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Olefin Hydrogenation with Rigid Mono-*P*-stereogenic Diphosphines: A Flexible Rhodium Ring to Rule Them All?

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The preparation of a rigid C_1-symmetric *P*-stereogenic diphosphine series possessing a *P*-*o*-diphenylphosphinophenyl moiety and its use in Rh^I-catalyzed hydrogenation of benchmark olefins, is presented. This simplified ligand design, wherein some specific features (backbone flexibility, identical nature of *P*,*P*′-substituents) of related C_2-symmetric ethylene-bridged diphosphines were knocked out, is a useful study-tool with which to better understand the role of essential motifs that guide catalysis in the original model.

Introduction

cis-Chelating *P*-stereogenic diphosphine ligands of transition-metal catalysts have continued to be a research topic of interest since Knowles' pioneering work in Rh^I-catalyzed asymmetric hydrogenation.[1,2] Although early advances in the field evolved toward C_2-symmetric diphosphines with backbone chirality, several *P*-stereogenic diphosphines or diphosphines possessing chiral *P*-substituents proved later to be superior in many cases under mild conditions.[3] In addition to the basic ethylene bridge spanning the two phosphorus atoms, 1,1′-biarene-2,2′-diyl, *o*-phenylene, or ferrocene-1,1′-diyl scaffolds can be identified in several successful ligand designs (Figure 1). Forming another category are nonsymmetric (C_1-symmetric) chiral diphosphines, which are embodied by the methylene-, ethylene-, or *o*-phenylene-bridged derivatives (Figure 2).[4] Among them, Hoge's all-aliphatic trichickenfootphos (TCFP) and Imamoto's 3H-BenzP* and 3H-QuinoxP* displayed an excellent performance in Rh^I-catalyzed hydrogenation in particular.

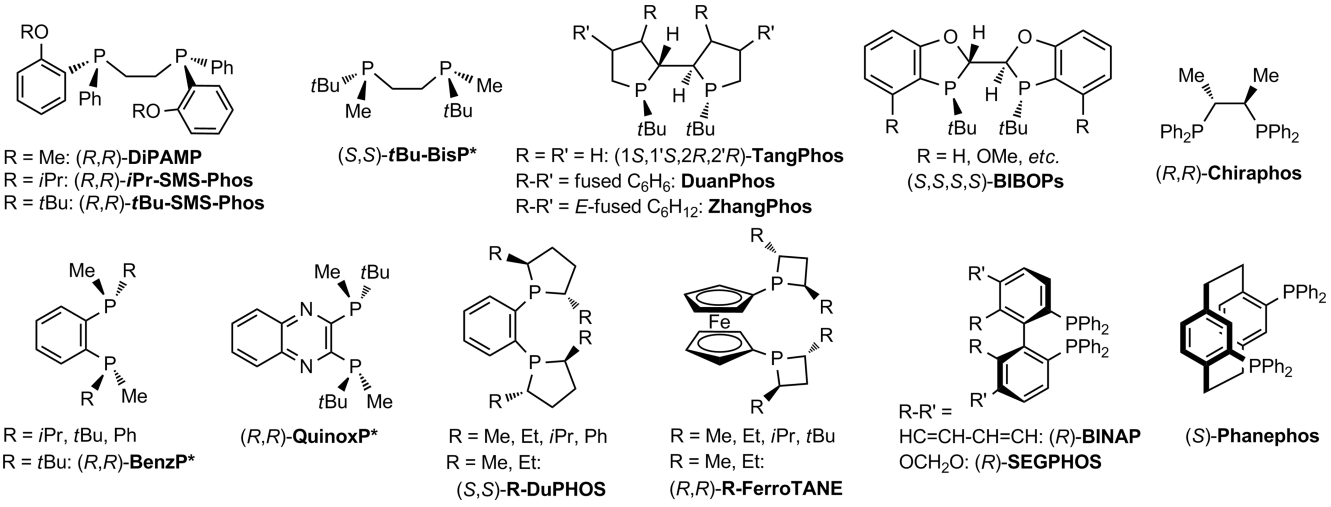

Figure 1. Selection of C_2-symmetric chiral diphosphines.

In some cases, C_1-symmetric designs furnished even better results than their C_2-symmetric bis(chiral phosphorus unit) counterparts.[5] In theory, efficient C_1-symmetric diphosphines, if easily accessed, would offer an economical synthetic advantage over the latter.

In our ongoing research program on metal-(chiral phosphine) complexes,[3a–3c,6] we present hereafter the synthesis

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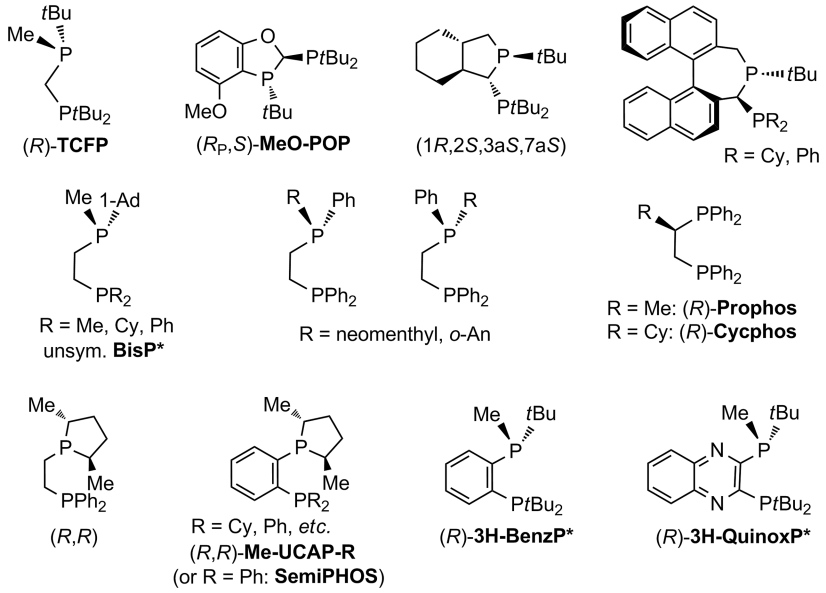


Figure 2. Selection of C_1-symmetric PCP- or PCCP-type chiral diphosphines.

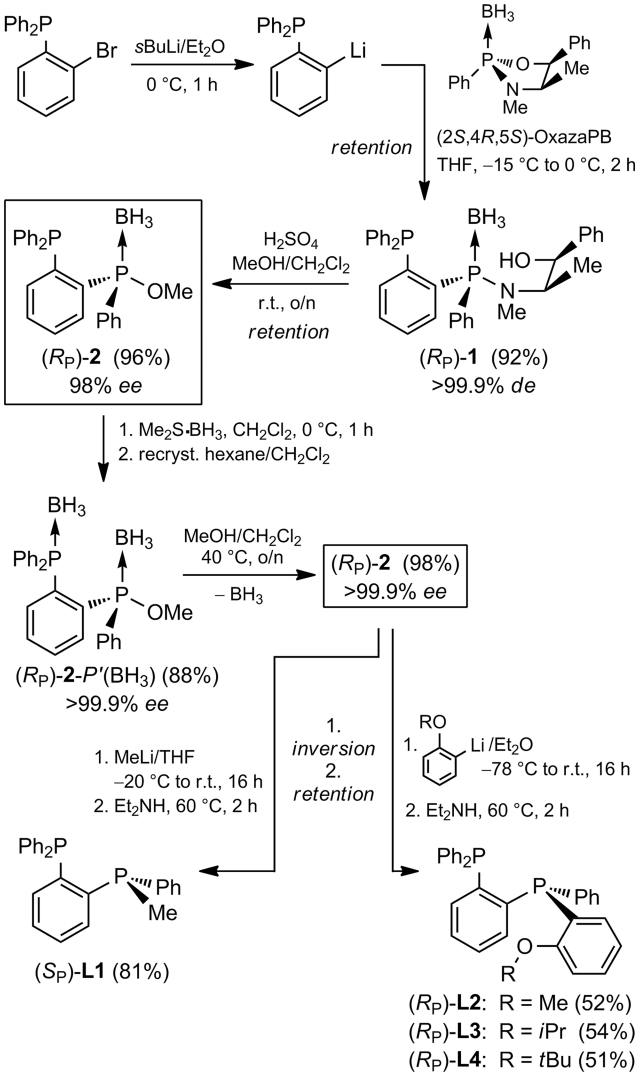
of an *o*-diphenylphosphinophenyl-based C_1-symmetric diphosphine series **L**, wherein the chirality is solely borne by a single phosphorus atom. Such combination has not been developed or investigated in catalysis.[7,8] The diphosphine ligands were screened in the Rh^I-catalyzed asymmetric hydrogenation of benchmark activated olefins.

Results and Discussion

Synthesis of the Diphosphine Series L

The mono-*P*-stereogenic diphosphines **L1**–**L4** were conveniently accessed in enantiopure form and with good overall yields (62, 39, 41, and 39% for **L1**, **L2**, **L3**, and **L4**, respectively) by following an adapted Jugé–Stephan asymmetric route to phosphines[9] (Scheme 1). This general strategy relies upon the sequential displacement with organolithium reagents of either (+)- or (–)-ephedrine auxiliary from the derived enantiopure 1,3,2-oxazaphospholidine-2-borane complex (oxazaPB), giving rise to either target enantiomer. In the present study, such an approach allowed advantageously simple tuning of the diphosphine structure at a late stage.

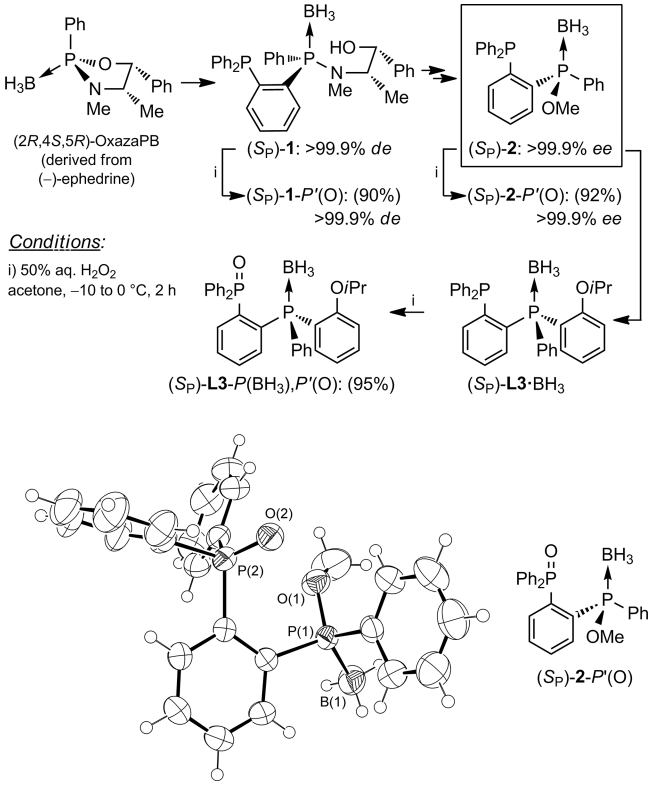
Thus, the diastereomerically pure phosphino-aminophosphine-*P*-borane **1** was obtained in 92% isolated yield by ring-opening of (2*S*,4*R*,5*S*)-(–)-oxazaPB [derived from (1*S*,2*R*)-(+)-ephedrine] with *o*-diphenylphosphino-phenyllithium. X-ray crystal-structure analysis of **1** confirmed its R_P absolute configuration. Notably, no by-products were formed, as is usually observed in this step during the introduction of bulky *ortho*-substituted phenyllithium derivatives.[10] The reactive phosphino-phosphinite-*P*-borane **2** intermediate was subsequently obtained as a viscous oil in 98%*ee* (by chiral HPLC) with 96% yield by H_2SO_4-catalyzed methanolysis of **1**. Its enantiopurity was enhanced to >99.9%*ee* through recrystallization of its borane bis ad-



Scheme 1. Synthesis of the ligand series **L1**–**L4** from ephedrine-derived enantiopure oxazaPB.

