2-butanol (m/z of 189 and 191 for ^{16}O and ^{18}O, respectively). The intensities of these peaks were measured by single ion monitoring of m/z 189 and 191 using the average of scans taken over each entire GC peak after appropriate background correction. The ratio of 191/(189 + 191) gives the percent ^{18}O in each sample. Repeat injections were reproducible to better than ±0.5%.

Stereochemical Experiments. A sample of enantiomerically enriched (*R*)-2-butylbrosylate (optical purity 88 ± 2%) was subjected to solvolysis conditions identical with those described above for the ^{18}O scrambling experiments. After two solvolysis half-lives the unsolvolyzed 2-butylbrosylate was recovered as described above and was reduced electrochemically. The recovered 2-butylbrosylate was reduced at a mercury pool electrode with use of controlled-potential electrolysis (CPE). Acetonitrile was used as the solvent and tetraethylammonium perchlorate (TEAP) served as the supporting electrolyte. CPE was conducted in a sealed electrochemical cell (IBM Instruments). Three milliliters of triply distilled mercury (Bethlehem Apparatus Co.) was used to form the mercury pool that served as the working electrode (surface area ca. 25 cm^2). A Pt wire was inserted into the pool to make contact. During CPE the mercury pool was stirred by a magnetic stirring bar. The auxillary electrode (Pt wire) compartment was a glass cylinder with a large Vycor tip, inset in the top of the cell. The Ag/Ag^+ reference electrode (a silver wire submerged in the 0.01 M $AgNO_3$–0.1 M TEAP acetonitrile solution) was separated from the electrolyzed solution by means of a salt bridge. The auxillary electrode compartment and the reference bridge were both filled with 0.1 M TEAP acetonitrile solution.

CPE of 2-butylbrosylate was carried out in 5-mL volumes of solutions prepared by dissolving approximately 15 mg of the compound in 0.1 M TEAP acetonitrile solution. Prior to CPE the solution was purged with argon for 20 min and then was kept under an argon blanket during CPE. Argon was purified from traces of moisture and oxygen and saturated with acetonitrile vapors by passing through a molecular sieve column, a copper catalyst column (Labclear), and two washing bottles filled with acetonitrile.

The progress of CPE was monitored coulometrically and by means of linear scan voltammetry (LSV) at a small mercury electrode (mercury coated platinum wire; surface area ca. 0.05 cm^2). The CPE and LSV measurements were conducted with a BAS-100 electrochemical analyzer (Bioanalytical Systems). The LSV voltammograms obtained for 2-butylbrosylate in 0.1 M TEAP in acetonitrile exhibited two peaks with peak potentials of −2.25 V and −2.53 V vs Ag/Ag^+. All of the CPE reductions of 2-butylbrosylate in this work were carried out at −2.80 V potential, which our preliminary CPE experiments had shown was sufficient to completely reduce the compound.

When the electrochemical reduction was complete the acetonitrile solution containing the 2-butanol was separated from the mercury pool and cooled to 0 °C. To the cooled acetonitrile solution was added, with stirring, 30 μL of pyridine and 150 μL of a 2 M solution of (*S*)-2-acetoxypropionyl chloride. The solution was warmed to room temperature, and stirring was continued for 2 h. The acetonitrile solution containing the derivatized alcohol was evaporated at room temperature under reduced pressure. To the resulting solid was added 1 mL of hexane followed by 10 drops of 0.1 N HCl; the hexane layer was separated and the HCl washed again with 1 mL of hexane. The combined hexane layers were dried ($MgSO_4$) and filtered, and the hexane was removed under reduced pressure at room temperature. After evaporation to dryness, 0.5 mL of hexane was added to the flask and the resulting solution used for gas chromatographic analysis. Gas chromatographic analysis was performed by injecting 1–2 μL of the hexane solution onto a 15 m × 0.25 mm J&W DB-1 fused silica capillary column operated at 70 °C. The linear flow velocity was 18 cm/min, and the split ratio was 100:1. The percent of each diasteriomer was determined by electronic integration of the peak areas. Several injections of each sample were made, and the average deviation was better than ±1.3%. Electrochemical reduction and derivatization of the starting 2-butylbrosylate and of 2-butylbrosylate isolated after two solvolysis half-lives was repeated twice and the results agreed within ±2%.

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Synthesis and Reactions of Phosphine–Boranes. Synthesis of New Bidentate Ligands with Homochiral Phosphine Centers via Optically Pure Phosphine–Boranes

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Abstract: Secondary and tertiary phosphine–boranes were synthesized in one-pot from phosphine oxides or substituted chlorophosphines without isolation of the intermediate phosphines. Phosphine–boranes having a methyl group were metalated with *sec*-butyllithium. The generated carbanions reacted with alkyl halides or carbonyl compounds to yield various phosphine–borane derivatives. The carbanions underwent copper(II)-promoted oxidative coupling without impairment of the borane functionality. Secondary phosphine–boranes reacted with alkyl halides, aldehydes, or α,β-unsaturated carbonyl compounds to give phosphine–borane derivatives having a functional group. The boranato group of phosphine–boranes was removed in a stereospecific manner with retention of configuration by treatment with a large excess of amine such as morpholine. A new route to bidentate ligands with homochiral phosphine centers has been explored by utilizing these characteristic reactivities of phosphine–boranes. Thus, optically pure (*S*,*S*)-1,2-bis(*o*-anisylphenylphosphino)ethane, (*R*,*R*)-1,2-bis(*tert*-butylphenylphosphino)ethane, and (*S*,*S*)-1,4-bis(*o*-anisylphenylphosphino)butane have been synthesized via phosphine–boranes.

