New Monodentate P,C-Stereogenic Bicyclic Phosphanes: 1-Phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole and 1-Phenyl-octahydrocyclopenta[*b*]phosphole

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Racemic 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]-phosphole (**4**) was separated into enantiomerically pure 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-oxides [(R_P)-**6** and (S_P)-**6**] by an oxidative resolution procedure involving treatment of **4** with menthyl bromoacetate, crystallization of the resulting diastereoisomeric phosphonium bromides **8**, and stereoselective hydrolysis of the diastereomerically pure salts to the corresponding enantiomerically pure phosphane oxides. Stereoretentive reduction of P=O in (R_P)-**6** gave enantiomerically pure (S_P)-**4**. Hydrogenation of (S_P)-**6** and subsequent reduction of P=O afforded saturated 1-phenyloctahydrocyclopenta[*b*]phosphole [(R_P)-**5**]. Monophosphanes (S_P)-**4** and (R_P)-**5** were tested as chiral ligands and catalysts in model asymmetric hydrogenation and C–C bond-forming reactions. Enantioselectivities of up to 95% were observed.

Introduction

Phosphanes are well known as most powerful and versatile ligands for use in catalysis involving transition metals.[1] Recently, monophosphanes with rigid bicyclic structures containing the phosphorus atom embedded in a five-membered ring (e.g., **1**–**3**) have been identified as both highly efficient chiral ligands and excellent chiral catalysts (Figure 1).[2–4]

In this paper we wish to demonstrate that the bicyclic P,C-stereogenic monophosphanes 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole [(S_P)-**4**][5] and 1-phenyl-octahydrocyclopenta[*b*]phosphole [(R_P)-**5**] can be readily obtained in the enantiomerically pure state by an efficient oxidative resolution procedure utilizing menthyl bromoacetates as resolving agents. The use of enantiopure monophosphanes (S_P)-**4** and (R_P)-**5** as ligands and catalysts in model asymmetric C–C bond-formation and hydrogenation processes is also reported.

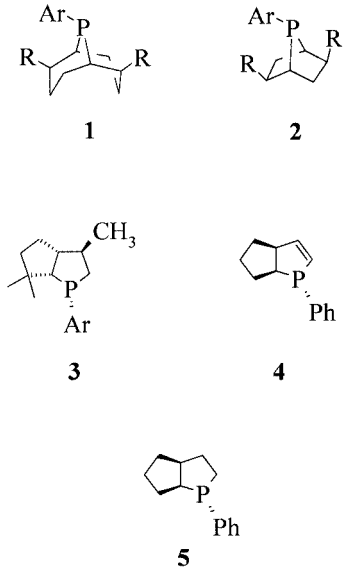

Figure 1. Selected chiral phosphanes

Results and Discussion

Racemic 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[-*b*]phosphole 1-oxide (**6**) was synthesized by a single-step cyclopentannulation route[5,6] involving deprotonation of 1-phenyl-2,5-dihydro-1*H*-phosphole 1-oxide (2.1 equiv. of LDA, −78 °C) and treatment of the resulting anionic intermediate with 1,3-diiodopropane. The annulation reaction

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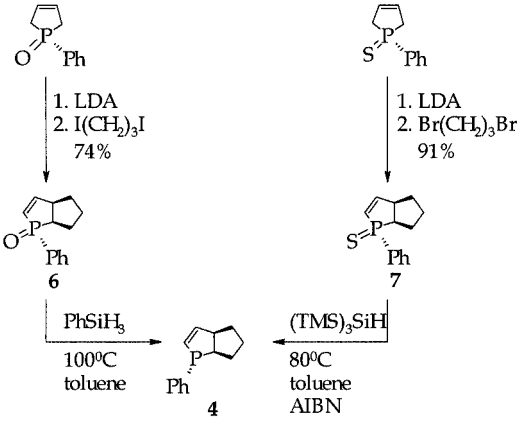
was found to be extremely difficult to scale up because of a strong exothermic effect, which caused dramatic decreases in the yields (74% on a 1 mmol scale, 47% on a 5 mmol scale, and only 15−20% on a 10 mmol scale). The analogous annulation with 1-phenyl-2,5-dihydro-1*H*-phosphole 1-sulfide proved to be less exothermic and afforded the expected 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-sulfide (**7**) in very high yield irrespective of the reaction scale used (91% yield for a 10 mmol scale).[5,6] Reduction of **6** with phenylsilane[7] and radical-based reduction of **7** with tris(trimethylsilyl)silane[8] gave 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole (**4**) quantitatively and with complete retention of configuration at P (Scheme 1).[5,7,8]



Scheme 1. Synthesis of racemic 1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole (**4**)

