 H, CH_3), 0.70 (dd, $^3J_{H,H}$ = 7.1 Hz, $^3J_{H,P}$ = 15.1 Hz, 6 H, CH_3), 0.78 (dd, $^3J_{H,H}$ = 6.8 Hz, $^3J_{H,P}$ = 13.6 Hz, 6 H, CH_3), 0.82 (m, 2 H, CH), 0.96 (dd, $^3J_{H,H}$ = 6.8 Hz, $^3J_{H,P}$ = 13.7 Hz, 6 H, CH_3), 1.22 (s, 6 H, CH_3), 1.79 (s, 6 H, CH_3), 1.94 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 1.99 (m, 2 H, CH), 2.12 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, CH_2), 2.18 (s, 6 H, CH_3), 6.68–6.71 (m, 2 ArH, CH), 7.01 (d, $^3J_{H,H}$ = 1.5 Hz, 2 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 27 °C): δ = 16.5 (d, $^2J_{C,P}$ = 3.7 Hz, CH_3), 19.0 (d, $^2J_{C,P}$ = 20.1 Hz, CH_3), 19.3 (d, $^2J_{C,P}$ = 15.7 Hz, CH_3), 19.7 (d, $^1J_{C,P}$ = 14.4 Hz, CH), 19.9 (s, CH_3), 20.2 (d, $^2J_{C,P}$ = 19.5 Hz, CH_3), 22.7 (d, $^1J_{C,P}$ = 16.0 Hz, CH), 29.4 (d, $^4J_{C,P}$ = 1.5 Hz, C_q), 32.0 (d, $^4J_{C,P}$ = 12.5 Hz, CH_3), 33.3 (s, CH_3), 46.1 (s, CH_2), 96.7 (s, C_q), 123.4 (d, $J_{C,P}$ = 20.1 Hz, C_q), 126.9 (s, CH_{Ar}), 128.1 (s, C_q), 129.4 (s, CH_{Ar}), 130.0 (d, $J_{C,P}$ = 2.6 Hz, C_q), 150.3 (d, $J_{C,P}$ = 16.3 Hz, C_q) ppm. ^{31}P NMR ($CDCl_3$, 27 °C): δ = –4.3(s) ppm. HRMS (ESI): calcd. for $C_{35}H_{55}O_2P_2$ [M + H^+] 569.3677; found 569.3674. $C_{35}H_{54}O_2P_2$ (568.76): calcd. C 73.90, H 9.57; found C 73.48, H 9.89.

Complex A: In a flame-dried flask, **1** (200 mg, 0.284 mmol, 1 equiv.) and [Pd(cod)Cl_2] (81 mg, 0.284 mmol) were dissolved in anhydrous CH_2Cl_2 (10 mL). The homogeneous yellow mixture was stirred at room temp. for 2 h, then the solvent was removed under reduced pressure, and the yellow solid was washed twice with anhydrous diethyl ether. After drying under vacuum, complex **A** (228 mg, 91%) was obtained as a yellow solid. Monocrystals suitable for X-ray diffraction could be obtained by slow diffusion of hexanes into a solution of complex **A** in CH_2Cl_2. ^{1}H NMR ($CDCl_3$, 27 °C): δ = 1.38 (s, 6 H, CH_3), 1.48 (s, 6 H, CH_3), 2.11 (d, $^3J_{H,H}$ = 12 Hz, 2 H, CH_2), 2.12 (s, 6 H, CH_3), 2.63 (d, $^3J_{H,H}$ = 12 Hz, 2 H, CH_2), 6.51 (ddd, $^4J_{H,H}$ = 2.1 Hz, $^4J_{H,H}$ = 0.5 Hz, $^3J_{H,P}$ = 4.7 Hz, 2 ArH, CH), 7.11 (dd, $^4J_{H,H}$ = 2.1 Hz, $^4J_{H,H}$ = 0.5 Hz, 2 ArH, CH), 7.23–7.34 (m, 7 ArH, CH), 7.43–7.54 (m, 7 ArH, CH), 7.98 (dd, $J_{H,H}$ = 4.7, 16 Hz, 6 ArH, CH) ppm. ^{13}C NMR ($CDCl_3$, 27 °C): δ = 21.0 (s, CH_3), 28.8 (s, C_q), 29.7 (s, CH_3), 31.4 (s, CH_3), 46.5 (s,