Phosphine–boranes, adducts of phosphines and boranes, constitute a unique class of organophosphorus compounds. These compounds have attracted the attention of chemists, and a number of preparative and physicochemical studies have been made so far, revealing their peculiar chemical properties as well as the inherent P–B bond nature.[1,2] In addition, it has been demon-

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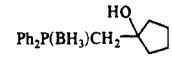
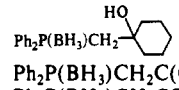
Table I. Preparation of Phosphine-Boranes

starting material	method	product[a]	yield (%)	mp or bp (°C)
Ph_2MePO	A	Ph_2MePBH_3	96	50–51 (lit.[b] oil)
Ph_2(▷)PO	A	Ph_2(▷)PBH_3	89	34
(*S*)-Ph(*o*-$MeOC_6H_4$)MePO[c]	A	Ph(*o*-$MeOC_6H_4$)$MePBH_3$[d]	62	75–76
Ph_2(1-$C_{10}H_7$)MePO	A	Ph_2(1-$C_{10}H_7$)$MePBH_3$	90	95–96
$Ph_2(H)PO$	A	$Ph_2(H)PBH_3$	65	45.5–46.5 (lit.[e] oil)
Ph_2PCl	B	$Ph_2(H)PBH_3$	94	
Ph(1-$C_{10}H_7$)(H)PO	A	Ph(1-$C_{10}H_7$)$(H)PBH_3$	66	oil
Ph(*t*-C_4H_9)(H)PO	A	Ph(*t*-C_4H_9)$(H)PBH_3$	82	bp 111–114/0.4 mm Hg
$PhPCl_2$, *t*-C_4H_9MgCl	B	Ph(*t*-C_4H_9)$(H)PBH_3$	67	
Ph(*o*-$MeOC_6H_4$)PO(OEt)	A	Ph(*o*-$MeOC_6H_4$)$(H)PBH_3$	91	95–96
Ph(*o*-$MeOC_6H_4$)PO(OH)	A	Ph(*o*-$MeOC_6H_4$)$(H)PBH_3$	15	
$PhPCl_2$, *o*-$MeOC_6H_4MgBr$	B	Ph(*o*-$MeOC_6H_4$)$(H)BPH_3$	60	
PhMePO(OMe)	A	$PhMe(H)PBH_3$	82	bp 110/0.1 mmHg

[a] All phosphine-boranes synthesized displayed satisfactory spectral data (IR and ^1H NMR) and elemental analysis. [b] Mathur, M. A.; Myers, W. H.; Sisler, H. H.; Ryschkewitsch, G. E. *Inorg. Synth.* **1974**, *15*, 128. [c] 93% ee. [d] 0% ee. [e] Nainan, K. C.; Ryschkewitsch, G. E. *Inorg. Chem.* **1969**, *8*, 2671.

Table II. Reaction of $Ph_2P(BH_3)CH_2Li$ with Electrophiles

entry	electrophile	product	yield (%)	mp (°C)
1	C_4H_9Br	$Ph_2P(BH_3)C_5H_{11}$	66	oil
2	CH_2=$CHCH_2Br$	$Ph_2P(BH_3)CH_2CH_2CH$=CH_2	62	oil
3	Me_3SiCl	$Ph_2P(BH_3)CH_2SiMe_3$	100	120–121
4	C_3H_7CHO	$Ph_2P(BH_3)CH_2CHOHC_3H_7$	92	oil
5	PhCHO	$Ph_2P(BH_3)CH_2CHOHPh$	93	oil
6	*p*-$O_2NC_6H_4CHO$	$Ph_2P(BH_3)CH_2CHOHC_6H_4NO_2$-*p*	85	117–118
7	PhCH=CHCHO	$Ph_2P(BH_3)CH_2CHOHCH$=$CHPh$	70	oil
8	Me_2CO	$Ph_2P(BH_3)CH_2C(OH)Me_2$	33	91–93
9			32	77–78
10			57	79–80
11	Ph_2CO	$Ph_2P(BH_3)CH_2C(OH)Ph_2$	94	130–131
12[a]	$PhCO_2Et$	$Ph_2P(BH_3)CH_2COPh$	54	99–101
13[a]	$(MeO)_2CO$	$Ph_2P(BH_3)CH_2CO_2Me$	83	oil
14[a]	$(t\text{-}C_4H_9OCO)_2O$	$Ph_2P(BH_3)CH_2CO_2C_4H_9$-*t*	90	82–83

[a] Lithium diisopropylamide was added to a mixture of methyldiphenylphosphine-borane and carbonyl compounds.

strated that these compounds have potential utility not only as olefin hydroboration agents[3] but also as useful intermediates in both synthetic organic chemistry and coordination chemistry.[4,5]

We have been interested in the characteristic properties of phosphine-boranes and have worked to develop syntheses and reactions of these compounds with a view to obtaining useful organophosphorus compounds. At first, we devised a one-step preparation of phosphine-boranes from phosphine oxides or substituted chlorophosphines without isolation of the intermediate phosphines. The synthesized phosphine-boranes were found to react with various organic functional groups to yield a variety of phosphine-borane derivatives possessing a functional group. The revealed reactivities of phosphine-boranes led us to explore a new route to bidentate phosphine ligands with homochiral phosphine centers.[6]