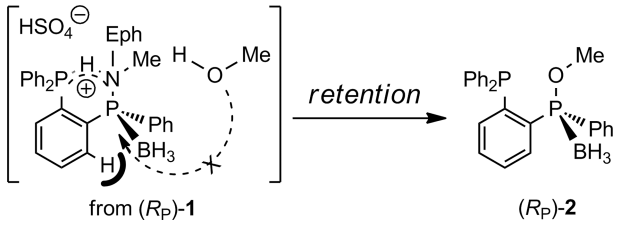
duct **2**-*P*′(BH$_3$). Most importantly, the use of CH_2Cl_2 instead of tetrahydrofuran (THF) ensured preservation of the otherwise labile *P*′-borane on Ph_2P during workup and isolation of **2**-*P*′(BH$_3$).

The *ent*-**2**-*P*′-oxide [derived from (1*R*,2*S*)-(–)-ephedrine] was prepared after failed attempts to determine the absolute configuration of **2** (Scheme 2).[11] Fortunately, its X-ray crystal-structure analysis was successful and revealed an unexpected (S_P)-configuration; therefore, an (R_P)-configuration was assigned to **2** in Scheme 1. This retention of *P*-configuration ensuing the P–N cleavage is in contrast to the inversion of stereochemistry encountered in this step of the Jugé–Stephan general route.[3a–3c,6,9] Given the high *ee* of (R_P)-**2**, this retention can be rationalized by a preferential MeOH attack from any less-encumbered face of the *P*-centered tetrahedron rather than from the hindered face by an adjacent phenylene-H, and leading to a transient trigonal bipyramidal (pentacoordinate) chiral phosphorus (Scheme 3). Such conformation is probably imposed by the six-membered ring formed by H^+-bridging of the N and P atoms of the ephedrino and Ph_2P moieties, respectively. To our knowledge, this is the first example of an S_N-type attack on a phosphorus atom with retention of *P*-configuration encountered in the aminophosphine-*P*-borane series.



Scheme 2. Preparation of (S_P)-**2**-*P*′(O) and X-ray determination of its absolute configuration.

Subsequently, the mono-*P*-borane-protected diphosphines **L1**·BH$_3$–**L4**·BH$_3$ were prepared through displacement of the *P*-OMe group of the enantioenriched (R_P)-**2** (>99.9%*ee*) with methyllithium (86%) or *o*-RO-phenyllithium (52–55%). Finally, the corresponding BH$_3$-free diphosphines **L1**–**L4** were readily obtained with 94–98% yield by decomplexation in Et_2NH (55–60 °C).[12]



Scheme 3. Proposed mechanism of H_2SO_4-catalyzed methanolysis of (R_P)-**1** leading to **2** with retention of *P*-configuration.[14] (*N*-ephedrino = MeN-Eph).

Moreover, Scheme 2 depicts the preparation of (S_P)-**L3**-*P*(BH$_3$),*P*′(O), which demonstrates the possibility of gaining access to such a dissymmetrically-protected and congested structure by following this strategy.[13]

The optical rotation sign of the reported diphosphine **L1**[7] indicated an (S_P)-configuration and the X-ray crystal-structure analysis of **L2** revealed an (R_P)-configuration (Figure 3). Consequently, an identical stereochemical outcome (inversion then retention from **2**) resulted, as expected in both cases taking into account the priorities of the groups according to CIP stereochemistry rules. By extension, an (R_P)-configuration was assigned to **L3** and **L4**.

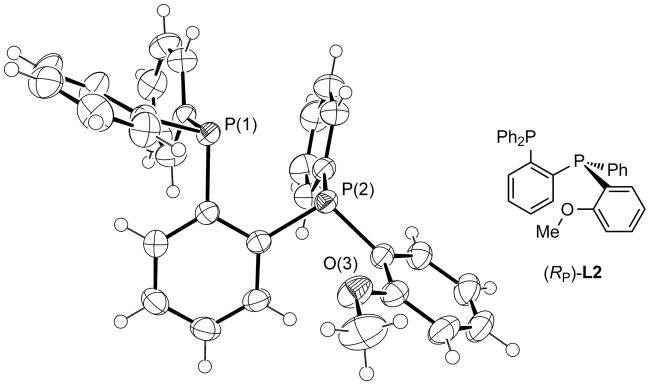


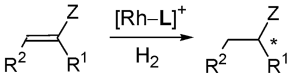
Figure 3. ORTEP of diphosphine **L2** drawn at the 50% probability level.

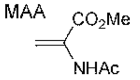
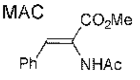
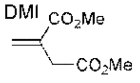
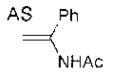
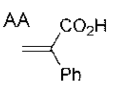
Assessment of the Diphosphine Series L in Rh^I-Catalyzed Hydrogenation

The mono-*P*-stereogenic diphosphine ligands **L1**–**L4** were screened in the Rh^I-catalyzed hydrogenation of methyl α-acetamidoacrylate (MAA), methyl (*Z*)-α-acetamidocinnamate (MAC), dimethyl itaconate (DMI), α-acetamidostyrene (AS), and atropic acid (AA) (Table 1).

Unfortunately, the overall outcome of Rh^I-**L** catalysis in terms of enantioselectivity and activity by current standards does not have a high synthetic value for the tested model substrates. Most notably, the highest *ee* of 87% was obtained for MAC and AS by using the fully arylic bulky ligand **L4** (*P*-*o*-*t*BuOPh-substituted) under 1 bar H_2, and this

Table 1. [Rh^{I}-**L**]-Catalyzed hydrogenation of benchmark activated olefins.[a]



Olefin	Ligand	pH_2 [bar]	t [h]	Conv. [%]	*ee* [%]
MAA 	(S_P)-**L1**	1	0.3	100	40 (*S*)
	(R_P)-**L2**	1	2	100	46 (*S*)
	(R_P)-**L3**	1	2	100	78 (*S*)
	(S_P)-**L1**	1	0.8	100	69 (*S*)
MAC 	(S_P)-**L1**	10	0.5	100	53 (*S*)
	(R_P)-**L2**	1	16	100	67 (*S*)
	(R_P)-**L2**	10	3	100	68 (*S*)
	(R_P)-**L3**	1	16	100	78 (*S*)
	(R_P)-**L3**	10	3	100	84 (*S*)
	(R_P)-**L4**	1	16	100	87 (*S*)
	(R_P)-**L4**	10	3	100	87 (*S*)
DMI 	(S_P)-**L1**	1	0.3	100	4 (*R*)
	(R_P)-**L3**	1	16	81	25 (*R*)
	(S_P)-**L1**	1	0.6	100	19 (*R*)
	(S_P)-**L1**	10	0.3	100	20 (*R*)
AS 	(R_P)-**L2**	1	2	100	25 (*S*)
	(R_P)-**L2**	10	1	100	25 (*S*)
	(R_P)-**L3**	1	3	100	79 (*S*)
	(R_P)-**L3**	10	1	100	80 (*S*)
	(R_P)-**L4**	1	3	100	87 (*S*)
	(R_P)-**L4**	10	1	100	90 (*S*)
	(S_P)-**L1**	10	16	100	2 (*R*)
AA 	(S_P)-**L1**[b]	10	16	100	6 (*R*)
	(R_P)-**L2**	10	16	45	20 (*S*)
	(R_P)-**L3**	10	16	100	34 (*S*)
	(R_P)-**L4**	10	16	100	67 (*S*)

[a] The catalysts were preformed in situ from [Rh(nbd)$_2$]BF$_4$ and the ligand **L**. Runs were carried out with 0.5 mmol substrate in MeOH (7.5 mL) by using a substrate/catalyst molar ratio (S/C) of 100 at 25 °C for the time indicated (progress at 1 bar was monitored for up to 3 h but reaction was continued for 16 h when conversion was not complete). Conversion and *ee* were determined by chiral GC analysis. [b] Et_3N (1.1 equiv.) added.

was improved to 90%*ee* for AS operating at 10 bar. The MAC and AS hydrogenation data with **L1**–**L4** and PCCP-type diphosphines relevant to this study are listed in Figure 4 (for additional listings, see the Supporting Information, Figure S1); because reported data related to AS hydrogenation and to the approximate hydrogenation rate for MAC is not complete, and because the adopted hydrogenation conditions vary, it is difficult to comment on this aspect. Notably, **L4** is enantioselectively competitive (within 7%) to DiPAMP for AS but the opposite is true for MAC.[15] Furthermore, **L4** and the phospholane-containing (stiffer) analogue Me-UCAP-Ph[4n,4o] results are comparable. Concerning the sense of induction of **L1**–**L4**, the same trend is observed as when applying the corresponding C_2-symmetric chiral ethylene- or *o*-phenylene-bridged diphosphines but, curiously, not for AS with **L1** [(*R*)-*N*-Ac-(1-phenylethyl)amine was obtained, albeit in very low 19%*ee*].

The following comparative observations can be made: (1) The Rh^{I} complex of the *P*-Me-substituted ligand **L1** displayed a much higher activity than the *P*-*o*-ROPh-containing **L2**–**L4** counterparts but afforded lower *ee* values. (2) The enantioselectivity consistently increased for all substrates with systematic increase in the RO bulk going from MeO (**L2**) to *i*PrO (**L3**) to *t*BuO (**L4**). (3) Testing the Rh^{I}-**L1** catalyst on MAC showed a noticeable H_2 pressure dependence (but not on AS) as enantioselectivity decreased with increase in pressure (shifting from 1 to 10 bar). Such variation was not substantially noticeable with **L2**–**L4** for MAC or AS. (4) The enantioselectivities (under 1 bar H_2) for MAC and AS with **L1** or **L2** were similar per substrate (69/67%*ee* for MAC and 19/25% for AS). (5) The enantioselectivities (under 1 bar H_2) for MAC and AS with **L3** or **L4** were similar per ligand (78%*ee* with **L3** and 87% with **L4**).

Notably, whereas the *ee* values and catalyst activity with **L2**–**L4** were inferior to those obtained by using the corresponding C_2-symmetric chiral ethylene-bridged diphosphines,[15] the *ee* value reached using **L1** for MAC (69%) is noticeably better than all the *ee* values obtained with the corresponding C_2-symmetric 1,2-bis[(methyl)(phenyl)phosphino]benzene,[16] or 1,2-bis[(aryl)(methyl)phosphino]ethanes (aryl = Ph,[17] Fc[18]), 1,2-bis[(*tert*-butyl)(phenyl)phosphino]ethane,[19] and the C_1-symmetric "unsymmetrical (1-Ad)-BisP*" ligands[4f,4g] (Figure 4).

To discuss enantioselectivity and hydrogenation rate for MAC and AS versus backbone rigidity, and due to the variety of PCCP-type diphosphines considering the backbone and *P*-substituents features (as in Figure 4), it seems necessary to differentiate between the diphosphines bearing a phospholano group, a (methyl)(phenyl)phosphino group, an (RO-substituted Ph)(phenyl)phosphino group, or an (RO-unsubstituted aryl)(phenyl)phosphino group (RO-unsubstituted aryl = ex. α-Nap).