Separation of **4** into its enantiomers was achieved by an oxidative resolution route,[9] as shown in Scheme 2. Addition of an ethyl acetate solution of racemic **4** to a solution of (−)-menthyl bromoacetate in ethyl acetate afforded crystalline phosphonium bromides in a 1:1 ratio. The crystals obtained were recrystallized twice from ethyl acetate/benzene/ethyl alcohol (20:1:1) to give one of the two epimeric phosphonium salts **8** in the form of a single diastereoisomer **8a** (29%). Hydrolysis of **8a** yielded virtually enantiomerically pure (R_P)-**6** (25% based on starting racemic **3**, >98% *ee*[10]). The collected filtrates enriched in the second P-epimer of **8** were evaporated and hydrolyzed to furnish the enantiomerically enriched oxide **6** (40% *ee*). Reduction of this oxide with phenylsilane and repetition of the above resolution procedure, but now with (+)-menthyl bromoacetate, gave (S_P)-**6** (37% based on starting racemic **6**, >98% *ee*[10]). The configuration of the intermediate diastereomerically pure phosphonium bromide **8a′** was established by X-ray crystallographic analysis (Figure 2).

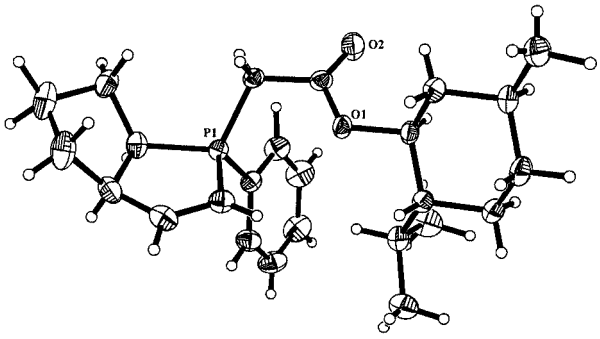
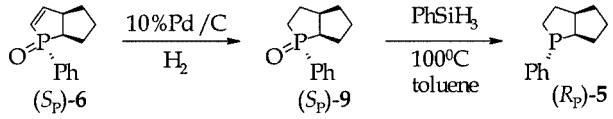


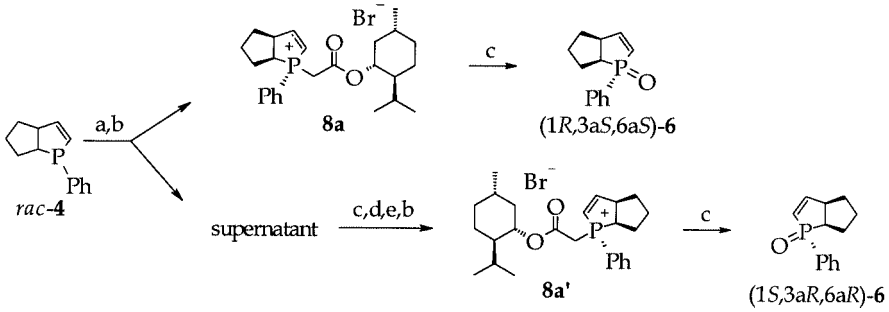
Figure 2. ORTEP drawing of salt **8a′**

Hydrogenation of (S_P)-**6** on 10% Pd / C afforded saturated 1-phenyloctahydrocyclopenta[*b*]phosphole 1-oxide [(S_P)-**9**, 92%], which, after reduction with phenylsilane, cleanly gave (R_P)-**5** (98%, Scheme 3). As we have found before,[5] the reduction proceeded with complete retention.



Scheme 3. Synthesis of (R_P)-**5**

The optical activities of the resolved compounds **6** and **9** were examined by circular dichroism (CD) spectroscopy. As can be seen in Figure 3, the CD spectra of compounds (1*R*,3a*S*,6a*S*)-**6** and (1*S*,3a*R*,6a*R*)-**6** have a perfect mirror-image relationship, as expected for enantiomers. In the case of compound (1*S*,3a*R*,6a*R*)-**9**, however, the expected CD bands could not be detected. This observation seems to indicate that the inclusion of the ring double bond in the chromophoric system in the 2,3-dihydro-1*H*-phosphole systems is of key importance. In corroboration of this, a nearly



Scheme 2. Oxidative resolution of *rac*-**4**; (a) (−)-menthyl bromoacetate, (b) double crystallization, (c) 10% aq NaOH, CH_2Cl_2, (d) $PhSiH_3$, toluene, 100 °C, (e) (+)-menthyl bromoacetate

ninefold decrease in the specific rotation value of the saturated **9** relative to the unsaturated **6** was observed. Further studies to explain this phenomenon are in progress in our laboratory.