Results and Discussion

Synthesis of Phosphine-Boranes. Phosphine-boranes are usually prepared by the reaction of phosphines with boranes. This currently employed method, however, is not always easily accomplished, because some phosphines, particularly secondary and primary phosphines, are very difficult to handle due to their corrosiveness and air-sensitivity. We tried to synthesize phos-

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(2) For recent works dealing with phosphine-boranes and related compounds: (a) Wisiam-Neilson, P.; Wilkins, M. A.; Weigel, F. C.; Foret, C. J.; Martin, D. R. *J. Inorg. Nucl. Chem.* **1981**, *43*, 457. (b) Martin, D. R.; Merkel, C. M.; Ruiz, J. P.; Mandal, J. U. *Inorg. Chem. Acta* **1985**, *100*, 293. (c) Das, M. K.; Roy, S. *Synth. React. Inorg. Met.-Org. Chem.* **1985**, *15*, 53. (d) Schmidbaur, H.; Weiss, E.; Müller, G. *Synth. React. Inorg. Met.-Org. Chem.* **1985**, *15*, 401, 415. (e) Kölle, P.; Nöth, H.; Paine, R. T. *Chem. Ber.* **1986**, *119*, 2681. (f) Arif, A. M.; Cowley, A. H.; Pakulski, M.; Power, J. M. *J. Chem. Soc., Chem. Commun.* **1986**, 889, (g) Arif, A. M.; Boggs, J. E.; Cowley, A. H.; Lee, J.-G.; Pakulski, M.; Power, J. M. *J. Am. Chem. Soc.* **1986**, *108*, 6083. (h) Bartlett, R. A.; Feng, X.; Power, P. P. *J. Am. Chem. Soc.* **1986**, *108*, 6817. (i) Narayana, C.; Periasamy, M. *J. Organomet. Chem.* **1987**, *323*, 145. (j) Köster, R.; Schüssler, W.; Synoradzki, L. *Chem. Ber.* **1987**, *120*, 1105. (k) Köster, R.; Tsay, Y.-H.; Synoradzki, L. *Chem. Ber.* **1987**, *120*, 1117. (l) Rasika Dias, H. V.; Power, P. P. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1270. (m) Driess, M.; Pritzkow, H.; Siebert, W. *Angew. Chem., Int. Ed. Eng.* **1988**, *27*, 399. (n) Köster, R.; Seidel, G.; Müller, G.; Böse, R.; Wrackmeyer, B. *Chem. Ber.* **1988**, *121*, 1381. (o) Köster, R.; Seidel, G.; Böse, R.; Wrackmeyer, B. *Chem. Ber.* **1988**, *121*, 1941. (p) Rasika Dias, H. V.; Power, P. P. *J. Am. Chem. Soc.* **1989**, *111*, 144. (q) Schmidbaur, H.; Wimmer, T.; Grohmann, A.; Steigelmann, O.; Müller, G. *Chem. Ber.* **1989**, *122*, 1607. (r) Wimmer, T.; Steigelmann, O.; Müller, G.; Schmidbaur, H. *Chem. Ber.* **1989**, *122*, 2109. (s) Imamoto, T.; Oshiki, T. *Tetrahedron Lett.* **1989**, *30*, 383. (t) Sood, A.; Spielvogel, B. F.; Shaw, B. R. *J. Am. Chem. Soc.* **1989**, *111*, 9234.

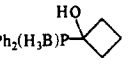
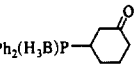
(3) (a) Pelter, A.; Rosser, R.; Mills, S. *J. Chem. Soc., Chem. Commun.* **1981**, 1014. (b) Bestmann, H. J.; Sühs, K.; Röder, T. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 1038. (c) Bestmann, H. J.; Röder, T. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 782. (d) Bestmann, H. J.; Röder, T.; Sühs, K. *Chem. Ber.* **1988**, *121*, 1509.

(4) Köster, R.; Richborn, B. *J. Am. Chem. Soc.* **1967**, *89*, 2782.

(5) Schmidbaur and his co-workers initially studied the reactions of chlorodimethylphosphine-borane and its derivatives, and they synthesized novel classes of metal complexes possessing P-B bond linkages. (a) Schmidbaur, H.; Müller, G. *Monatsch. Chem.* **1980**, *111*, 1233. (b) Schmidbaur, H.; Weiss, E. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 283. (c) Schmidbaur, H.; Müller, G.; Dash, K. C.; Milewski-Mahrla, B. *Chem. Ber.* **1981**, *114*, 441. (d) Müller, G.; Neugebauer, D.; Geike, W.; Köher, F. H.; Pebler, J.; Schmidbaur, H. *Organometallics* **1983**, *2*, 257. (e) Schmidbaur, H.; Weiss, E.; Graf, W. *Organometallics* **1985**, *4*, 1233.

(6) A preliminary account of a portion of this work has appeared: Imamoto, T.; Kusumoto, T.; Suzuki, N.; Sato, K. *J. Am. Chem. Soc.* **1985**, *107*, 5301.