In the case of phospholano-containing diphosphines and as reported by the Pringle group for AS, Rh^{I}-catalyzed hydrogenation by using Me-UCAP-Ph was completed much more rapidly than with Me-DuPHOS, and 1,2-bis(diphenylphosphino)benzene was in an intermediate position.[4n,22] This implies that the incorporation of a rigid aliphatic phospholano group slows down hydrogenation compared with incorporation of a flexible arylic diphenylphosphino group, but the electronic dissymmetry of Me-UCAP-Ph could be responsible for its observed rate enhancement. However, the impact on hydrogenation kinetics of Me-UCAP-Ph versus its ethylene-bridged analogue[4o] or of R-DuPHOS versus its ethylene-bridged analogue R-BPE was, to our knowledge, never clearly exposed. Nevertheless in these cases, the enantioselectivity (for MAC and AS) was higher with ligands having a rigid *o*-phenylene backbone.[3n,4n,4o]

In the case of (methyl)(phenyl)phosphino-containing diphosphines, the results demonstrate that MAC and AS hydrogenation rates are lower with the rigid *o*-phenylene backbone than with the flexible ethylene backbone {**L1** compared with 1,2-bis[(methyl)(phenyl)phosphino]eth-

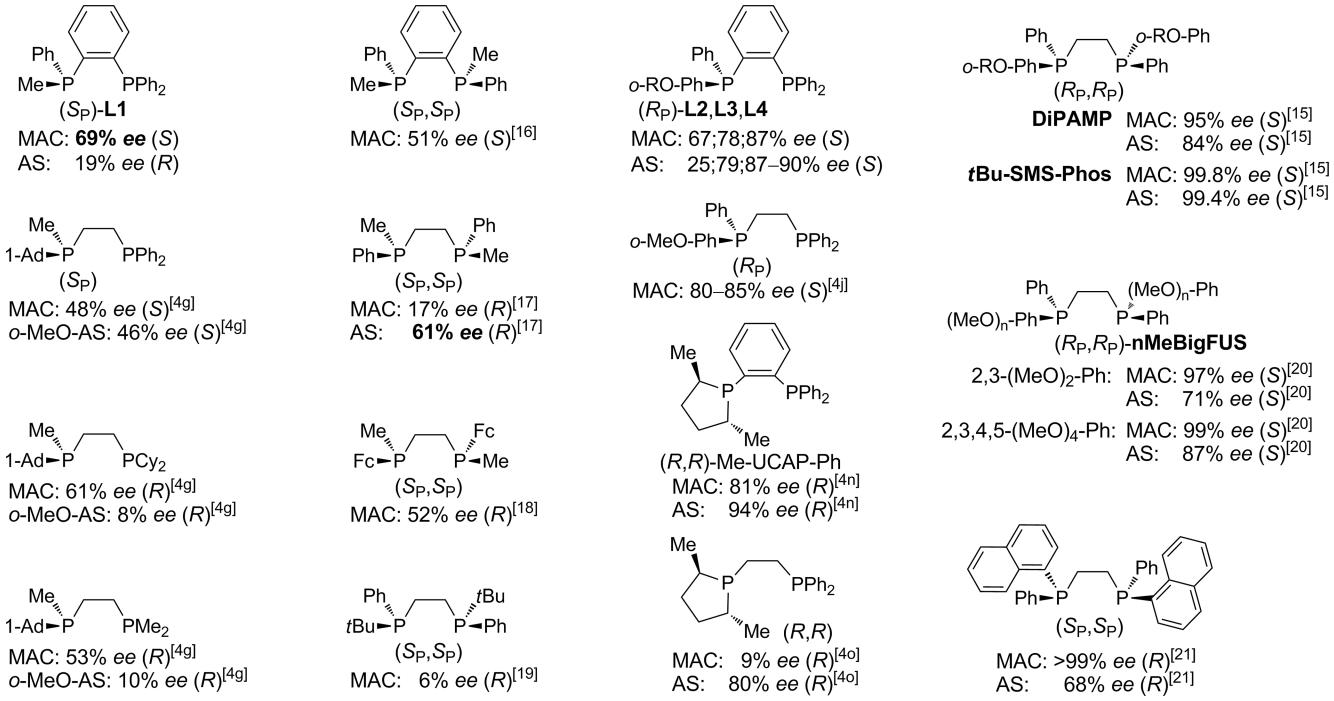


Figure 4. Selection of *P*-stereogenic or phospholano-containing PCCP-type diphosphines with a summary of their Rh^I-catalyzed hydrogenation results against MAC and AS (for additional results, see the Supporting Information, Figure S1).

ane[17a]} but the enantioselectivity for MAC is better with the rigid *o*-phenylene backbone.

Most importantly, the hydrogenation rates for MAC and AS were much higher with 1,2-bis[(aryl)(phenyl)phosphino]ethanes [wherein aryl = *o*-RO-Ph,[6a,15] 2,3-$(MeO)_2$-Ph, 2,3,4,5-$(MeO)_4$-Ph[20]] than with **L1**–**L4**, demonstrating a clear beneficial impact on the hydrogenation kinetics of the flexible CH_2CH_2 backbone in such *P*,*P*,*P*′,*P*′-tetraaryl PCCP-type bridged structure. However, the *P*-α-Nap-substituted analogue[21] displayed much lower hydrogenation rates for MAC and AS compared with DiPAMP[15] or 1,2-bis[(methyl)(phenyl)phosphino]ethane[17a] (having comparable rates), and 1,2-bis{[2,3-$(MeO)_2$-Ph](phenyl)phosphino}ethane,[20] but gave the same level of enantioselectivities as with the latter, pointing here also to the unfavorable increase in the overall rigidity of the system.

It thus seems that the decreased steric demands of **L1** compared with **L2**–**L4** are responsible for its higher hydrogenation rates in the series. This is also seen from the low hydrogenation rate of the unhindered MAA substrate.

Finally, comparing MAC results using **L2**–**L4** (67%*ee* with **L2**, 78%*ee* with **L3**, 87%*ee* with **L4**) against (*o*-An)(Ph)$PCH_2CH_2PPh_2$ (80–85%*ee*),[4j] suggests that the negative impact on enantioselectivity due, in this case, to the severely restricted flexibility of the *o*-phenylene backbone, can be offset by an increase in the *P*-*o*-ROPh bulk. Based on these results, it seems that the highest *ee* values and hydrogenation rates for MAC and AS are obtained by using Rh^I complexes of flexible ethylene-bridge backboned diphosphines having an appropriate arrangement of the (RO-substituted Ph)(phenyl)phosphino groups.

Background

Since the early advances in asymmetric hydrogenation, much effort has been directed towards elucidating the mode of action and the origin of enantioselection of the chiral Rh^I-(*cis*-chelating C_2-symmetric diphosphine) catalysts.[3e,23] In particular, the complex mechanistic aspects of asymmetric hydrogenation of prochiral α-amido-olefins [especially (*Z*)-α-amidocinnamates and α-acetamidostyrene] catalyzed by Rh^I-(*P*-stereogenic PCCP-type diphosphine) complexes are by now well-substantiated and diverse. It seems that either a different or a combination of mechanisms (dihydride vs. unsaturated) can occur depending on the conditions, catalytic system, and the steric and electronic properties of the substrate.[23,24] The basicity and CH_2CH_2 bridge flexibility of diphosphines may play a major role in the rate-determining step by favoring an increase in the Rh^I complex affinity to H_2, facilitating the oxidative H_2 addition, positioning of the two hydrides, and influencing the H-transfer.

Some studies point out that the five-membered ring Rh-(*P*,*P*,*P*′,*P*′-tetraaryl CH_2CH_2-backboned diphosphine) chelates possess just the appropriate conformational mobility.[23c] Accommodating incoming molecules (olefin, H_2, coordinating solvent), the diphosphine is able to adapt to a certain extent by P–C bond free-rotation of the *P*-substituents, flexing the chelate ring with positional switching of these groups. Thus, substrate control as well as Rh-complex control can occur.

Interestingly, Rh-diphosphine quadrant diagrams allow a simple illustration of the primary steric interaction be-

tween the chiral Rh proximal environment and the incoming olefin substrate, and rationalize the sense of induction.[25,26]

As ligand optimization and fine-tuning involve partial alteration of the *P*-substituents, this can severely impact the phosphine basicity and/or bulk, the catalyst overall conformation, and can present difficulties in predicting catalyst performance. A seemingly slight modification of the original ligand structure can lead to a dramatic positive or negative effect on stereoselectivity. As observed in several cases, just an optimal design matches a given substrate [for example in the case of R-BPE vs. R-DuPHOS against a series of β-substituted or unsubstituted (*Z*)-dehydro-α-acetamido methyl esters[3n,3o]]. Therefore in addition to the hydrogenation conditions, the substrate structure is critical when discussing the efficacy of a ligand. Unfortunately, mostly sketchy hydrogenation conditions and data for MAC are found in the early reports and rarely for AS or other by-now benchmark olefins, rendering comparison difficult. However, it is suggested that (*Z*)-dehydro-α-amido acids/esters are more strongly bound, are less bulky than α-amidostyrenes, and are generally hydrogenated faster.

Stereochemical and Profile Considerations for Rh^I-L

In this investigation, our particular interest was to determine the impact on hydrogenation of rigidifying the CH_2CH_2 backbone of *P*-stereogenic *P*,*P*,*P*′,*P*′-tetraarylic diphosphines. Screening on basic benchmark substrates revealed that catalyst activity clearly decreased with the rigid *o*-phenylene-backboned Rh^I catalysts, especially with **L2**–**L4** (*P*-*o*-ROPh-substituted) compared with **L1** (*P*-Me-substituted).

Taking into account the incidence of the backbone switch on *P*-configuration according to the CIP rules, the sense of stereochemical outcome was, as expected, from the "same side" of the olefin (*re*-face for MAA, MAC, AS, and AA, and *si*-face for DMI), by analogy to the corresponding C_2-symmetric chiral ethylene- or *o*-phenylene-bridged counterparts. However, **L1** afforded the opposite configuration for *N*-Ac-(1-phenylethyl)amine with a low but noticeable value (19%*ee*) pointing to a reversal in the major hydrogenation course seen for MAC.[27]

Although the use of Rh^I-**L1** and Rh^I-**L2** led to comparable enantioselectivities for MAC (69/67%*ee*) and AS (19/25%*ee*) under 1 bar H_2, operating at 10 bar resulted in a noticeable decrease in *ee* for MAC (from 69 to 53%*ee*) but not for AS (19/20%*ee*) by using the former,[28] whereas *ee* values were not affected (for both MAC and AS) by using the latter (or the rest of catalysts). Furthermore, hydrogenation rates for MAC and AS with Rh^I-**L1** (100% conv. within 0.8 h) were much higher than with the rest of the Rh^I-**L** catalysts (**L** = **L2**–**L4**), and, in particular, hydrogenation rates with the latter for MAC (100% conv. within 16 h) were significantly lower than for AS (100% conv. within 2–3 h). It is clear that the *ee* values of MAC and AS hydrogenation products improved consistently with increased steric bulk from **L2** to **L3** to **L4**, which, in turn, increases the overall rigidity. This points to a steric factor in the control of enantioselectivity and substrate (or H_2) approach.