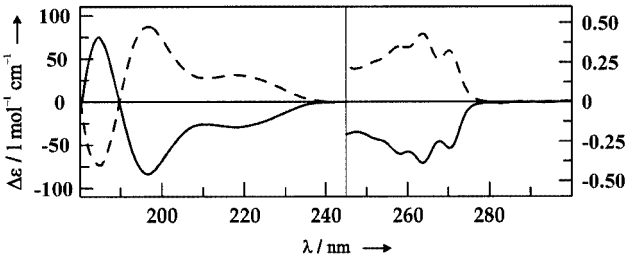
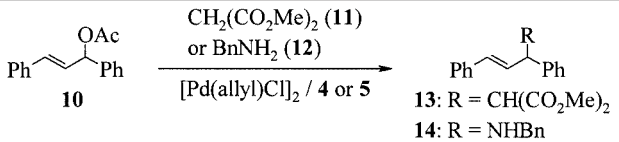


Figure 3. CD spectra of (R_P)-**6** (dashed) and (S_P)-**6** (solid) in acetonitrile solution

The enantiopure P,C-stereogenic phosphanes (S_P)-**4** and (R_P)-**5** were tested as chiral catalysts and ligands in a series of model asymmetric reactions known to be efficiently catalyzed by monophosphanes or their organometallic complexes. Firstly, we tested the Pd-catalyzed allylic substitution reaction[11] (Table 1). Treatment of (*E*)-1,3-diphenylallyl acetate (**10**) with dimethyl malonate (**11**) in the presence of (S_P)-**4** or (R_P)-**5** and [Pd(allyl)Cl]$_2$ as catalyst precursor gave the allylated malonate **13**[12] (20% *ee* with **4** and 31% *ee* with **5**). The same procedure with benzylamine (**12**) as nucleophile gave the allylamine derivative **14**[13] in 86% yield, but with only 15% *ee*. However, an analogous reaction with cyclopentenyl carbonate **15**[14] as substrate and phthalimide (**16**) as nucleophile (Table 2) afforded the cyclopentenylamine derivative **17** in excellent chemical yield (96%) and with very high enantioselectivity (95% *ee*).

The last result underlines the potential effectiveness of P-stereogenic bicyclic monophosphane ligands in the asymmetric allylic substitution of cyclic carbonates and constitutes a good lead for further developments of ligands containing 2-phosphabicyclo[3.3.0]octane skeletons.

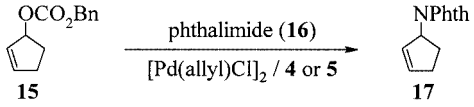
Table 1. Palladium-catalyzed allylic substitution



Entry	Starting materials	Solvent	Ligand[a] (mol %)	Product	Yield (%)	*ee* (%)
1	**10** + **11**	CH_2Cl_2	**4** (10)	**13**	86	13[b]
2	**10** + **11**	toluene	**4** (12.5)[c]	**13**	52	18[b]
3	**10** + **11**	THF	**4** (12.5)	**13**	46	20[b]
4	**10** + **11**	THF	**5** (12.5)	**13**	86	31[b]
5	**10** + **12**	THF	**5** (10)	**14**	86	15[d]

[a] [Pd(allyl)Cl]$_2$ was used as catalyst precursor (1.25 mol %); [b] % *ee* was measured by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_2$ shift reagent; [c] A solution of KCl (30 mol %) and 18-c-6 (20 mol %) in toluene was added; [d] % *ee* was measured by HPLC with Chiralcel OD-R column (methanol, water −8:2).

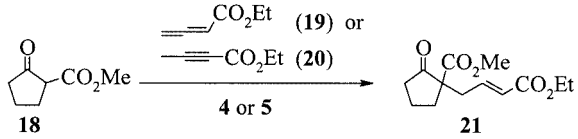
Table 2. Palladium-catalyzed allylic substitution



Entry	Starting materials	Solvent	Ligand[a] (mol %)	Product	Yield (%)	*ee* (%)[b]
1	**15** + **16**	CH_2Cl_2/THF	**4** (5)	**17**	96	95
2	**15** + **16**	CH_2Cl_2	**4** (5)	**17**	83	69
3	**15** + **16**	CH_2Cl_2/THF	**5** (5)	**17**	96	56

[a] [Pd(allyl)Cl]$_2$ was used as catalyst precursor (0.5 mol %). [b] % *ee* was determined by comparing the optical rotation with literature value.[15]

Table 3. C−C bond formation (24 h, room temp., benzene)



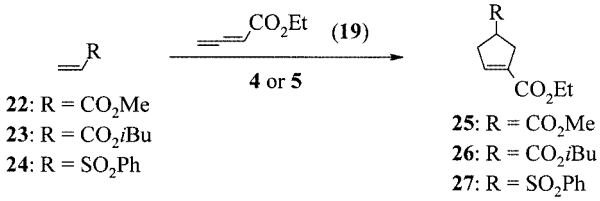
Entry	Starting materials	Product	Cat. (10 mol %)[a]	Yield (%)	*ee* (%)
1	**18** + **19**	**21**	**4**	63	51[b]
2	**18** + **19**	**21**	**5**	67	48[b]
3	**18** + **20**	**21**	**4**	64[c]	29[b]

[a] The reaction was carried out under Ar with chiral phosphane (10 mol %), **19** or **20** (100 mol %), **18** (100 mol %), NaOAc (50 mol %), and AcOH (50 mol %).[3c] [b] % *ee*s were measured by GC with γ-Dex 225 column.[3c] [c] 24 h, 80 °C.