Table III. Reaction of Secondary Phosphine–Boranes with Electrophiles

secondary phosphine–borane	electrophile	conditions[a]	product[b]	yield (%)	mp (°C)
$Ph_2(H)PBH_3$	CH_2=$CHCH_2Br$	MeOH, KOH	$Ph_2P(BH_3)CH_2CH$=CH_2	92	oil
$Ph_2(H)PBH_3$	C_4H_9Br	MeOH, KOH	$Ph_2P(BH_3)C_4H_9$	86	oil
$Ph_2(H)PBH_3$	$C_{10}H_{21}Br$	MeOH, KOH	$Ph_2P(BH_3)C_{10}H_{21}$	80	oil
$Ph_2(H)PBH_3$	$Br(CH_2)_3Br$	THF, NaH	$Ph_2P(BH_3)(CH_2)_3P(BH_3)Ph_2$	94	150–151
$Ph_2(H)PBH_3$	$ClCH_2OMe$	MeOH, KOH	$Ph_2P(BH_3)CH_2OMe$	36	oil
$Ph_2(H)PBH_3$	$ClCH_2COMe$	MeOH, KOH	$Ph_2P(BH_3)CH_2COMe$	37	oil
$Ph_2(H)PBH_3$	$BrCH_2COC_6H_4Br$-*p*	MeOH, MeONa	$Ph_2P(BH_3)CH_2COC_6H_4Br$-*p*	56	102–103
$Ph_2(H)PBH_3$	$ClCH_2CO_2Me$	MeOH, KOH	$Ph_2P(BH_3)CH_2CO_2Me$	79	oil
(*o*-An)Ph(H)PBH_3	$ClCH_2CO_2Me$	THF, NaH	(*o*-An)Ph$P(BH_3)CH_2CO_2Me$	92	oil
$Ph_2(H)PBH_3$	trimethylene oxide	MeOH, KOH	$Ph_2P(BH_3)(CH_2)_3OH$	20	oil
$Ph_2(H)PBH_3$	HCHO	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH_2OH$	90	oil
$Ph_2(H)PBH_3$	C_3H_7CHO	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CHOHC_3H_7$	58	oil
$Ph_2(H)PBH_3$	PhCHO	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CHOHPh$	75	104–105
$Ph_2(H)PBH_3$	*p*-ClC_6H_4CHO	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH(OH)C_6H_4Cl$-*p*	72	96–98
$Ph_2(H)PBH_3$	PhCH=CHCHO	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH(OH)CH$=$CHPh$	28	139–140
			$Ph_2P(BH_3)CH(Ph)CH_2CHO$	68	101–103
$Ph_2(H)PBH_3$	Me_2CO	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)C(OH)Me_2$	60	129–130
$Ph_2(H)PBH_3$	cyclobutanone	MeOH, KOH (5 mol %)		71	106–107
$Ph_2(H)PBH_3$	2-cyclohexenone	MeOH, KOH (5 mol %)		88	116–118
$Ph_2(H)PBH_3$	PhCH=CHCOPh	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH(Ph)CH_2COPh$	92	151–153
$Ph_2(H)PBH_3$	CH_2=$CHCO_2Et$	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH_2CH_2CO_2Et$	73	oil
$Ph_2(H)PBH_3$	CH_2=$CHCONH_2$	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH_2CH_2CONH_2$	71	136–137
$Ph_2(H)PBH_3$	CH_2=$CHCN$	MeOH, KOH (5 mol %)	$Ph_2P(BH_3)CH_2CH_2CN$	50	oil
$Ph_2(H)PBH_3$	$H_3BP(CH$=$CH_2)_3$	MeOH, KOH (5 mol %)	$[Ph_2P(BH_3)CH_2CH_2]_3PBH_3$	65	72–74
(*o*-An)Ph(H)PBH_3	$(CH_2$=$CH)Ph_2PBH_3$	MeOH, KOH (5 mol %)	(*o*-An)Ph$P(BH_3)CH_2CH_2P(BH_3)Ph_2$	49	147–148
$Ph_2(H)PBH_3$	CH_2=$CMeCMe$=CH_2	THF, reflux	$Ph_2P(BH_3)CH_2CMe$=CMe_2	30	oil
$Ph_2(H)PBH_3$	cyclohexene	C_6H_6, AIBN, reflux	$Ph_2P(BH_3)C_6H_{11}$	7	88–89
$Ph_2(H)PBH_3$	CH_2=CHC_6H_{13}	C_6H_6, AIBN, reflux	$Ph_2P(BH_3)C_8H_{17}$	35	oil
$PhMe(H)PBH_3$	*o*-iodoanisole	PhMe, K_2CO_3[c]	Ph(*o*-$MeOC_6H_4$)$MePBH_3$	91	75–76

[a] All reactions were carried out at from 0 °C to room temperature unless otherwise stated. [b] All compounds synthesized displayed satisfactory spectral (IR and ^1H NMR) and elemental analysis. [c] $(Ph_3P)_4Pd$ (5 mol %), 70–80 °C.

phine–boranes directly from phosphine oxides or chlorophosphines by the following two methods:

Method A:

$$R^1R^2R^3P(O) \xrightarrow{LiAlH_4/NaBH_4/CeCl_3} R^1R^2R^3PBH_3$$

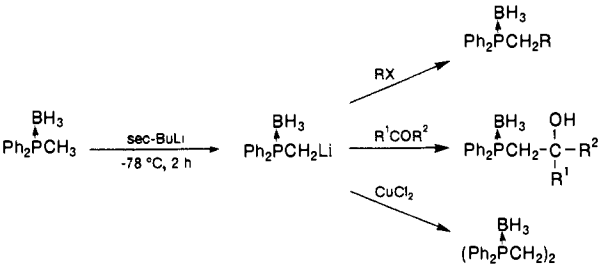
Method B:

$$R^1R^2PCl \xrightarrow{LiAlH_4/BH_3\cdot THF} R^1R^2P(H)BH_3$$

The results are shown in Table I. Tertiary phosphine oxides were converted into the corresponding phosphine–boranes in good yields by method A.[7] Secondary phosphine oxides and phosphinic acid esters also reacted under similar conditions to give secondary phosphine–boranes. It is noted that this reaction did not proceed in the absence of cerium(III) chloride. Trivalent cerium presumably plays dual roles in this reaction: it activates phosphine oxides by coordination so that the deoxygenation with $LiAlH_4$ proceeds readily,[8] and it activates $NaBH_4$ to facilitate reaction with intermediate phosphines to form phosphine–boranes.

We attempted to obtain optically active phosphine–boranes from the corresponding phosphine oxides by using (*S*)-*o*-anisylmethylphenylphosphine oxide as a model substrate. Unfortunately, however, the isolated *o*-anisylmethylphenylphosphine–borane was found to be a racemate. This result is explained by assuming that the phosphorane intermediate formed by reversible addition of $LiAlH_4$ to the phosphine oxide rapidly undergoes pseudorotation prior to the formation of the phosphine.[9,10]

Scheme I



Some secondary phosphine–boranes were prepared in good yields by method B. It is worth mentioning that unsymmetrical secondary phosphine–boranes were synthesized in one-pot from dichlorophenylphosphine by successive treatments with Grignard reagent, $LiAlH_4$, and borane.

Synthesis of Phosphine–Borane Derivatives. We next examined the synthesis of a variety of functionalized phosphine–boranes by using methyldiphenylphosphine–borane as a model substrate. The compound was metalated with *sec*-BuLi in THF at −78 °C.[11] The generated carbanion was allowed to react with various electrophiles such as allyl bromide, chlorotrimethylsilane, or carbonyl compounds.

(7) Köster et al. initially found that triphenylphosphine oxide, on treatment with amine–borane at 120 °C, is converted into triphenylphosphine–borane in quantitative yield. Köster, R.; Morita, Y. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 593.

(8) Phosphine oxides were rapidly deoxygenated by $LiAlH_4$–$CeCl_3$ in THF at 20–40 °C to afford the corresponding phosphines in high yields. Imamoto, T.; Takeyama, T.; Kusumoto, T. *Chem. Lett.* **1985**, 1491.

(9) The authors previously reported that the reaction of (*S*)-*o*-anisylmethylphenylphosphine oxide (93% ee) with $LiAlH_4/CeCl_3$ at 40 °C for 0.5 h provided racemic *o*-anisylmethylphenylphosphine in 90% yield. See ref 8.

(10) The $LiAlH_4$-induced stereomutation of optically active phosphine oxides was reported. (a) Henson, P. D.; Naumann, K.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 5645. (b) Campbell, I. G. M.; Way, J. K. *J. Chem. Soc.* **1960**, 5034. (c) Campbell, I. G. M.; Way, J. K. *J. Chem. Soc.* **1961**, 2133. (d) Aguiar, A. M.; Aguiar, H. J.; Archibald, T. G. *Tetrahedron Lett.* **1966**, 3187.

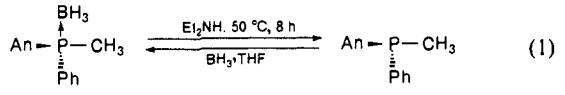
(11) Schmidbaur et al. initially generated phosphine–borane-stabilized carbanions and found that they are subjected to C-alkylation. See ref 1a and references cited therein.

As shown in Table II, all the reactions examined proceeded smoothly to afford the phosphine–borane derivatives, some of which possessed a functional group such as alkenyl, hydroxy, and carbonyl groups. The carbanion underwent copper(II)-promoted oxidative coupling without impairment of the borane functionality to give 1,2-bis(boranatodiphenylphosphino)ethane in 81% yield.[12]

Our subsequent trial was concerned with the use of secondary phosphine–boranes. Secondary phosphine–boranes are expected to react with various electrophiles in a similar reaction pattern as secondary phosphine oxides and related compounds.[13] As summarized in Table III, diphenylphosphine–borane reacted readily with electrophiles in the presence of a base under mild conditions to afford functionalized phosphine–boranes in good to high yields. Thus, the substitution reactions with several halides proceeded in the presence of a stoichiometric amount of KOH or NaH. The addition to carbonyl groups was also induced by KOH (5 mol %), although the method was limited to aldehydes and to some less sterically crowded ketones such as acetone or cyclobutanone. The reaction with trimethylene oxide proceeded with ring opening to furnish the corresponding alcohol. The Michael-type addition to olefins possessing an electron-withdrawing group proceeded smoothly under similar conditions. It is noted that vinyl phosphine–boranes also underwent the Michael-type addition with diphenylphosphine–borane,[14] This method may provide a route to polydentate ligands or unsymmetrical phosphine ligands.[15]

A palladium-catalyzed substitution reaction of secondary phosphine–borane with aromatic and vinylic halides was also tried under various conditions. It was found that methylphenylphosphine–borane reacted with *o*-iodoanisole in the presence of a catalytic amount of $(Ph_3P)_4Pd$ in toluene at 70–80 °C.[16] It may be worthy to note that the boranato function remained unchanged under these relatively drastic conditions. However, the reaction of aryl bromides or vinyl bromide was sluggish under the conditions.