CH_2), 104.8 (s, C_q), 120.2 (m, C_q), 127.1 (m, CH_{Ar}), 127.6 (s, CH_{Ar}), 128.4 (m, CH_{Ar}), 129.5 (m, CH_{Ar}), 129.6 (s, C_q), 131.1 (s, CH_{Ar}), 131.4 (s, C_q), 132.5 (s, C_q), 134.3 (m, CH_{Ar}), 137.6 (m, CH_{Ar}), 151.8 (s, C_q) ppm. ^{31}P NMR ($CDCl_3$, 27 °C): δ = 20.03 (s) ppm. HRMS (ESI): calcd. for $C_{47}H_{46}Cl_2O_2P_2Pd$ [M^+] 880.1385; found 880.1515. $C_{47}H_{46}Cl_2O_2P_2Pd$ (882.13): calcd. C 63.99, H 5.26; found C 63.71, H 5.38.

Typical Catalytic Procedure: Palladium acetate trimer (1.125 mg, 1.67 μmol) and enantiopure (–)-**1** (4.2 mg, 6 μmol) were placed in a tube under an inert gas. Anhydrous and degassed ethanol (0.5 mL) was added, and the mixture was stirred for 30 min, during which time the mixture became homogeneous. The cyanoacetate (0.1 mmol) was diluted in ethanol (0.5 mL) and then added to the catalyst. NFSI (35 mg, 0.11 mmol) was introduced in one portion, and the resulting mixture was stirred for the indicated time. The crude mixture was then filtered through a short pad of Celite, and ethanol was removed under reduced pressure. The pure product was obtained as a colorless oil after silica gel column chromatography (diethyl ether/pentane, 5%). The conversion was determined by ^1H NMR analysis of the crude product, and the enantiomeric excess by HPLC analysis on the pure product with a Chiralpak IC column.

Ethyl 2-Cyano-2-fluoro-2-phenylacetate (10a): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.33 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 4.37 (m, 2 H), 7.52 (m, 3 ArH), 7.66 (m, 2 ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.8, 63.4, 86.1, 88.1, 125.5, 129.2, 131.3, 131.7, 162.8 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –145.8 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 11.5, t_{R2} = 12.4 min.

Methyl 2-Cyano-2-fluoro-2-phenylacetate (10b): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 3.92 (s, 3 H), 7.52 (m, 3 ArH), 7.66 (m, 2 ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 54.6, 86.1, 114.1, 125.5, 129.3, 131.3, 131.5, 162.9 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –145.6 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 14.4, t_{R2} = 15.5 min.

***tert*-Butyl 2-Cyano-2-fluoro-2-phenylacetate (10c):** NMR and HPLC data are in accordance with those described by Kim.[6b]

Ethyl 2-(2-Chlorophenyl)-2-cyano-2-fluoroacetate (10d): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.38 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 4.44 (q, $^3J_{H,H}$ = 7 Hz, 2 H), 7.47 (m, 3 ArH), 7.79 (d, J = 8 Hz, 1 ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.7, 64.7, 85.8, 127.5, 128.5, 128.6, 129.5, 129.8, 131.1, 132.3, 162.0 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –147.8 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 19.9, t_{R2} = 21.2 min.

Ethyl 2-(2-Bromophenyl)-2-cyano-2-fluoroacetate (10e): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.39 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 4.44 (q, $^3J_{H,H}$ = 7 Hz, 2 H), 7.40 (ddd, J = 2, 8, 8 Hz, 1 H, ArH), 7.52 (ddd, J = 2, 8, 8 Hz, 1 H, ArH), 7.66 (d, J = 8 Hz, 1 H, ArH), 7.79 (d, J = 8 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 15.6, 66.5, 87.7, 129.3, 130.4, 130.5, 131.4, 131.6, 133.0, 134.2, 163.8 ppm. ^{19}F NMR: δ = –146.1 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 23, t_{R2} = 25 min.