We also tested phosphane-catalyzed C−C bond formation in reactions between 2-butynoates and malonate-type nucleophiles (Table 3).[3c,16] Activation of ethyl 2,3-butadienoate (**19**) with chiral phosphane (S_P)-**4** or (R_P)-**5**, followed by addition of the active intermediate[16,17] to 2-methoxycarbonyl cyclopentanone (**18**), gave the known optically active adduct **21** in 48−51% *ee*s depending on the phosphane used (Table 3, Entries 1,2). Similar transformations utilizing ethyl 2-butynoate (**20**) as substrate required higher reaction temperatures and gave significantly lower enantioselectivities (Table 3, Entry 3).

The catalytic activity of phosphanes (S_P)-**4** and (R_P)-**5** was also screened in [3+2] cycloadditions between ethyl 2,3-butadienoate (**19**) and selected olefins to afford functionalized cyclopentenes.[3b,17,18] The tested olefins included methyl acrylate and isobutyl acrylate as described in the original paper,[3b] and phenyl vinyl sulfone was also used as a new substrate. With these three substrates only moderate enantioselectivities (up to 33% *ee*) were observed (Table 4). Apparently, the size of the ester group in the electron-deficient olefins did not affect the enantioselectivity.[3b] In terms of regioselectivity, phosphane **5** was found to be more selective than **4** as it favored the formation only of the 1,4-substituted cyclopentene, whereas in the presence of **4** small

Table 4. C−C Bond formation (24 h, room temp., benzene)



22: R = CO_2Me
23: R = CO_2iBu
24: R = SO_2Ph

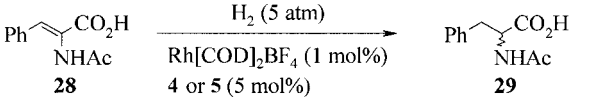
25: R = CO_2Me
26: R = CO_2iBu
27: R = SO_2Ph

Entry	Starting materials	Cat. (10 mol %)[a]	Product	Yield (%)[b]	*ee* (%)
1	**19** + **22**	**4**	**25**	42[c]	21[d]
6	**19** + **22**	**5**	**25**	62	26[d]
5	**19** + **23**	**4**	**26**	46[e]	0[f]
4	**19** + **23**	**5**	**26**	63	14[f]
5	**19** + **24**	**4**	**27**	46	29[g]
6	**19** + **24**	**5**	**27**	71	33[g][h]

[a] The reaction was carried out under Ar with chiral phosphane (10 mol %), **19** (100 mol %) and electron-deficient olefins (1000 mol %).[3b] [b] 1,4 vs. 1,5 substitution was assigned by ^1H NMR spectroscopy. [c] 6% of the 1,5-isomer was also isolated. [d] % *ee* values were measured by GC on a γ-Dex 225 column.[3b] [e] 18% of the 1,5-isomer was also isolated. [f] % *ee* values were measured by HPLC on a Chiralcel OD-H column (hexane, isopropyl alcohol 99:1). [g] % *ee* values were measured by HPLC on a Chiralcel OD-H column (hexane, isopropyl alcohol 8:2). [h] $[\alpha]_D^{20} = -2.4$ (c = 0.8, chloroform).

amounts of 1,5-substituted isomers were always detected (6−18%). For phenyl vinyl sulfone the formation of only 1,4-substituted product was observed regardless of the phosphane used.

Recently, monophosphanes have also been found to be efficient ligands for Rh-, Ru-, and Ir-catalyzed asymmetric hydrogenation, although high *ee*s of the hydrogenated products are still rarely achieved.[19,20] Rhodium-catalyzed asymmetric hydrogenation of (*Z*)-*N*-acetylaminocinnamic acid (**28**) in the presence of (S_P)-**4** and $Rh[COD]_2BF_4$ as catalyst precursor gave *N*-acetylphenylalanine (**29**) with only 10% *ee* (Scheme 4). The same reaction in the presence of (R_P)-**5**, however, afforded the product with 62% *ee*. In both cases quantitative conversion of the starting material took place (Scheme 4).



ligand **4**: 10% *ee*
ligand **5**: 62% *ee*

Scheme 4. Hydrogenation of **28** in the presence of $Rh[COD]_2BF_4$ and **4** or **5** (MeOH/THF, 24 h, room temp.)

Conclusions

In summary, we have demonstrated that the readily available enantiomerically pure bicyclic phosphanes (S_P)-**4** and (R_P)-**5** are efficient catalysts and ligands for asymmetric C−C bond-forming and hydrogenation reactions.