Reaction of Phosphine–Boranes with Amines. Our attention was next turned to the reactions of the boronato group. Our cursory experiments led to the finding that the boronato group of phosphine–boranes was removed on treatment with a large excess of an amine such as morpholine or diethylamine. This reaction has been proven to proceed in a stereospecific manner with retention of configuration. Thus, (*S*)-*o*-anisylmethylphenylphosphine–borane (89% ee) was converted in essentially quantitative yield into (*S*)-*o*-anisylmethylphenylphosphine (89% ee) on treatment with a large excess of diethylamine at 50 °C for 8 h.



(1)

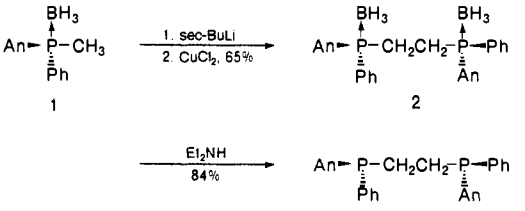
An = *o*-Anisyl

It has been well documented that this type of reaction is reversible.[17] Most work reported hitherto rather emphasizes the formation of phosphine–boranes from phosphines and amine–borane,[18] and the reverse reaction to produce phosphines from phosphine–boranes has been scarcely recognized from the synthetic point of view. Our results clearly demonstrate that parent phosphines can be obtained from phosphine–boranes in high yield by the use of a large excess of amine which has strong nucleophilicity.

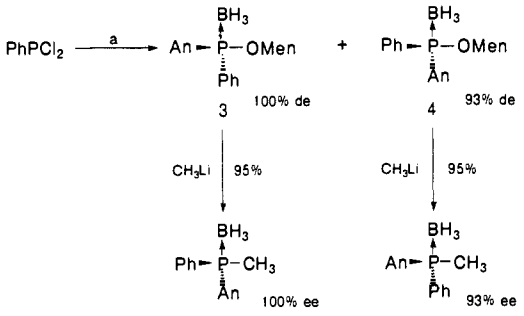
The reactions mentioned above may offer a possible route to such phosphine derivatives that are not easily accessible by other previously existing methods. It is particularly worth mentioning that in these reaction sequences the boranato group acts both as an activating group and as a protecting group. That is, as was initially demonstrated by Schmidbauer et al.,[5b] the boranato group bonding with the phosphorus atom activates the adjacent methyl group as well as the P–H bond to deprotonation with a strong base; at the same time it protects the phosphine group which is generally sensitive toward oxygen and other electrophiles such as alkyl halides.

Synthesis of (*S*,*S*)-1,2-Bis(*o*-anisylphenylphosphino)ethane. On the basis of the experimental facts mentioned above, we have

Scheme II

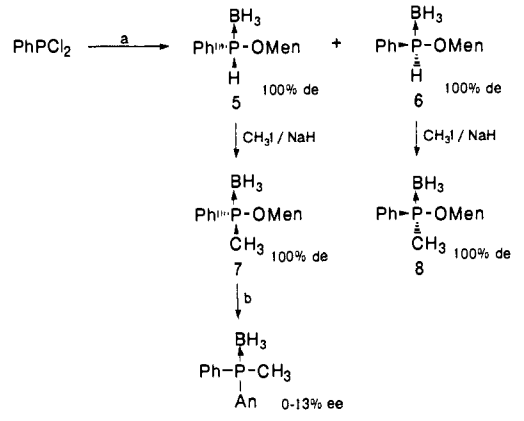


Scheme III[a]



[a](a) (i) *o*-Anisylmagnesium bromide; (ii) (−)-menthol/pyridine; (iii) BH_3·THF.

Scheme IV[a]



[a](a) (i) (−)-Menthol/pyridine; (ii) BH_3·THF; (iii) $LiAlH_4$; (b) *o*-anisyllithium, benzene or THF, reflux.

(12) Maryanoff, C. A.; Maryanoff, B. E.; Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 5839.

(13) Smith, D. J. H. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Sutherland, I. O., Ed.; Pergamon: London, 1979; Vol. 3, p 1121. (b) Pudovik, A. N.; Konovalova, I. V. *Synthesis* **1979**, 81. (c) Weissermel, K.; Kleiner, H.-J.; Finke, M.; Felcht, U.-H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 223. (d) Lu, X.; Zhu, J.; Huang, J.; Tao, X. *J. Mol. Catal.* **1987**, *41*, 235.

(14) The Michael-type reaction of vinyl phosphine, vinyl phosphine oxides, and vinyl phosphine sulfides with nucleophiles have been reported. (a) King, R. B.; Cloyd, J. C. *J. Am. Chem. Soc.* **1975**, *97*, 53. (b) Johnson, C. R.; Imamoto, T. *J. Org. Chem.* **1987**, *52*, 2170. (c) Pietrusiewicz, K. M.; Zablocka, M. *Tetrahedron Lett.* **1988**, *29*, 1987, 1991.