When (R_P/S_P)-**L1** was resolved with {(*S*)-*o*-[1-(dimethylamino)ethyl]phenyl}palladium(II) chloride,[7] two diastereomeric Pd complexes were obtained, wherein the stereogenic phosphorus atom and the Me_2N group were in the *trans*-position. However, when (*o*-An)(Ph)$PCH_2CH_2PPh_2$ was enantioenriched [70% ee (S_P)] with {(*R*)-1-[1-(dimethylamino)ethyl]-2-naphthyl}palladium(II) chloride,[4i] all four possible mixed diastereomeric Pd complexes were obtained, with the major complex having the Ph_2P group and the Me_2N group in *trans*-position. Similar to the last case, addition of MAC to Rh^I-[(R_P)-(*o*-An)(Ph)$PCH_2CH_2PPh_2$] led to all four possible mixed diastereomeric Rh complexes in slight favor (56:44) of the pair having the Ph_2P group and the C=C in *trans*-position (the stereogenic P-atom and the amide oxygen atom are in *trans*-position).[4j,29] This indicates that some coordination mode(s) of the nonsymmetrical bidentate ligand to metal complexes can be favored based on a pronounced dissymmetry in their electronic characters.

Given the low *ee* values of the present system, further mechanistic studies were not undertaken.[30] From the results described above it seems likely that the Rh^I-**L1** and Rh^I-**L** (**L** = **L2**–**L4**) catalysts operate differently in hydrogenation due to the unequal steric and electronic nature of the *p*-alkyl versus *p*-aryl substituent. In the case of **L1**, this may privilege a reduced number of Rh intermediates and affect the H-positioning (electronic and steric factors visible), but in the case of **L2**–**L4** this seems to hinder the approach of the incoming substrate or H_2 (more steric factors visible).

With their *o*-phenylene backbone, the Rh^I-**L** complexes are more rigid than the Rh^I-DiPAMP system but they are more supple than the Rh^I-(Me-UCAP-Ph) complex. The *P*,*P*′-phenyls and *P*-*o*-ROPh (or *P*-Me) substituents have more rotational freedom around the corresponding P–C bonds. Although the **L** ligands provide only one half of the chiral array of the corresponding C_2-symmetric chiral diphosphines, the Ph_2P group phenyls (both isoclinal) can also participate to the induction process in the complex by mutually affecting each other in response to the incoming molecules (olefin, H_2) (Figure 5).[31,32] Thus, the reaction rate with **L2**–**L4** should be comparable to that with 1,2-bis(diphenylphosphino)benzene, and the electronic dissymmetry of **L1** could be responsible for the increased rate, as observed with Me-UCAP-Ph.[4n,22]

Finally, it is the geminal substituent of *P*-Me that induces the steric hindrance with 1,2-bis[(Ar)(Me)phosphino]ethanes or -benzenes, as in the case of R-BisP* (the *P*-Me mimics the bulkiest *P*-substituent of the corresponding *P*,*P*,*P*′,*P*′-tetraarylic diphosphines). The geminal *P*-Ar substituent is able to orient the sense of enantioselectivity by more effectively blocking a quadrant. Thus, Imamoto and Gridnev "reformulated quadrant rule"[26] accounts for the observed sense of induction with the *P*-stereogenic 1,2-bis-

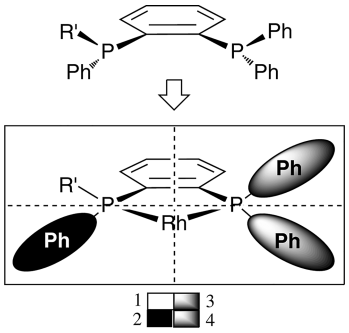


Figure 5. Quadrant diagram for [Rh^{I}-**L**] (R′ = Me, *o*-RO-Ph) [quadrants: unhindered (1), hindered (2), and quasi-hindered depending on olefin accommodation (3, 4)].

[(Ar)(Me)phosphino]ethanes (wherein Ar = Ph, Fc), and 1,2-bis[(Ph)(Me)phosphino]benzene (Figure 4). Similarly for **L1**, it is the *P*-Ph substituent geminal to *P*-Me that induces the steric hindrance and the phenyls of the Ph_2P group (which are not influenced by the *P*-stereogenic center as much as in CH_2CH_2-bridged diphosphines due to δ/λ-conformations deletion) can adopt against each other either a hindering or unhindering conformation to accommodate molecules (Figure 5).

Conclusions

A series of mono-*P*-stereogenic (*P*-*o*-diphenylphosphinophenyl)-based PCCP-type diphosphines **L** was prepared by following the Jugé–Stephan asymmetric route, and studied in Rh^{I}-catalyzed hydrogenation of benchmark activated olefins. The observed retention of *P*-configuration during the H_2SO_4-catalyzed methanolysis step of an aminophosphine-*P*-borane means that extra caution must be taken when attributing *P*-configuration to products derived from intermediates possessing "non-standard" substituents in the vicinity of the reactive phosphorus center.

This "knockout diphosphine design" brought a further mechanistic insight into the relationship between steric and electronic factors affecting the Rh^{I}-catalyzed hydrogenation of olefins. Consequently, this system can serve as a study-tool for the translation of skeletal modifications of *P*-stereogenic *P*,*P*,*P*′,*P*′-tetraarylic ethylene-bridged diphosphines to catalysis.

The thoroughly studied asymmetric hydrogenation mechanism can be sensitive to operating conditions, and achieving an ideal match between a chiral catalyst system and a given substrate towards highest enantioselective efficiency remains largely an empirical process. The design and screening of complementary new chiral ligands provides probes with which to extend our knowledge. As Heller rightfully put it "a chiral ligand is a necessary but not sufficient condition for stereoselection".[33]

Experimental Section

Materials and Methods: The following compounds were prepared according to reported procedures: (2-bromophenyl)diphenylphosphine[34] and (2*S*,4*R*,5*S*)-(–)-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphospholidine-2-borane [(–)-oxazaPB; derived from (1*S*,2*R*)-(+)-ephedrine] and (+)-oxazaPB [derived from (1*R*,2*S*)-(–)-ephedrine];[9] noncommercial olefin: α-acetamidostyrene [*N*-(1-phenylvinyl)acetamide, AS].[35] All reactions were conducted under an inert atmosphere (nitrogen or argon) with anhydrous solvents. Analytical thin-layer chromatography (TLC) was performed with Silica Gel 60 F254 pre-coated plates (0.25 mm thickness). R_f values are reported and visualization was accomplished by irradiation with a UV lamp (254 nm) and/or staining with $KMnO_4$ solution. Flash column chromatography was performed with Silica Gel 60 (40–63 μm). ^{1}H (299.9 MHz; internal Me_4Si), ^{13}C (75.4 MHz; internal $CDCl_3$, δ = 77.00 ppm), and ^{31}P (120 MHz, external 85% H_3PO_4) NMR spectra were recorded with a Varian Unity plus 300 spectrometer for solutions in $CDCl_3$. HRMS measurements were obtained with a Waters Micromass Q-TOF Premier instrument equipped with an orthogonal Z-spray ESI interface.

(R_P)-(2-Diphenylphosphinophenyl)[(1*S*,2*R*)-(*N*-ephedrino)](phenyl)phosphine-*P*-borane [(R_P)-1]: To a cold (0 °C) solution of (2-bromophenyl)diphenylphosphine (6.10 g, 17.88 mmol, 1.32 equiv.) in Et_2O (100 mL) was added *s*BuLi (1.2 M in cyclohexane/hexane, 92:8; 14.6 mL, 1.3 equiv.) and the mixture was stirred for 1 h. To this mixture at –15 °C, a solution of (–)-oxazaPB (3.86 g, 13.52 mmol) in THF (10 mL) was added. The resulting mixture was warmed to 0 °C and stirred for 2 h, then the reaction was quenched with H_2O (10 mL). The residue was partitioned between Et_2O (150 mL) and H_2O (50 mL), and the organic layer was dried (Na_2SO_4) and concentrated. The residue was purified on silica gel (toluene (R_f 0.2), then toluene/EtOAc, 9:1), and recrystallized (hexane/CH_2Cl_2) to afford the product (6.82 g, 92%) as colorless crystals; m.p. 130–132 °C; $[a]_D^{25}$ = –14.8 (*c* = 1.0, $CHCl_3$) (>99.9% *de* by ^{1}H NMR). ^{1}H NMR: δ = 0.88–1.98 (br. m, 3 H), 1.21 (d, *J* = 7 Hz, 3 H), 1.68 (br. s, 1 H), 2.63 (d, *J* = 7 Hz, 3 H), 4.35–4.57 (m, 1 H), 4.94–5.03 (m, 1 H), 7.06–7.45 (m, 21 H), 7.52–7.63 (m, 3 H) ppm. ^{13}C NMR: δ = 11.5 (m), 31.9 (m), 58.4 (m), 78.9 (m), 125.9 (m), 127.2–133.4 (m), 137.1–139.0 (m), 141.4 (dd, *J* = 23, 13 Hz), 142.5 ppm. ^{31}P NMR: δ = –16.5 (d, *J* = 23 Hz), 72.6 (br. m) ppm. MS (ESI): *m*/*z* (%) = 548.2 (30) [M + H]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{34}H_{37}BNOP_2$ [M + H]$^+$ 548.244; found 548.243. Absolute configuration determination: X-ray single-crystal-structure analysis revealed its (R_P)-configuration.[36]

(S_P)-(2-Diphenylphosphinophenyl)[(1*R*,2*S*)-(*N*-ephedrino)](phenyl)phosphine-*P*-borane [(S_P)-1]: By following a similar procedure to that described for (R_P)-**1**, starting from (+)-oxazaPB, a crystalline material (>99.9% *de* by ^{1}H NMR) was obtained with identical spectral characteristics to those described above; $[a]_D^{25}$ = +14.9 (*c* = 1.0, $CHCl_3$).

(S_P)-(2-Diphenylphosphinoylphenyl)[(1*R*,2*S*)-(*N*-ephedrino)](phenyl)phosphine-*P*-borane [(S_P)-1-*P*′(O)]: To a solution of (S_P)-**1** (84 mg, 0.153 mmol, >99.9% *de*) in acetone (10 mL) was added 50% aq. H_2O_2 (0.1 mL) at 0 °C and the mixture was stirred for 2 h. The reaction was quenched with 10% aq. Na_2SO_3, concentrated, and partitioned between CH_2Cl_2/H_2O. The organic layer was filtered through a pad of SiO_2/Na_2SO_4 eluting with CH_2Cl_2 then with EtOAc to afford the product (78 mg, 90%) as a colorless oil. $[a]_D^{25}$ = –52.1 (*c* = 1.0, $CHCl_3$) (>99.9% *de* by ^{1}H NMR). ^{1}H NMR: δ = 0.21–1.50 (br. m, 3 H), 1.19 (d, *J* = 7 Hz, 3 H), 3.12 (d, *J* = 11 Hz, 3 H), 3.67–3.94 (m, 1 H), 4.57 (t, *J* = 4 Hz, 1 H), 4.68–4.77 (m, 1 H), 7.06–6.91 (m, 2 H), 7.67–7.07 (m, 21 H), 7.85–7.73 (m, 1 H) ppm. ^{13}C NMR: δ = 12.1 (d, *J* = 3 Hz), 33.3 (d, *J* = 8 Hz), 58.6 (d, *J* = 3 Hz), 75.9, 126.6–132.2 (m), 133.5–136.0 (m), 137.1–138.7 (m), 141.9 ppm. ^{31}P NMR: δ = 36.2 (d, *J* = 4.4 Hz), 74.8 (br. m) ppm.