The asymmetric induction at the level of 96% *ee* achieved in the studied Pd-catalyzed allylic substitution reaction of a cyclic carbonate points to potential usefulness of the bicyclo[3.3.0]octane structural motif in ligand design.

Experimental Section

The solvents were purified and dried by literature methods. All reactions were performed under Ar. TLC was performed on silica gel (HF-254) and column chromatography on silica gel (230−400 mesh, Merck). NMR spectra were recorded with a Varian Mercury 400BB instrument at 400 MHz (for ^1H) or 100 MHz (for ^{13}C) and a Bruker AM 500 spectrometer at 500 MHz (for ^1H) or 125 MHz (for ^{13}C) in deuteriochloroform ($CDCl_3$) or deuteriobenzene (C_6D_6) with Me_4Si as internal standard. CD spectra were measured on a JASCO 715 spectropolarimeter in acetonitrile. High-resolution mass spectra (HR-MS) were measured with AMD-604 and MARINER mass spectrometers. Optical rotations were measured with a JASCO DIP-360 automatic polarimeter.

1-Phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-Oxide (6): A solution of 1-phenyl-2,5-dihydro-1*H*-phosphole 1-oxide (178 mg, 1.0 mmol) in THF (2 mL) was added at −78 °C to a solution of freshly prepared LDA (2.1 mmol) in THF (6 mL). The resulting deep red solution was stirred at −78 °C for 10 min, and a solution of 1,3-diiodopropane (235 mg, 1.1 mmol) in THF (2 mL) was then added in one portion. Stirring at −78 °C was continued for 1 h and the reaction mixture was quenched by addition of a few drops of water at −78 °C and then allowed to come to room temperature. Solvents were evaporated. Column chromatography of the residue (hexane/ethyl acetate/methanol, 5:3:1 as eluent) gave pure **6** (161 mg, 74%). HR-MS(EI) calcd. for $C_{13}H_{15}PO$ $[M]^+$: 218.0860; found 218.0857.

1-Phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-Sulfide (7): A solution of 1-phenyl-2,5-dihydro-1*H*-phosphole 1-sulfide (1.94 mg, 10.0 mmol) was added at −78 °C to a solution of freshly prepared LDA (30 mmol) in THF (170 mL). The resulting red solution was stirred at −78 °C for 10 min, and a solution of 1,3-dibromopropane (2.12 g, 10.5 mmol) in THF (5 mL) was then added in one portion. Stirring at −78 °C was continued for 1 h, and the reaction mixture was quenched by addition of a few drops of water at −78 °C and then allowed to come to room temperature. Solvents were evaporated. Column chromatography of the residue (hexane/ethyl acetate 9:1 as eluent) gave pure **7** (2.13 g, 91%). HR-MS(EI) calcd. for $C_{13}H_{15}PS$ $[M]^+$: 234.0632; found 234.0631.

1-Phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole (4). Method A. From 1-Phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-Oxide (6): A solution of racemic phosphane oxide **6** (4.111 g, 18.8 mmol) and phenylsilane (3.36 g, 31.0 mmol) in toluene (8 mL) was heated under argon at 100 °C (bath temperature) for 5 h. Solvents were evaporated, and the residue was filtered through silica gel with hexane as eluent and evaporated again to give phosphane **4**, which was used for separation of enantiomers without further purification.

Method B. From 1-Phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-Sulfide (7): Tris(trimethylsilyl)silane (1.58 mL, 5.1 mmol) and AIBN (40 mg) were added to a solution of racemic phosphane sulfide **7** (1.171 g, 5.0 mmol) in toluene (25 mL), and the mixture was heated at 80 °C for 16 h. Volatiles were evaporated to dryness, and the residue was filtered through silica gel with hexane as eluent and evaporated again to yield **4**, which was used for separation of

enantiomers without further purification. ^{1}H NMR (C_6D_6): δ = 7.47 (m, 2 H, Ar), 7.10 (m, 3 H, Ar), 5.99 (ddd, $J_{H,P}$ = 43.5, $J_{3,4}$ = 7.5, J = 2.4 Hz, 1 H, H-3), 5.93 (ddd, $J_{H,P}$ = 69.0, J = 7.5, J = 2.6 Hz, 1 H, H-4), 3.28 (m, 1 H), 2.32 (m, 1 H), 1.78 (m, 2 H), 1.43 (m, 2 H), 1.28 (m, 2 H) ppm. ^{13}C NMR (C_6D_6): δ = 148.1 (d, $J_{C,P}$ = 1.7 Hz), 132.6 (d, $J_{C,P}$ = 18.9 Hz), 128.5, 128.6, 128.2 (d, $J_{C,P}$ = 6.0 Hz), 53.7 (d, $J_{C,P}$ = 4.3 Hz, CH), 45.1 (d, $J_{C,P}$ = 6.8 Hz, CH), 33.7 (d, $J_{C,P}$ = 33.5 Hz, CH_2), 31.5 (d, $J_{C,P}$ = 3.4 Hz, CH_2), 26.0 (d, $J_{C,P}$ = 5.1 Hz, CH_2) ppm. ^{31}P NMR (C_6D_6): δ = 25.4 ppm.