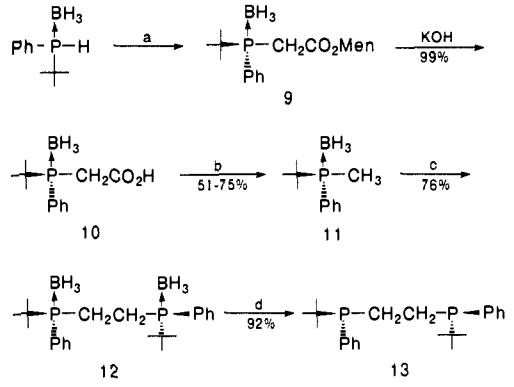
(15) King, R. B. *Acc. Chem. Res.* **1972**, *5*, 177.

(16) Similar reactions of aryl halides with phosphinous acids or phosphinic acid esters have been reported. (a) Hirao, T.; Masunaga, T.; Yamada, N.; Ohshiro, Y.; Agawa, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 909. (b) Xu, Y.; Li, Z.; Guo, H.; Huang, Y. *Synthesis* **1984**, 781. (c) Xia, J.; Guo, H. *Synthesis* **1986**, 691. (d) Zhang, J.; Xu, Y.; Huang, G.; Guo, H. *Tetrahedron Lett.* **1988**, *29*, 1955. (e) Holt, D. A.; Erb, J. M. *Tetrahedron Lett.* **1989**, *30*, 5393.

(17) (a) Young, D. E.; McAchran, G. E.; Schore, S. G. *J. Am. Chem. Soc.* **1966**, *88*, 4390. (b) VanPaasschen, J. M.; Geanangel, R. A. *Inorg. Chem.* **1978**, *17*, 3302.

(18) Reetz, T.; Katlafsky, B. *J. Am. Chem. Soc.* **1960**, *82*, 5036. (b) Reetz, T. *J. Am. Chem. Soc.* **1960**, *82*, 5039. (c) Baldwin, R. A.; Smitheman, K. A.; Washburn, R. M. *J. Org. Chem.* **1961**, *26*, 3547. (d) Baldwin, R. A.; Washburn, R. M. *J. Org. Chem.* **1961**, *26*, 3549.

Scheme V[a]



[a] (a) $ClCH_2CO_2Men$, NaH, THF, followed by recrystallization from hexane; (b) 110 °C in anisole, 2.5 h; (c) *sec*-BuLi, $CuCl_2$; (d) morpholine, 70 °C, 2 h.

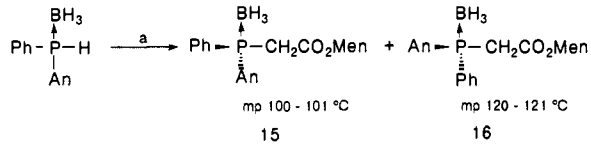
worked to develop a new method for the preparation of bidentate phosphine ligands homochiral at phosphorus. Our first trial was conducted with the preparation of optically pure 1,2-bis(*o*-anisylphenylphosphino)ethane (diPAMP), which is an extremely useful ligand in catalytic asymmetric hydrogenation.[19] The *S*-enantiomer **1** (89% ee) was converted via copper(II)-promoted oxidative coupling to (*S,S*)-1,2-bis(*o*-anisylboranatophenylphosphino)ethane **2** in 65% yield.[12] This compound was then treated with diethylamine at 50 °C for 10 h to furnish optically pure (*S,S*)-diPAMP in 84% yield.

This new method involves the following characteristic features. (1) The product bisphosphine, (*S,S*)-diPAMP, is almost optically pure, even though the optical purity of the phosphine–borane is not very high (89% ee), since the meso isomer can be removed by chromatography.[20] (2) The precursor bis(phosphine–borane) is a stable crystalline solid and easily handled. (3) The final step of removing the boranato group proceeds without racemization, and the product can be easily separated from the amine–borane complex and unreacted amine.

These results led us to explore a new method for the synthesis of the key intermediate, optically active *o*-anisylmethylphenylphosphine–borane. Dichlorophenylphosphine was successively treated in one-pot with *o*-anisylmagnesium bromide, (−)-menthol/pyridine, and borane–THF complex to furnish the diastereomeric mixture of *o*-anisyl(menthyloxy)phenylphosphine–boranes (**3** and **4**). Each diastereomer was separated by preparative TLC on silica gel. The separated diastereomers were treated with MeLi in benzene to afford the desired products in almost quantitative yield.

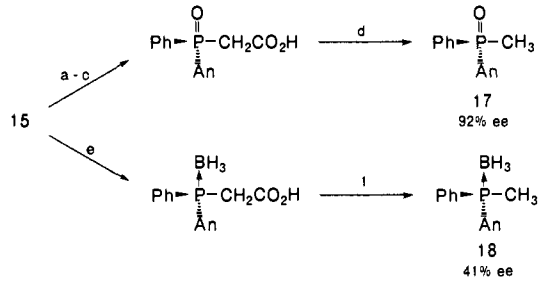
Another attempt is illustrated in Scheme IV. Dichlorophenylphosphine was successively treated with (−)-menthol/pyridine, borane–THF, and $LiAlH_4$ to give a mixture of diastereomers **5** and **6**. Each diastereomer, after separation by fractional crystallization from hexane, was converted to **7** and **8**, respectively.[21] The reaction of compound **7** with *o*-anisyllithium in refluxing benzene, 1,2-dimethoxyethane (DME), or THF afforded *o*-anisylmethylphenylphosphine–borane in good yield. Unfortunately, this compound was found to be almost racemic,[22]

Scheme VI[a]



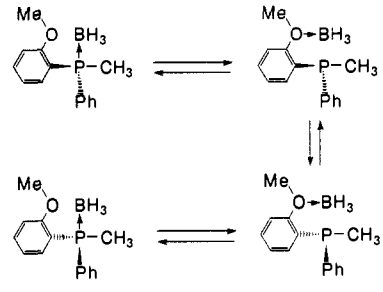
[a] (a) (−)-Menthyl chloroacetate, NaH, THF.