Methyl (R_P)-(2-Diphenylphosphinophenyl)(phenyl)phosphinite-*P*-borane [(R_P)-2]: To a solution of (R_P)-**1** (6.00 g, 10.96 mmol) in CH_2Cl_2 (30 mL) and absolute MeOH (120 mL), a solution of 96% H_2SO_4 (1.11 g, 10.86 mmol) in absolute MeOH (30 mL) was added at room temp. while stirring. The mixture was stirred overnight, filtered through a bed of silica gel, and concentrated. The crude product was purified on silica gel (toluene) to give the title compound (4.32 g, 96%) as a colorless viscous oil. R_f = 0.7 (toluene); $[a]_D^{25}$ = +2.3 (c = 1.7, $CHCl_3$); 98.2%*ee* by HPLC (Chiralpak AD-H; hexane/2-PrOH, 98:2; 1.0 mL/min; λ 254 nm): t_R = 7.6 (R_P), 8.2 (S_P) min [racemic mixture prepared by weighing equal amounts of (R_P)- and (S_P)-**2**]. ^{1}H NMR: δ = 0.59–1.74 (br. m, 3 H), 3.48 (d, J = 12 Hz, 3 H), 6.82–7.15 (m, 4 H), 7.17–7.53 (m, 12 H), 7.59–7.74 (m, 2 H), 8.00–8.15 (m, 1 H) ppm. ^{13}C NMR: δ = 53.6 (m), 128.0–129.0 (m), 132.5–134.1 (m), 136.4–138.5 (m), 141.5 (dd, J = 23, 9 Hz) ppm. ^{31}P NMR: δ = –14.5 (d, J = 23 Hz), +111.2 (br. m) ppm. MS (ESI): m/z (%) = 415.1 (90) [M + H]$^+$. HRMS (ESI): m/z calcd. for $C_{25}H_{26}BOP_2$ [M + H]$^+$ 415.155; found 415.156.

Methyl (S_P)-(2-Diphenylphosphinophenyl)(phenyl)phosphinite-*P*-borane [(S_P)-2]: By following a similar procedure to that described for (R_P)-**2**, starting from (S_P)-**1**, a viscous oil (98.4%*ee* by HPLC) was obtained with identical spectral characteristics to those described above.

Methyl (R_P)-[2-(Diphenylphosphino-*P*-borane)phenyl](phenyl)phosphinite-*P*-borane [(R_P)-2-*P*′(BH$_3$)]: To a cold (0 °C) solution of (R_P)-**2** (4.14 g, 10.0 mmol, 98.2%*ee*) in CH_2Cl_2 (30 mL) was added $Me_2S{\cdot}BH_3$ (5.0 mL, 50 mmol). After stirring for 1 h, the mixture was filtered through a bed of silica gel and carefully concentrated at room temp. to afford the product (4.36 g, 100% yield) as a white powder; m.p. 141–143 °C; $[a]_D^{25}$ = –178.6 (c = 1.0, CH_2Cl_2). Recrystallization (hexane/CH_2Cl_2) afforded the product (3.77 g, 88%) as fine white needles in enantiomerically pure form: >99.9%*ee* [by HPLC analysis of regenerated (R_P)-**2**]; $[a]_D^{25}$ = –183.3 (c = 1.0, CH_2Cl_2). ^{1}H NMR: δ = 0.07–2.61 (br. m, 6 H), 2.91 (d, J = 12 Hz, 3 H), 7.07–7.22 (m, 1 H), 7.32 (ddd, J = 8, 3, 1 Hz, 1 H), 7.36–7.56 (m, 10 H), 7.57–7.74 (m, 5 H), 7.74–7.89 (m, 2 H) ppm. ^{13}C NMR: δ = 52.2 (d, J = 3 Hz), 128.5–128.9 (m), 130.2–131.1 (m), 131.8–132.6 (m), 133.9 (d, J = 9 Hz), 135.0 (dd, J = 23, 8 Hz), 136.5 (dd, J = 9, 7 Hz) ppm. ^{31}P NMR: δ = +57.7 (br. m), +143.4 (br. m) ppm.

Methyl (S_P)-[2-(Diphenylphosphino-*P*-borane)phenyl](phenyl)phosphinite-*P*-borane [(S_P)-2-*P*′(BH$_3$)]: By following a similar procedure to that described for (R_P)-**2**-*P*′(BH$_3$), starting from (S_P)-**2** (98.4%*ee*), a white powder was obtained with identical spectral characteristics to those described above with $[a]_D^{25}$ = +183.4 (c = 1.0, CH_2Cl_2); >99.9%*ee* [by HPLC analysis of regenerated (S_P)-**2**].

Methyl (R_P)-(2-Diphenylphosphinophenyl)(phenyl)phosphinite-*P*-borane [(R_P)-2; >99.9%*ee*]: A solution of (R_P)-**2**-*P*′(BH$_3$) (2.90 g, 6.77 mmol, >99.9%*ee*) in CH_2Cl_2 (50 mL) and 96% MeOH (50 mL) was stirred at 40 °C overnight then concentrated. The residue was filtered through a bed of silica gel (toluene) to afford the title regenerated compound (2.75 g, 98%) as a colorless viscous oil; $[a]_D^{25}$ = +2.4 (c = 1.7, $CHCl_3$); >99.9%*ee* by HPLC. ^{1}H NMR data were in accordance with those of **2** prepared as described above.

Methyl (S_P)-(2-Diphenylphosphinophenyl)(phenyl)phosphinite-*P*-borane [(S_P)-2; >99.9%*ee*]: By following a similar procedure to that described for (R_P)-**2** (>99.9%*ee*), starting from (S_P)-**2**-*P*′(BH$_3$) (>99.9%*ee*), a viscous oil (>99.9% ee by HPLC) was obtained with identical spectral characteristics to those detailed above.

Methyl (S_P)-(2-Diphenylphosphinoylphenyl)(phenyl)phosphinite-*P*-borane [(S_P)-2-*P*′(O)]: To a solution of (S_P)-**2** (60 mg, 0.145 mmol, >99.9%*ee*) in acetone (10 mL) was added 50% aq. H_2O_2 (0.5 mL) at 0 °C and the mixture was stirred for 2 h. The reaction mixture was quenched with 10% aq. Na_2SO_3, and partitioned between EtOAc and H_2O. The organic layer was filtered through a pad of silica gel/Na_2SO_4 followed by recrystallization from MeOH to afford the product (57 mg, 92%) as white crystals; m.p. 100 °C; $[a]_D^{25}$ = +95.4 (c = 1.0, abs. MeOH). ^{1}H NMR: δ = 0.3–1.7 (br. m, 3 H), 3.25 (d, J = 12 Hz, 3 H), 7.26–7.69 (m, 16 H), 7.78 (ddd, J = 11, 8, 1 Hz, 2 H), 8.07 (ddd, J = 10, 8, 4 Hz, 1 H) ppm. ^{13}C NMR: δ = 53.5 (d, J = 3 Hz), 128.0–128.5 (m), 130.1–130.4 (m), 131.1–132.3 (m), 135.0–135.7 (m) ppm. ^{31}P NMR: δ = 59.9 (d, J = 5 Hz), 140.6 (br. m, J = 5 Hz) ppm. HRMS (ESI): m/z calcd. for $C_{25}H_{23}BO_2P_2$ [M – H]$^+$ 428.1375; found 428.1375. Absolute configuration determination: X-ray single-crystal-structure analysis revealed its (S_P)-configuration.[36]

(S_P)-(2-Diphenylphosphinophenyl)(methyl)(phenyl)phosphine-*P*-borane [(S_P)-L1·BH$_3$]: To a cold (–20 °C) solution of (R_P)-**2** (2.00 g, 4.83 mmol, >99.9%*ee*) in THF (50 mL) was added dropwise MeLi (1.6 M in Et_2O, 5.0 mL). The mixture was warmed to room temp. overnight then the reaction was quenched with H_2O (10 mL) and the mixture was concentrated and extracted with Et_2O. The organic layer was filtered through a bed of silica gel/Na_2SO_4 and concentrated to afford the product (1.65 g, 86%) as a colorless syrup; R_f 0.3 (hexane/EtOAc, 9:1); $[a]_D^{25}$ = –28.1 (c = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.56–1.71 (br. m, 3 H), 2.16 (d, J = 10 Hz, 3 H), 6.78–6.90 (m, 2 H), 6.92–7.02 (m, 2 H), 7.09–7.30 (m, 9 H), 7.40–7.52 (m, 5 H), 8.12–8.27 (m, 1 H) ppm. ^{13}C NMR: δ = 13.2 (m), 128.1–137.8 (m), 141.8 (dd, J = 20, 4 Hz) ppm. ^{31}P NMR: δ = –15.7 (d, J = 23 Hz), 15.3 (br. m) ppm. MS (ESI): m/z (%) = 421.1 (15) [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{25}H_{25}BP_2Na$ [M + Na]$^+$ 421.142; found 421.142. Absolute configuration of the title compound was assigned as (S_P) based on configuration of its BH_3-free derivative **L1** (a reported compound,[7] the configuration of which has been determined by X-ray analysis of a palladium complex), which was determined by optical rotation measurement (see below), and assumed retention of *P*-configuration during decomplexation as in the case of related reported compounds such as (R_P,R_P)-DioxyBenzP*·BH$_3$ and *P*-stereogenic phosphine-*P*-boranes in general.[3j,12]

(R_P)-(2-Anisyl)(2-diphenylphosphinophenyl)(phenyl)phosphine-*P*-borane [(R_P)-L2·BH$_3$]: To a cold (0 °C) solution of 2-bromoanisole (0.450 g, 2.40 mmol, 1.3 equiv.) in Et_2O (10 mL) was added dropwise *s*BuLi (1.25 M in cyclohexane/hexaane, 92:8; 1.9 mL, 1.3 equiv.). After stirring at 0 °C for 45 min, a solution of (R_P)-**2** (0.760 g, 1.83 mmol, >99.9%*ee*) in Et_2O (10 mL) was slowly added at –78 °C. The reaction mixture was stirred at room temp. overnight, quenched with H_2O (1 mL), and concentrated. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and extracted with CH_2Cl_2 (2× 10 mL). The organic layer was dried (Na_2SO_4), concentrated, and the residue was recrystallized (EtOAc) to afford the product (0.476 g, 54%) as a white powder; m.p. 166–168 °C; R_f 0.2 (hexane/EtOAc, 9:1); >99.9%*ee* by HPLC (Chiralpak AD-H; hexane/2-PrOH, 95:5; 1.0 mL/min; λ 254 nm): t_R = 11.0 (S_P), 12.9 (R_P) min [a racemic mixture was prepared by weighing equal amounts of (R_P)- and (S_P)-**L2**·BH$_3$]. ^{1}H NMR: δ = 0.94–2.09 (br. m, 3 H), 3.25 (s, 3 H), 6.42 (ddd, J = 8, 4, 1 Hz, 1 H), 6.91–7.05 (m, 5 H), 7.13–7.45 (m, 13 H), 7.46–7.62 (m, 1 H), 7.72–7.87 (m, 2 H), 7.93 (ddd, J = 14, 8, 2 Hz, 1 H) ppm. ^{13}C NMR: δ = 54.6 (m), 110.1–138.4 (m), 141.1 (dd, J = 21, 10 Hz), 160.7 ppm. ^{31}P NMR: δ = –16.6 (d, J = 30 Hz), 20.7 (br. m) ppm. MS (ESI): m/z (%) = 489.2 (45) [M – H]$^+$. HRMS (ESI): m/z calcd. for $C_{31}H_{28}BOP_2$ [M – H]$^+$ 489.171; found 489.171. Absolute configuration of the title compound was assigned as (R_P) based on config-

uration of its BH_3-free derivative **L2**, which was determined by X-ray crystal diffraction analysis (see below), and assumed retention of *P*-configuration during decomplexation as in the case of related reported compounds such as (R_P,R_P)-DioxyBenzP*·BH_3 and *P*-stereogenic phosphine-*P*-boranes in general.[3j,12]

(S_P)-(2-Anisyl)(2-diphenylphosphinophenyl)(phenyl)phosphine-*P*-borane [(S_P)-L2·BH_3]: By following a similar procedure to that described for (R_P)-**L2**·BH_3, starting from (S_P)-**2** (>99.9%*ee*), a white powder was obtained with identical spectral characteristics to those described above.