Resolution of *rac*-4 into its Enantiomers: Crude phosphane **4** (18.8 mmol) was dissolved in ethyl acetate (50 mL). This solution was added in one portion to a solution of (−)-menthyl bromoacetate[21] (5.85 g, 21.1 mmol) in ethyl acetate (10 mL) and the resulting mixture was left overnight at room temperature. The precipitated crystals were collected on sintered glass, washed with ethyl acetate/hexane (1:1), and dried under vacuum to afford a mixture of diastereoisomeric phosphonium salts (7.430 g, 82%). Crystallization from ethyl acetate/ethyl alcohol/benzene (20:1:1) yielded crystals **A** (2.635 g, 29%, *ee* > 92%) and filtrate **A**. Crystals were recrystallized from the same solvent mixture to afford diastereomerically pure salt **8a** (2.260 g, 25%, >98% *ee*) and filtrate **B**.

Compound 8a: $[\alpha]_D^{20}$ = 78.1 (*c* = 0.3, chloroform). ^{1}H NMR ($CDCl_3$), δ = 8.20 (m, 2 H, Ar), 7.67 (m, 1 H, Ar), 7.60 (m, 2 H, Ar), 7.22 (ddd, $J_{H,P}$ = 45.9, J = 2.2, J = 7.9 Hz, 1 H, H-3), 7.01 (ddd, $J_{H,P}$ = 26.3, J = 2.4, J = 7.9 Hz, 1 H, H-2), 4.80 (dd, $J_{H,P}$ = 13.5, $J_{H,CH}$ = 17.4 Hz, 1 H, C*H*P), 4.62 (m, J = 4.4 Hz, J = 10.9 Hz, 1 H, OC*H*-menthyl), 4.51 (dd, $J_{H,P}$ = 13.1, $J_{H,CH}$ = 17.4 Hz, 1 H, C*H*P), 3.82 (m, 1 H), 3.54 (m, 1 H), 2.63 (m, 1 H), 2.15 (m, 1 H), 2.06 (m, 1 H), 1.60−1.88 (m, 7 H), 1.52 (m, 1 H), 1.36 (m, 1 H), 1.29 (m, 1 H), 0.92 (m, 2 H), 0.85 (d, J = 6.5 Hz, 3 H, *i*Pro-CH_3), 0.79 (d, J = 7.0 Hz, 3 H, *i*Pro−CH_3), 0.58 (d, J = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 165.2 (d, $J_{C,P}$ = 3.9 Hz), 163.6 (d, $J_{C,P}$ = 20.4 Hz), 134.3 (d, $J_{C,P}$ = 3.1 Hz), 132.6 (d, $J_{C,P}$ = 10.7 Hz), 129.8 (d, $J_{C,P}$ = 13.1 Hz), 120.1 (d, $J_{C,P}$ = 84.8 Hz), 113.8 (d, $J_{C,P}$ = 76.2 Hz), 77.7 (s), 53.3 (d, $J_{C,P}$ = 12.7 Hz), 46.4 (s), 40.3 (s, CH_2), 37.7 (d, $J_{C,P}$ = 55.0 Hz), 33.8 (s, CH_2), 31.8 (d, $J_{C,P}$ = 54.2 Hz, CH_2), 31.4 (s), 31.1 (d, $J_{C,P}$ = 3.8 Hz, CH_2), 29.5 (d, $J_{C,P}$ = 1.5 Hz, CH_2), 26.7 (d, $J_{C,P}$ = 7.6 Hz, CH_2), 25.8 (s), 22.9 (s, CH_2), 21.8 (s), 20.7 (s), 15.8 (s) ppm. ^{31}P NMR ($CDCl_3$), δ = 55.6 ppm. HR-MS/LSIMS calcd. for $C_{25}H_{36}O_2P$ [M − Br]$^+$: 399.2453; found 399.2436.