Ethyl 2-Cyano-2-fluoro-2-(naphthalen-1-yl)acetate (10f): Yellowish oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.25 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 4.36 (m, 2 H), 7.61 (m, 3 H, ArH), 7.97 (m, 3 H, ArH), 8.23 (m, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.7, 64.6, 89.9, 101.9, 123.8, 124.7, 126.8, 127.0, 127.1, 127.8, 129.2, 132.5, 134.2, 162.8 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –142.2 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 16.5, t_{R2} = 17.8 min.

Ethyl 2-Cyano-2-fluoro-2-*p*-tolylacetate (10g): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.32 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 2.4 (s, 3 H), 4.36 (m, 2 H), 7.30 (d, J = 8 Hz, 2 H, ArH), 7.54 (d, J = 8 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.8, 21.3, 64.3, 86.2, 114.1, 125.6, 128.5, 128.8, 129.9, 141.7, 163.1 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –143.7 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 12.3, t_{R2} = 13.8 min.

Ethyl 4-(1-Cyano-2-ethoxy-1-fluoro-2-oxoethyl)benzoate (10h): Yellow oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.32 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 1.43 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 4.36 (m, 2 H), 4.42 (q, $^3J_{H,H}$ = 7 Hz, 2 H), 7.74 (d, $^3J_{H,H}$ = 9 Hz, 2 H, ArH), 8.17 (d, $^3J_{H,H}$ = 9 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.8, 14.3, 61.6, 64.7, 87.7, 113.6, 125.4, 130.4, 133.2, 135.6, 162.3, 165.3 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –148.6 ppm. HPLC (Chiralpak IC; hexane/*i*PrOH, 95:5): t_{R1} = 8.4, t_{R2} = 9.1 min.

Ethyl 2-Cyano-2-fluoro-2-(4-methoxyphenyl)acetate (10i): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.33 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 3.87 (s, 3 H), 4.37 (m, 2 H), 7.00 (d, J = 9 Hz, 2 H, ArH), 7.58 (d, J = 9 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.8, 55.5, 64.2, 87.9, 114.0, 114.3, 123.3, 127.4, 161.8, 163.1 ppm. ^{19}F NMR ($CDCl_3$, 25 °C): δ = –140.4 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 21, t_{R2} = 23 min.

Ethyl 2-Chloro-2-cyano-2-phenylacetate (11): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.32 (t, $^3J_{H,H}$ = 7 Hz, 3 H),4.36 (m, 2 H), 7.49 (m, 3 H, ArH), 7.75 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.7, 60.0, 65.1, 115.2, 126.5, 129.2, 130.6, 132.9, 163.2 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 19.5, t_{R2} = 20.8 min.

Ethyl 2-Bromo-2-cyano-2-phenylacetate (12): Colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.35 (t, $^3J_{H,H}$ = 7 Hz, 3 H), 4.37 (m, 2 H), 7.47 (m, 3 H, ArH), 7.80 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): δ = 13.7, 45.4, 65.1, 115.5, 127.3, 129.2, 130.5, 132.8, 163.2 ppm. HPLC (Chiralpak IC; hexane/CH_2Cl_2, 9:1): t_{R1} = 19.8, t_{R2} = 22.3 min.

***mesoldl* Diethyl 2,3-dicyano-2,3-diphenylsuccinate (13):** NMR spectroscopic data are in accordance with those reported in the literature.[22]

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra of ligands, complex **A** and fluorinated products.

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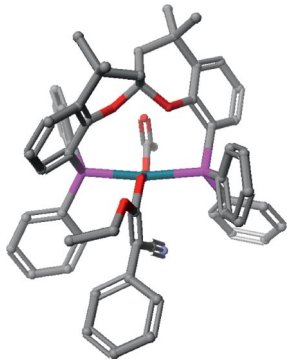
Asymmetric Fluorination

A *trans*-coordinating diphosphane in asymmetric fluorination catalysis? New enantiopure wide-bite-angle diphosphanes were synthesized and used in the palladium-catalyzed asymmetric fluorination of α-cyanoacetates. Enantiomeric excesses up to 93% were obtained using $Pd(OAc)_2$-SPANphos as the catalyst for the fluorination of ethyl 2-cyano-2-phenylacetate with *N*-fluorobenzenesulfonimide (NFSI).



Keywords: Asymmetric catalysis / Ligand design / Palladium / Halogenation / Fluorine