(R_P)-(2-Diphenylphosphinophenyl)(2-isopropoxyphenyl)(phenyl)phosphine-*P*-borane [(R_P)-L3·BH_3]: By following a similar procedure to that described for (R_P)-**L2**·BH_3 from *o*-bromo-isopropoxybenzene (0.516 g, 2.40 mmol, 1.3 equiv.), the product (0.513 g, 55%) was obtained as a white powder; m.p. 170–173 °C; R_f 0.3 (hexane/EtOAc, 9:1); $[a]_D^{25}$ = –15.5 (*c* = 0.8, $CHCl_3$). ^{1}H NMR: δ = 0.51–1.89 (br. m, 3 H), 0.70 (d, *J* = 6 Hz, 3 H), 0.96 (d, *J* = 6 Hz, 3 H), 4.06 (sept, *J* = 6 Hz, 1 H), 6.32–6.46 (m, 1 H), 6.91–7.05 (m, 5 H), 7.11–7.46 (m, 13 H), 7.54–7.69 (m, 1 H), 7.75–7.91 (m, 2 H), 7.99 (ddd, *J* = 14, 8, 2 Hz, 1 H) ppm. ^{13}C NMR: δ = 21.1 (m), 69.1 (m), 111.1 (m), 117.5 (dd, *J* = 58, 4 Hz), 120.3 (m), 127.9–138.7 (m), 141.3 (dd, *J* = 22, 11 Hz), 158.9 ppm. ^{31}P NMR: δ = –16.7 (d, *J* = 30 Hz), 20.7 (br. m) ppm. MS (ESI): *m*/*z* (%) = 517.2 (80) $[M - H]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{33}H_{32}BOP_2$ $[M - H]^+$ 517.202; found 517.203. Absolute configuration of the title compound is assumed to be (R_P) by extension from **L2**·BH_3.

(S_P)-(2-Diphenylphosphinophenyl)(2-isopropoxyphenyl)(phenyl)phosphine-*P*-borane [(S_P)-L3·BH_3]: By following a similar procedure to that described for (R_P)-**L3**·BH_3, starting from (S_P)-**2** (>99.9%*ee*), the product was obtained as a white powder with identical spectral characteristics to those described above.

(R_P)-(2-*tert*-Butoxyphenyl)(2-diphenylphosphinophenyl)(phenyl)phosphine-*P*-borane [(R_P)-L4·BH_3]: To a solution of *tert*-butoxybenzene (300 mg, 2.00 mmol, 1.4 equiv.) in cyclohexane (2 mL), *t*BuLi (1.6 M in pentane, 1.25 mL, 1.4 equiv.) was added dropwise at room temp. After stirring at 60 °C for 6 h, the solution was cooled to –78 °C and a solution of (R_P)-**2** (637 mg, 1.54 mmol, >99.9%*ee*) in Et_2O (5 mL) was added slowly. The mixture was stirred at room temp. overnight, then the reaction was quenched with H_2O (1 mL), and concentrated. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and extracted with CH_2Cl_2 (2 × 10 mL). The organic layer was dried (Na_2SO_4), concentrated, and purified on silica gel (hexane then hexane/EtOAc, 95:5 to 90:10) to give the product (0.426 g, 52%) as a white powder; m.p. 132–134 °C; $[a]_D^{25}$ = –13.7 (*c* = 1, $CHCl_3$). ^{1}H NMR: δ = 0.76–2.40 (br. m, 3 H), 1.05 (s, 9 H), 6.53–6.62 (m, 1 H), 6.81–6.94 (m, 2 H), 6.94–7.04 (m, 2 H), 7.08–7.23 (m, 4 H), 7.23–7.45 (m, 9 H), 7.45–7.57 (m, 1 H), 7.61–7.76 (m, 4 H) ppm. ^{13}C NMR: δ = 28.4, 79.6, 115.2 (d, *J* = 5 Hz), 119.9 (d, *J* = 11 Hz), 127.9–128.1 (m), 128.8 (d, *J* = 11 Hz), 130.3–130.7 (m), 132.3 (m), 133.0–133.4 (m), 134.1–134.2 (m), 134.7–135.0 (m), 135.7–135.9 (m), 137.6–137.8 (m), 158.4 ppm. ^{31}P NMR: δ = –16.1 (d, *J* = 31 Hz), 22.4 (br. m) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{34}H_{34}BOP_2$ $[M - H]^+$ 531.2176; found 531.2176. Absolute configuration of the title compound is assumed to be (R_P) by extension from **L2**·BH_3.

(S_P)-(2-Diphenylphosphinophenyl)(methyl)(phenyl)phosphine [(S_P)-L1]: (S_P)-**L1**·BH_3 (1.10 g, 2.76 mmol) in Et_2NH (30 mL) was heated to reflux for 2–3 h under argon then concentrated. The residue was filtered through a pad of silica gel with toluene under an inert atmosphere to afford the product (0.998 g, 94%) as a colorless syrup; R_f 0.5 (hexane/EtOAc, 9:1); $[a]_D^{25}$ = –30.1 (*c* = 1.0, $CHCl_3$), $[a]_D^{23}$ = –74.1 (*c* = 2.5, acetone). ^{1}H NMR: δ = 1.47 (d, *J* = 4 Hz, 3 H), 6.91–7.00 (m, 1 H), 7.17–7.34 (m, 18 H) ppm. ^{13}C NMR: δ = 12.4 (m), 127.7–129.1 (m), 131.7–134.1 (m), 137.1 (dd, *J* = 12, 6 Hz), 137.6 (dd, *J* = 12, 6 Hz), 140.2 (dd, *J* = 13, 5 Hz), 143.5 (dd, *J* = 32, 11 Hz), 145.9 (dd, *J* = 31, 13 Hz) ppm. ^{31}P NMR: δ = –36.2 (d, *J* = 158 Hz), –13.2 (d, *J* = 158 Hz) ppm. MS (ESI): *m*/*z* (%) = 385.1 (40) $[M + H]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{23}P_2$ $[M + H]^+$ 385.128; found 385.127. Absolute configuration of the title compound was determined as (S_P) by comparing its optical rotation with the reported compound [(*S*)-isomer: $[a]_{589}$ = –51 (*c* = 2.38, acetone); (*R*)-isomer: $[a]_{589}$ = +51 (*c* = 2.50, acetone)].[7]

(R_P)-(2-Anisyl)(2-diphenylphosphinophenyl)(phenyl)phosphine [(R_P)-L2]: Prepared by following a similar procedure to that described for **L1**, from (R_P)-**L2**·BH_3 (0.40 g, 0.81 mmol, >99.9%*ee*), to afford the product (0.373 g, 96%) as colorless crystals; m.p. 158–160 °C; R_f 0.6 (toluene); $[a]_D^{25}$ = –49.7 (*c* = 1.2, $CHCl_3$). ^{1}H NMR: δ = 3.63 (s, 3 H), 6.63 (ddd, *J* = 7, 4, 2 Hz, 1 H), 6.72–6.85 (m, 2 H), 6.94–7.08 (m, 2 H), 7.11–7.29 (m, 18 H) ppm. ^{13}C NMR: δ = 55.6, 110.2 (m), 120.8, 126.0 (dd, *J* = 14, 7 Hz), 128.1–130.0 (m), 133.7–134.3 (m), 136.5 (dd, *J* = 12, 5 Hz), 137.4 (dd, *J* = 12, 5 Hz), 137.5 (dd, *J* = 12, 4 Hz), 143.3 (dd, *J* = 32, 11 Hz), 143.7 (dd, *J* = 33, 10 Hz), 161.0 (d, *J* = 15 Hz) ppm. ^{31}P NMR: δ = –22.9 (d, *J* = 166 Hz), –13.4 (d, *J* = 166 Hz) ppm. MS (ESI): *m*/*z* (%) = 477.2 (100) $[M + H]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{27}OP_2$ $[M + H]^+$ 477.154; found 477.155. Absolute configuration determination: X-ray single-crystal-structure analysis revealed its (R_P)-configuration.[36]

(S_P)-(2-Anisyl)(2-diphenylphosphinophenyl)(phenyl)phosphine [(S_P)-L2]: By following a similar procedure to that described for (R_P)-**L2**, starting from (S_P)-**L2**·BH_3 (>99.9%*ee*), the product was obtained as colorless crystals with identical spectral characteristics to those described above.

(R_P)-(2-Diphenylphosphinophenyl)(2-isopropoxyphenyl)(phenyl)phosphine [(R_P)-L3]: Prepared by following a similar procedure to that described for **L1**, from (R_P)-**L3**·BH_3 (0.40 g, 0.77 mmol) to afford the product (0.381 g, 98%) as colorless crystals; m.p. 130–132 °C; R_f 0.6 (toluene); $[a]_D^{25}$ = –50.9 (*c* = 1.5, $CHCl_3$). ^{1}H NMR: δ = 0.97 (d, *J* = 6 Hz, 3 H), 1.09 (d, *J* = 6 Hz, 3 H), 4.44 (sept, *J* = 6 Hz, 1 H), 6.61 (ddd, *J* = 8, 4, 2 Hz, 1 H), 6.67–6.83 (m, 2 H), 7.02–7.28 (m, 20 H) ppm. ^{13}C NMR: δ = 21.7, 21.8, 70.1, 111.9 (m), 120.3, 127.4 (dd, *J* = 14, 8 Hz), 128.0–129.5 (m), 133.7–134.7 (m), 136.5 (dd, *J* = 11, 4 Hz), 137.4 (dd, *J* = 12, 5 Hz), 137.7 (dd, *J* = 13, 7 Hz), 143.4 (dd, *J* = 32, 10 Hz), 143.9 (dd, *J* = 32, 10 Hz), 159.0 (d, *J* = 14 Hz) ppm. ^{31}P NMR: δ = –21.4 (d, *J* = 164 Hz), –14.0 (d, *J* = 164 Hz) ppm. MS (ESI): *m*/*z* (%) = 505.2 (100) $[M + H]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{33}H_{31}OP_2$ $[M + H]^+$ 505.185; found 505.185.

(S_P)-(2-Diphenylphosphinophenyl)(2-isopropoxyphenyl)(phenyl)phosphine [(S_P)-L3]: By following a similar procedure to that described for (R_P)-**L3**, starting from (S_P)-**L3**·BH_3, colorless crystals were obtained with identical spectral characteristics to those described above.

(R_P)-(2-*tert*-Butoxyphenyl)(2-diphenylphosphinophenyl)(phenyl)phosphine [(R_P)-L4]: Prepared by following a similar procedure to that described for **L1**, from (R_P)-**L4**·BH_3 (0.35 g, 0.657 mmol), to afford the product (0.174 g, 98%) as colorless crystals; m.p. 128–130 °C; R_f 0.7 (toluene); $[a]_D^{25}$ = –19.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR: δ = 1.28 (s, 9 H), 6.50–6.70 (m, 1 H), 6.74–6.78 (m, 1 H), 6.93–7.42 (m, 21 H) ppm. ^{13}C NMR: δ = 29.0 (d, *J* = 1 Hz), 79.5, 118.4 (m), 121.5, 128.0–129.0 (m), 131.1 (dd, *J* = 12, 8 Hz), 133.7–134.7 (m), 136.8–137.9 (m), 143.2 (dd, *J* = 32, 11 Hz), 144.1 (dd, *J* = 32, 11 Hz), 158.3 (d, *J* = 16 Hz) ppm. ^{31}P NMR: δ = –14.1 (d, *J* = 166 Hz),

–20.4 (d, J = 166 Hz) ppm. HRMS (ESI): m/z calcd. for $C_{34}H_{33}OP_2$ $[M + H]^+$ 519.2007; found 519.2011.