Filtrates **A** and **B** were combined, and the solvents were evaporated to dryness to give a mixture of salts (4.892 g, 54%) enriched in the P-epimer of **8a** (ca. 40% *ee*). ^{1}H NMR ($CDCl_3$): δ selected signals of the predominant epimer: 7.23 (ddd, $J_{H,P}$ = 46.0, J = 2.2 Hz, J = 8.0 Hz, 1 H, H-3), 6.90 (ddd, $J_{H,P}$ = 29.0, J = 2.3, J = 7.9 Hz, 1 H, H-2), 4.60 (d, 2 H, PCH_2), 4.56 (m, J = 4.5 Hz, J = 10.9 Hz, 1 H, OC*H*−menthyl), 0.49 (d, J = 7.0 Hz, 3 H, CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 55.5 ppm. The mixture was dissolved in dichloromethane (60 mL), aqueous sodium hydroxide (10%, 50 mL) was added, and the resulting two-phase reaction mixture was stirred at room temp. for 3 h. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The organic layers were combined, washed with water (2 × 10 mL), dried over Na_2SO_4, and filtered, and the solvents were evaporated to dryness. Column chromatography of the residue (hexane/ethyl acetate/methanol, 5:3:1) gave enantioenriched phosphane oxide **6** (2.027 g, 91%, 40% *ee*). $[\alpha]_D^{25}$ = −152.5 (*c* = 0.42, chloroform). The enantioenriched phosphane oxide **6** (655 mg, 3.0 mmol) was treated with phenylsilane (815 mg, 7.5 mmol) as described above, and the resulting crude phosphane was dissolved in ethyl acetate (2 mL) and added to a solution of (+)-menthyl bromoacetate[21] (890 mg, 3.2 mmol) in ethyl acetate (8 mL). The crystals that precipitated (1.025 g, 71%) were recrystallized twice from ethyl acetate/ethyl alcohol/benzene (20:1:1) as described above for salt **8a** to afford the diastereomerically pure salt **8a′** (538 mg, 37%, >98% *ee*). $[\alpha]_D^{20}$ = −80.4 (*c* = 0.34, chloroform). NMR spectroscopic data of **8a′** were identical to those of **8a**. HR-MS/LSIMS calcd. for $C_{25}H_{36}O_2P$ [M − Br]$^+$: 399.2453; found 399.2459.

The remaining filtrates were combined, evaporated to dryness, and hydrolyzed as described above, and yielded recovered **6** (355 mg, 54% calculated for starting racemic **6**), $[\alpha]_D^{20}$ = −2.0 (*c* = 0.41, chloroform), which could be recycled in the resolution process.

Hydrolysis of **8a** (2.260 g, 4.7 mmol) as described above gave (1*R*,3a*S*,6a*S*)-(+)-**6** (990 mg, 96%). $[\alpha]_D^{20}$ 365.1 (*c* = 0.55, chloroform).

Hydrolysis of **8a′** (515 mg, 1.07 mmol) as described above gave (1*S*,3a*R*,6a*R*)-(−)-**6** (222 mg, 95%). $[\alpha]_D^{20}$ = −363.6 (*c* = 0.33, chloroform).

X-Ray Crystallographic Study and Crystal Data for 8a′: Diffraction data were collected on a Kappa CCD diffractometer with graphite monochromated Mo-K_α radiation. Structure was solved by direct methods (SHELXS-97) and refined on F^2 by the full-matrix, least-squares method (SHELXL-97).[22] The non-hydrogen atoms were refined anisotropically; hydrogen atoms were refined isotropically with a riding model.

Formula: $C_{25}H_{36}O_2P^+$ Br^-, M = 479.42, orthorhombic, space group $P2_12_12_1$, a = 7.1060(2), b = 11.3810(4), c = 30.3240(10) Å, V = 2452.40(14) Å^3, Z = 4, $F(000)$ = 1008, R_1 = 0.0329 [$I > 2\sigma(I)$], wR_2 = 0.0844 for all data. The absolute configuration was known from the reference (1*S*,2*R*,5*S*)-menthyl fragment.

CCDC-238149 contains the crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

(1*S*,3a*R*,6a*R*)-1-Phenyloctahydrocyclopenta[*b*]phosphole 1-Oxide (9): Pd/C (10%, 100 mg) was added to a solution of (−)-1-phenyl-1,3a,4,5,6,6a-hexahydrocyclopenta[*b*]phosphole 1-oxide [(−)-**6**, 218 mg, 1.0 mmol] in methanol (8 mL), and the reaction mixture was kept under hydrogen atmosphere (balloon) at room temp. for 24 h. The mixture was then filtered through a short silica column with methanol as eluent. The filtrate was evaporated to dryness to yield the title compound (203 mg, 92%) as an oil. $[\alpha]_D^{20}$ = −43.2 (*c* = 0.53, chloroform). M.p. 40−42 °C. HR-MS(EI) calcd. for $C_{13}H_{17}PO$ [M]$^+$: 220.1017; found 220.1009.