(S_P)-(2-Diphenylphosphinoylphenyl)(2-isopropoxyphenyl)(phenyl)-phosphine-*P*-borane [(S_P)-L3-*P*(BH_3),*P*′(O)]: To a solution of (S_P)-**L3**·BH_3 (50 mg, 0.097 mmol) in CH_2Cl_2 (10 mL) was added 50% aq. H_2O_2 (0.1 mL) at –10 °C and the mixture was stirred for 2 h. The reaction was quenched with 10% aq. Na_2SO_3, and the mixture was partitioned between CH_2Cl_2 and H_2O, and the organic layer was filtered through a pad of $MgSO_4$/Na_2SO_4 to afford the product (48 mg, 95%) as a colorless oil. $[a]_D^{25}$ = +101.9 (c = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.61–2.10 (br. m, 3 H), 0.78 (d, J = 6.1 Hz, 3 H), 1.01 (d, J = 6.0 Hz, 3 H), 3.97 (sept, J = 6.0 Hz, 1 H), 6.05–6.15 (m, 1 H), 6.79–6.89 (m, 1 H), 7.02–7.54 (m, 16 H), 7.55–7.70 (m, 2 H), 7.73–7.84 (m, 2 H), 8.49–8.63 (m, 1 H) ppm. ^{13}C NMR: δ = 20.3, 21.6, 68.6, 110.6 (d, J = 6 Hz), 119.1 (d, J = 10 Hz), 127.3–128.3 (m), 129.3–132.2 (m), 134.1 (d, J = 9 Hz), 135.0 (dd, J = 14, 7 Hz), 135.5–135.6 (m), 138.4 (dd, J = 19, 10 Hz), 158.2 (d, J = 4 Hz) ppm. ^{31}P NMR: δ = 26.0 (m), 29.7 (d, J = 5.4 Hz) ppm.

Preparation of [Rh(L)(MeOH)$_2$]BF_4 Solvate: To a solution of bis(2,5-norbornadiene)rhodium tetrafluoroborate {[Rh(nbd)$_2$]BF_4} (9.3 mg, 0.025 mmol) in MeOH (0.5 mL), a solution of ligand **L** (0.025 mmol, 1 equiv. to Rh atom) in MeOH (0.5 mL) was added dropwise at room temp. The mixture was hydrogenated at 1 atm H_2 for 30 min, and this amount was equally divided for five hydrogenation tests. The same procedure was followed for the preparation of Rh^I complexes of (S_P,S_P)-1,2-bis[(methyl)(phenyl)phosphino] ethane and (S_P,S_P)-1,2-bis[(1-naphthyl)(phenyl)phosphino]ethane.

Procedure for Hydrogenation Tests (S/C 100): To a solution of the substrate (0.5 mmol) in MeOH (7.5 mL), three freeze-pump-thaw cycles were applied and the system was filled with argon. To the substrate solution was added under argon a solution of the above preformed [Rh(**L**)(MeOH)$_2$]BF_4 solvate (0.2 mL, 0.005 mmol). A vacuum was applied to this system then it was backfilled with H_2. The mixture was stirred at room temp. and H_2 pressure as indicated. Progress of the hydrogenation was monitored by the diminution of the volume of the closed reaction system at 1 bar (until H_2 uptake ceased and the color of the solution changed); for reactions at 10 bar, analyses were carried out after 16 h. The reaction mixture was analyzed by chiral GC and the absolute configuration was assigned by comparison with the reported data of t_R.[6] The following hydrogenation products with the mentioned absolute configurations were obtained by using (R_P)-**L3** or **L4** (Table 1).

(*S*)-*N*-Acetyl-alanine Methyl Ester: ^{1}H NMR: δ = 1.41 (d, J = 7 Hz, 3 H), 2.02 (s, 3 H), 3.76 (s, 3 H), 4.60 (m, 1 H), 6.26 (br. s, 1 H) ppm. GC (Lipodex-E; 25m × 0.25 mm; 120 °C): t_R = 8.2 (*S*), 9.2 (*R*) min.

(*S*)-*N*-Acetyl-phenylalanine Methyl Ester: ^{1}H NMR: δ = 1.99 (s, 3 H), 3.13 (m, 2 H), 3.73 (s, 3 H), 4.90 (dt, J = 6, 8 Hz, 1 H), 5.90 (br. d, J = 6 Hz, 1 H), 7.09 (m, 2 H), 7.28 (m, 3 H) ppm. GC (Chiralsil-L-Val; 25m × 0.25 mm; 160 °C): t_R = 4.7 (*R*), 4.9 (*S*) min.

Dimethyl (*R*)-2-Methylsuccinate: ^{1}H NMR: δ = 1.23 (d, J = 7 Hz, 3 H), 2.42 (dd, J = 6, 16 Hz, 1 H), 2.75 (dd, J = 8, 16 Hz, 1 H), 2.93 (m, 1 H), 3.68 (s, 3 H), 3.70 (s, 3 H) ppm. GC (Lipodex-E; 25m × 0.25 mm; 80 °C): t_R = 8.6 (*S*), 9.0 (*R*) min.

(*S*)-*N*-Acetyl-(1-phenylethyl)amine: ^{1}H NMR: δ = 1.48 (d, J = 6.9 Hz, 3 H), 1.97 (s, 3 H), 5.12 (m, 1 H), 5.84 (br. s, 1 H), 7.22–7.39 (m, 5 H) ppm. GC (CP-Chiralsil-DEX CB; 25m × 0.25 mm; 140 °C): t_R = 10.6 (*S*), 11.7 (*R*) min.

(*S*)-2-Phenylpropionic Acid: ^{1}H NMR: δ = 1.52 (d, J = 7 Hz, 3 H), 3.74 (q, J = 7 Hz, 1 H), 7.31 (m, 5 H) ppm. GC analysis after esterification with $TMSCHN_2$ (CP-Chiralsil-DEX CB; 25m × 0.25 mm; 90 °C): t_R = 19.7 (*S*), 20.5 (*R*) min.

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[11] Obtaining **2**-*P′*(BH_3) as fine needles was favorable for its enantioenrichment, but the crystals were unfortunately unsuitable for X-ray diffraction analysis.

[12] We assume full retention of *P*-configuration in the decomplexation step with Et_2NH by analogy to reported related compounds such as the mono-BH_3-protected (R_P,R_P)-DioxyBenzP*·BH_3.[3j] Furthermore, decomplexation of *P*-stereogenic phosphine-*P*-boranes occurs with full retention of *P*-configuration, see: T. Imamoto, T. Kusumoto, N. Suzuki, K. Sato, *J. Am. Chem. Soc.* **1985**, *107*, 5301–5303.

[13] For the synthesis of Me-DuPHOS-*P*(BH_3),*P′*(O), see: A. A. Boezio, J. Pytkowicz, A. Côté, A. B. Charette, *J. Am. Chem. Soc.* **2003**, *125*, 14260–14261.

[14] Methanolysis attempt with (S_P)-**1**-*P′*(O) (prepared as shown in Scheme 2) led to acidolysis compounds [*o*-(diphenylphosphoryl)phenyl](hydroxy)(phenyl)phosphine-*P*-borane and [*o*-(diphenylphosphoryl)phenyl](phenyl)phosphine *P*-oxide (probably resulting from slow BH_3 loss of the latter) according to ^{31}P NMR analysis of the crude reaction mixture before workup (products not isolated).

[15] Rh^I[(R_P,R_P)-diphosphine] hydrogenation (1 bar H_2, MeOH, room temp., S/C = 100) of MAC and AS afforded (*S*)-products. With DiPAMP: 95%*ee* within 18 min and 84%*ee* within 11 min, respectively; with *i*Pr-SMS-Phos: 99.7%*ee* within 4 min and 97.8%*ee* within 3 min, respectively; and with *t*Bu-SMS-Phos: 99.8%*ee* within 2 min and 99.4%*ee* within 2 min, respectively.[3b,3c,6a]

[16] MAC was hydrogenated (1 atm H_2, EtOH, 20 °C, S/C = 100) in 51%*ee* (*S*) with Rh^I-{(S_P,S_P)-1,2-bis[(methyl)phenylphosphino]-benzene}. For this, see: D. G. Allen, S. B. Wild, D. L. Wood, *Organometallics* **1986**, *5*, 1009–1015.

[17] a) For this work, we have prepared (S_P,S_P)-1,2-bis[(methyl)-(phenyl)phosphino]ethane by following ref.[17b] and tested it in Rh^I-catalyzed hydrogenation (1 bar H_2, MeOH, room temp., S/C = 100) of MAC (15 min, 100% conv., 17%*ee* (*R*)), AS (20 min, 100% conv., 61%*ee* (*R*)), and DMI (20 min, 100% conv., 23%*ee* (*S*)). (S_P,S_P)-1,2-Bis[(methyl)(phenyl)phosphino]-ethane was prepared but not evaluated in catalysis; for this, see: b) F. Chaux, S. Frynas, H. Laureano, C. Salomon, G. Morata, M. L. Auclair, M. Stephan, R. Merdes, P. Richard, M. J. Ondel-Eymin, J. C. Henry, J. Bayardon, C. Darcel, S. Jugé, *C. R. Chim.* **2010**, *13*, 1213–1226; c) A. R. Muci, K. R. Campos, D. A. Evans, *J. Am. Chem. Soc.* **1995**, *117*, 9075–9076; therein it is claimed that (S_P,S_P)-1,2-bis[(aryl)(methyl)phosphino]ethanes wherein aryl = Ph, *o*-An, *o*-Tol, or α-Nap, were found to be configurationally unstable in $CDCl_3$, which was not the case in our hands for aryl = Ph.

[18] N. Oohara, K. Katagiri, T. Imamoto, *Tetrahedron: Asymmetry* **2003**, *14*, 2171–2175.

[19] F. Maienza, F. Spindler, M. Thommen, B. Pugin, C. Malan, A. Mezzetti, *J. Org. Chem.* **2002**, *67*, 5239–5249.

[20] a) B. Zupančič, B. Mohar, M. Stephan, *Adv. Synth. Catal.* **2008**, *350*, 2024–2032; therein, MAC was hydrogenated (1 bar H_2, MeOH, room temp., S/C = 100) within 3–4 min, leading to 97/99%*ee* (*S*) using (R_P,R_P)-1,2-bis[(aryl)(phenyl)phosphino]ethanes (ex. aryl = 2,3-$(MeO)_2$-Ph and 2,3,4,5-$(MeO)_4$-Ph); b) B. Zupančič, B. Mohar, M. Stephan, *Tetrahedron Lett.* **2009**, *50*, 7382–7384; therein, AS was hydrogenated (1 bar H_2, MeOH, room temp., S/C = 100) within 4 min leading to 71/87%*ee* (*S*) using (R_P,R_P)-1,2-bis[(aryl)(phenyl)phosphino]ethanes (ex. aryl = 2,3-$(MeO)_2$-Ph and 2,3,4,5-$(MeO)_4$-Ph); c) Using the *P*-(*o*-unsubstituted MeO-aryl)-containing (R_P,R_P)-1,2-bis[(MeO-aryl)(phenyl)phosphino]ethanes, wherein MeO-aryl is 3-MeO-Ph, 4-MeO-Ph, 3,4-$(MeO)_2$-Ph, and 3,5-$(MeO)_2$-Ph, Rh^I-catalyzed hydrogenation (1 bar H_2, MeOH, room temp., S/C = 100) led respectively to 6, 17, 25, and 12%*ee* (*S*) for MAC (100% conv. within <10 min), and to 1, 15, 27, and 5%*ee* (*S*) for AS[20b] (100% conv. within <10 min). For the former set, see: B. Zupančič, PhD Thesis **2011**, University of Ljubljana, Slovenia.

[21] a) For this work, we have tested (S_P,S_P)-1,2-bis[(1-naphthyl)(phenyl)phosphino]ethane ($[a]_D^{22}$ = –19 (*c* = 1, $CHCl_3$), >99%*ee*, 95% purity, purchased from Sigma–Aldrich Co.) in Rh^I-catalyzed hydrogenation (1 bar H_2, MeOH, room temp., S/C = 100) of MAC [1.5 h, 100% conv., >99%*ee* ((*R*)-configuration with measured $[a]_D^{22}$ = –15.6 (*c* = 1.0, abs. MeOH))], AS (2.4 h, 100% conv., 68%*ee* (*R*)), DMI (2.3 h, 100% conv., 40%*ee* (*S*)), and AA (10 bar H_2 in the presence of 1.1 equiv. Cy_2NH; 16 h, 100% conv., 20%*ee* (*R*)). Thus, in light of these results, it is clear that the reported[19] MAC hydrogenation using Rh^I-{(S_P,S_P)-1,2-bis[(1-naphthyl)(phenyl)phosphino]ethane} (1.1 bar H_2, MeOH, 25 °C) in 98.6%*ee* (*S*), and the authors advising to apply the "quadrant rule" with caution, no longer hold for this ligand. Moreover, and in line with our findings, MAC was hydrogenated (3 atm H_2, *i*PrOH, 50 °C) in 92 to >99%*ee* (*R*) by using the closely related Rh^I-{(S_P,S_P)-1,2-bis[(aryl)(phenyl)phosphino]ethane} catalysts, wherein aryl = *o*-Tol, *o*-Et-Ph, *o*-*i*Pr-Ph, or 5,6,7,8-tetrahydronaphth-1-yl; for this, see: b) Y. Wada, T. Imamoto, H. Tsuruta, K. Yamaguchi, I. D. Gridnev, *Adv. Synth. Catal.* **2004**, *346*, 777–788; Rh^I-catalyzed hydrogenation (3 atm H_2, *i*PrOH, 50 °C) of α-acetamidocinnamic acid (ACA) using (R_P,R_P)-1,2-bis[(*o*-An)(Cy)-phosphino]ethane (DiCAMP) led to 64%*ee* (*S*), (R_P,R_P)-1,2-bis[(*o*-F-Ph)(Ph)phosphino]ethane to 60%*ee* (*S*), and (R_P,R_P)-1,2-bis[(*o*-An)(Et)phosphino]ethane to 60%*ee* (*S*). For this, see: c) W. S. Knowles, W. C. Christopfel, K. E. Koenig, C. F. Hobbs, *Adv. Chem., Ser.* **1982**, 325–336.

[22] In ref.[4n] the catalysts were formed in situ from [Rh(cod or nbd)(diphosphine)]BF_4 in the presence of AS during hydrogenation (5 bar H_2, 3 h), hence the induction period toward the formation of the active species was not eliminated. We learned

from the corresponding author that the H_2 uptake plots vs. time actually correspond to different reaction scales and that the H_2 uptake values derive from pressure variation taking into account H_2 solubility. The slopes of the plots indicate a 10:2:1 hydrogenation rate ratio for the Rh^I-catalysts of Me-UCAP-Ph, 1,2-bis(diphenylphosphino)benzene, and Me-DuPHOS, respectively.

[23] a) C. R. Landis, J. Halpern, *J. Am. Chem. Soc.* **1987**, *109*, 1746–1754; b) B. Mcculloch, J. Halpern, M. R. Thompson, C. R. Landis, *Organometallics* **1990**, *9*, 1392–1395; c) J. S. Giovannetti, C. M. Kelly, C. R. Landis, *J. Am. Chem. Soc.* **1993**, *115*, 4040–4057; d) S. Feldgus, C. R. Landis, *Organometallics* **2001**, *20*, 2374–2386; e) A. Ohashi, *Chirality* **2002**, *14*, 573–577; f) T. Schmidt, W. Baumann, H. J. Drexler, A. Arrieta, D. Heller, H. Buschmann, *Organometallics* **2005**, *24*, 3842–3848; g) P. J. Donoghue, P. Helquist, O. Wiest, *J. Org. Chem.* **2007**, *72*, 839–847; h) T. Schmidt, Z. Dai, H. J. Drexler, M. Hapke, A. Preetz, D. Heller, *Chem. Asian J.* **2008**, *3*, 1170–1180; i) I. D. Gridnev, T. Imamoto, G. Hoge, M. Kouchi, H. Takahashi, *J. Am. Chem. Soc.* **2008**, *130*, 2560–2572; j) I. D. Gridnev, T. Imamoto, *Chem. Commun.* **2009**, 7447–7464; k) P. J. Donoghue, P. Helquist, P. O. Norrby, O. Wiest, *J. Am. Chem. Soc.* **2009**, *131*, 410–411. For studies related to electronic effects, see: l) D. Z. Wang, *Tetrahedron* **2005**, *61*, 7125–7133; m) H. C. Wu, S. A. Hamid, J. Q. Yu, J. B. Spencer, *J. Am. Chem. Soc.* **2009**, *131*, 9604–9605; n) S. Giri, D. Z. Wang, P. K. Chattaraj, *Tetrahedron* **2010**, *66*, 4560–4563. For a study of enantioselectivity and hydrogenation rate vs. conformation of five-membered chelate rings of [Rh(PP)(diene)]$^+$-type, wherein PP is a stereogenic DPPE-derived ligand with chirality on the ethylene bridge, see ref.[4l]

[24] For example, the extent and sense of enantioselection in α-substituted acetamidoethylenes hydrogenation has been shown to be quite sensitive to the nature of the α-substituent influencing the substrate orientation.[3e,23d,23g,23j]

[25] Knowles early empirical "quadrant rule"[1] predicts, in many cases, and for α-amido acids/esters in particular, the sense of the product enantioselectivity in relation to the C_2-symmetric *P*-stereogenic diphosphine chirality. It states that (*S*)-α-amino acid derivatives are obtained by using (R_P,R_P)-diphosphines and vice versa (note that the α-substituent of the resulting amido acid/ester should have the 3rd CIP priority number). This is valid for *P*-stereogenic 1,2-bis[(Ar)(Ph)phosphino]ethanes such as DiPAMP, R-SMS-Phos, and 1,2-bis[(*o*-alkyl-Ph)(Ph)phosphino]ethanes.

[26] Imamoto and Gridnev[21b] reformulated Knowles "quadrant rule" in order to fit the selectivity observed with the new introduced *P*-stereogenic ligands: (1) the bulky *P*,*P*′-substituents in the top-left and bottom-right quadrants give (*R*)-hydrogenation products and the opposite orientation gives (*S*); (2) if the *P*,*P*′-substituents are the same or very similar in size, more steric hindrance is given by the *quasi*-axial substituents: viz. (*R*)-α-amino acid derivatives are obtained using (S_P,S_P)-1,2-bis[(bulky alkyl)(Me)phosphino]ethanes (e.g., *t*Bu-BisP*) and (R_P,R_P)-1,2-bis[(bulky alkyl)(Me)phosphino]methanes (e.g., *t*Bu-MiniPHOS). For this, see also: D. Gridnev, N. Higashi, K. Asakura, T. Imamoto, *J. Am. Chem. Soc.* **2000**, *122*, 7183–7194.

[27] Interestingly, a reverse in induction in Rh^I-[(S_P)-(1-Ad)(Me)-$PCH_2CH_2PR_2$] MAC and *o*-MeO-AS hydrogenations occurred upon swapping R = Cy (or Me) with R = Ph (Figure 4).[4g] This demonstrates that Ph_2P and $(alkyl)_2P$ have different effects on the mechanism.

[28] The more rigid *i*Pr-SMS-Phos was shown to be less sensitive to H_2 pressure than DiPAMP.[3c]

[29] Some supporting information (spectra and other proofs) related to the study in ref.[4j] is unfortunately lacking and no archives were kept as we learned from the corresponding author.

[30] ^{31}P NMR analysis at room temperature of {Rh[(R_P)-**L2**](MAC)}BF_4 showed four diastereomeric adducts in ca. 50:25:20:5 ratio (see the Supporting Information, Figure S2).

[31] X-ray spectroscopic analysis of {Pt[(*R*,*R*)-Me-UCAP-Ph]-Cl_2}[4n] revealed two molecules in the unit cell, wherein in one the two phenyls have an edge-face disposition[32] and a face-edge disposition in the second, however X-ray analysis of {Pt[(*R*,*R*)-1-(2,5-diMe-phospholano)-2-diphenylphosphino-ethane]Cl_2}[4o] revealed the two phenyls to be in an edge-face disposition (starting from the Me-blocked quadrant). Furthermore, X-ray analysis of *cis*-{Pd[(S_P)-**L1**][(*S*)-*o*-(1-(dimethylamino)ethyl)phenyl]}PF_6[7] revealed the three phenyls in an edge-edge-face arrangement (from below the *P*-Me quadrant). Unfortunately, the X-ray analysis of *cis*-{Pd[(S_P)-(*o*-An)(Ph)-$CH_2CH_2PPh_2$][(*R*)-1-(1-(dimethylamino)ethyl)-2-naphthyl]}-BF_4[4i] is poorly characterized and its cif is lacking. Independently, a C_2-symmetric diarsine complex {Pd[(R_{As},R_{As})-1,2-bis-[(methyl)(phenyl)arsino]benzene][(*S*)-*o*-(1-(dimethylamino)ethyl)phenyl]}PF_6 revealed the two phenyls to have edge dispositions. For this, see: B. W. Skelton, A. H. White, *J. Chem. Soc., Dalton Trans.* **1980**, 1556–1566.

[32] For *P*-aryl edge/face-exposed determination in metal complexes, see: a) H. Brunner, A. Winter, J. Breu, *J. Organomet. Chem.* **1998**, *553*, 285–306; b) J. M. Brown, P. L. Evans, *Tetrahedron* **1988**, *44*, 4905–4916.

[33] H. J. Drexler, S. L. Zhang, A. L. Sun, A. Spannenberg, A. Arrieta, A. Preetz, D. Heller, *Tetrahedron: Asymmetry* **2004**, *15*, 2139–2150.

[34] D. Quintard, M. Keller, B. Breit, *Synthesis* **2004**, 905–908.

[35] a) J. T. Reeves, Z. L. Tan, Z. X. S. Han, G. S. Li, Y. D. Zhang, Y. B. Xu, D. C. Reeves, N. C. Gonnella, S. L. Ma, H. Lee, B. Z. Lu, C. H. Senanayake, *Angew. Chem. Int. Ed.* **2012**, *51*, 1400–1404; b) M. J. Burk, G. Casy, N. B. Johnson, *J. Org. Chem.* **1998**, *63*, 6084–6085.

[36] CCDC-1034830 [for (R_P)-**1**], -1034831 [for (R_P)-**L2**], and -1034832 [for (S_P)-**2**-*P*′(O)] 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.

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