(1*R*,3a*R*,6a*R*)-1-Phenyloctahydrocyclopenta[*b*]phosphole (5): Reduction of (−)-1-phenyloctahydrocyclopenta[*b*]phosphole 1-oxide [(−)-**9**, 191 mg, 0.87 mmol] with phenylsilane as described for **4** gave the title compound (175 mg, 98%) as an oil. ^{1}H NMR (C_6D_6): δ = 7.26 (m, 2 H, Ar), 7.08 (m, 2 H, Ar), 7.01 (m, 1 H, Ar), 2.54 (m, 1 H), 2.46 (m, 1 H), 2.00 (m, 1 H), 1.46−1.80 (m, 7 H), 1.22 (m, 1 H), 0.90 (m, 1 H) ppm. ^{13}C NMR (C_6D_6): δ = 131.0 (d, $J_{C,P}$ = 14.6 Hz), 128.2, 128.0, 127.8, 46.2 ($J_{C,P}$ = 3.4 Hz), 45.3 (d, $J_{C,P}$ = 12.1 Hz), 34.1 (d, $J_{C,P}$ = 30.2 Hz, CH_2), 33.9 (s, CH_2), 33.8 (d, $J_{C,P}$ = 3.4 Hz, CH_2), 27.9 (d, $J_{C,P}$ = 8.6 Hz, CH_2), 26.0 (d, $J_{C,P}$ = 14.6 Hz, CH_2) ppm. ^{31}P NMR (C_6D_6): δ = 7.1 ppm.

General Procedure for Palladium-Catalyzed Allylic Substitution: Dimethyl malonate (0.76 mmol) and BSA (1 mmol) were dissolved in THF (2 mL), and the solution was stirred at room temp. for 30 min. It was then cooled to −20 °C, and a solution of $[Pd(allyl)Cl]_2$ (1.25 mol %) and ligand (**4** or **5**, 12.5 mol %) in benzene (0.2 mL) was

added. The resulting mixture was stirred at −20 °C for 30 min and at 0 °C for 20 min and was cooled again to −20 °C, a solution of (*E*)-1,3-diphenylallyl acetate (0.4 mmol) in THF (1 mL) was added, and the mixture was stirred at room temp. overnight. Solvents were evaporated to dryness, and column chromatography of the residue gave **13** (hexane/acetone, 15:1, as eluent), **14** (hexane/ethyl acetate, 9:1), or **17** (hexane/acetone, 10:1 as eluent).

Ethyl 4-(Phenylsulfonyl)cyclopent-1-ene-1-carboxylate (27): The chiral phosphane **5** (120 μL of a 0.42 M solution in benzene, 0.05 mmol) was added to a solution of ethyl 2,3-butadienoate (**19**, 56 mg, 0.5 mmol) and methyl phenyl sulfone (**24**, 101 mg, 0.6 mmol) in benzene (2 mL), and the mixture was stirred at room temp. for 24 h. Solvents were evaporated, and the residue was purified by column chromatography (hexane/ethyl acetate, 7:3), which gave **27** (100 mg, 71%) as a thick oil. ^{1}H NMR ($CDCl_3$): δ = 7.90 (m, 2 H, Ar), 7.65 (m, 1 H, Ar), 7.56 (m, 2 H, Ar), 6.58 (m, 1 H, CH=), 4.15 (q, *J* = 7.1 Hz, 2 H, OCH_2), 3.92 (m, 1 H, CHS), 3.08 (m, 2 H, CH_2), 2.80 (m, 2 H, CH_2), 1.24 (t, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.6 (C=O), 139.4 (CH=), 137.9 (C=), 134.4, 133.8, 129.3, 128.5, 61.6 (CHS), 60.5 (OCH_2), 34.1 (CH_2), 32.9 (CH_2), 14.1 (CH_3) ppm. HR-MS (ESI) calcd. for $C_{14}H_{16}NaO_4S$ $[M + Na]^+$: 303.0662; found 303.0677.

***N*-Acetylphenylalanine (29):** A ligand (**4** or **5**, 5 mol %) was added to a cooled (−70 °C) solution of $Rh[COD]_2BF_4$ (1 mol %) in THF (2 mL) and the resulting solution was stirred at −70 °C for 30 min and additionally at 0 °C for 20 min. The solution of rhodium catalyst was transferred to an autoclave, (*Z*)-*N*-acetylaminocinnamic acid (**28**, 1.5 mmol) and Et_3N (0.02 mL) in methanol (7 mL) was added, and hydrogen pressure was applied (5 atm, 24 h). Solvents were evaporated, and the residue was dissolved in aqueous NaOH (1 M) and washed with dichloromethane (2 × 15 mL). The aqueous phase was acidified with H_2SO_4 (3 M), saturated with sodium sulfate, and extracted with chloroform. The organic extracts were dried (Na_2SO_4), and the solvents were evaporated to yield *N*-acetylphenylalanine (**29**) of $[\alpha]_D^{20}$ = −4.1 (*c* = 1.0, methanol) in the case of **4**, and $[\alpha]_D^{20}$ = −24.9 (*c* = 1.2, methanol) in case of **5**. ref.[23] $[\alpha]_D^{20}$ = +40.1 (*c* = 1.0, methanol) for (*S*) enantiomer.

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