Scheme VII[a]



[a] (a) *N*-Methylmorpholine, 70 °C, 1 h, 88%; (b) H_2O_2, 100%; (c) KOH/MeOH, 25 °C, 3 h, 96%; (d) xylene, reflux, 5 h, 100%; (e) KOH/MeOH–THF, 25 °C, 4 h, 89%; (f) xylene, 130 °C, 1 h, 41%.

Scheme VIII



Synthesis of (*R,R*)-1,2-Bis(*tert*-butylphenylphosphino)ethane. The preparation of diPAMP via phosphine–boranes anticipates that the method can be applied to the synthesis of analogous ligands. We next tried to synthesize a new ligand, (*R,R*)-1,2-bis(*tert*-butylphenylphosphino)ethane, exploring a new method for the synthesis of optically pure phosphine–boranes having a methyl group. Our methodology is illustrated in Scheme V.

The reaction of *tert*-butylphenylphosphine–borane with (−)-menthyl chloroacetate in the presence of NaH afforded a mixture of two diastereomers of menthyl ester as a pasty oil, from which one diastereomer was obtained as a crystalline solid. The pure diastereomer **9** was hydrolyzed, and the resulting carboxylic acid **10** was subjected to decarboxylation[23] to afford optically pure (*R*)-(*tert*-butyl)methylphenylphosphine–borane (**11**).[24,25] Oxidative dimerization of **11** provided bis(phosphine–borane) **12**, which was treated with morpholine to furnish optically pure bidentate ligand **13** as a colorless crystalline solid.

Synthesis of (*S,S*)-1,4-Bis(*o*-anisylphenylphosphino)butane. There have been reported a number of chiral ligands for catalytic

(19) (a) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2567. (b) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946. (c) Knowles, W. S. *J. Chem. Educ.* **1986**, *63*, 222.

(20) Oxidative coupling proceeds through a radical intermediate; therefore, the reaction leading to homochiral isomers {(*S,S*) and (*R,R*)} has almost the same rate as that to produce meso isomer (*RS*). When *S*-enantiomer possessing 89% ee is employed, the ratio of coupling products is calculated to be (*SS*)/(*RR*)/(*RS*) = 296:1:34, removal of the meso isomer provides the product possessing 99.3% ee.

(21) The conversion of diastereomerically pure **6** to compound **4** was also examined. The treatment of **6** with *o*-iodoanisole (2 equiv) in the presence of $(Ph_3P)_4Pd$ (7 mol %) in DME at 70 °C afforded **4** with 93% de in 70% yield.

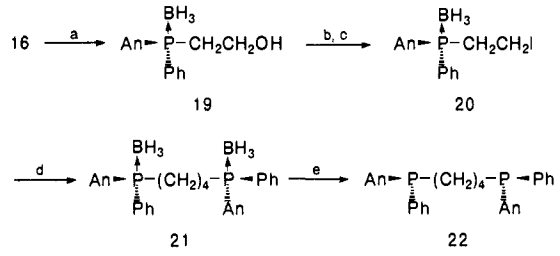
(22) *m*-Anisyllithium or *p*-anisyllithium were allowed to react with compound **7** in refluxing benzene or DME, and the products were analyzed by HPLC with "CHIRALCEL OJ". In contrast to the reaction of *o*-anisyllithium, these reactions provided the corresponding substitution products that possessed high enantiomeric excesses {*m*-anisyl: 82% ee (benzene), 95% ee (DME); *p*-anisyl: 72–88% ee (benzene), 95–99% ee (DME)}.

(23) Similar decarboxylation of phosphine oxides has been described. (a) Bodalski, R.; Rutkowska-Olma, E.; Pietrusiewicz, K. M. *Tetrahedron* **1980**, *36*, 2353. (b) Pietrusiewicz, K. M.; Zablocka, M.; Monkiewicz, J. *J. Org. Chem.* **1984**, *49*, 1522. (c) Imamoto, T.; Sato, K.; Johnson, C. R. *Tetrahedron Lett.* **1985**, *26*, 783.

(24) Absolute configuration of this compound **11** was determined to be *R* by the following transformation. Compound **11** was treated with large excess of diethylamine at 50 °C for 7 h, followed by reaction with H_2O_2 to furnish (*S*)-*tert*-butylmethylphenylphosphine oxide (mp 99.5–100.5 °C; $[\alpha]^{25}_D$ −21.6° (*c* 1.0, MeOH) (lit,[23c] mp 99–100 °C; $[\alpha]^{25}_D$ −21.8° (*c* 1.0, MeOH)).

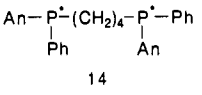
(25) Another enantiomer may be obtained in a similar procedure by the use of (+)-menthyl chloroacetate.

Scheme IX[a]



[a](a) $LiAlH_4$, 87%; (b) $MeSO_2Cl$, pyridine, 96%; (c) NaI/acetone, 74%; (d) Cu(0)–PEt_3, 64%; (e) morpholine, 70 °C, 2 h, 85%.

asymmetric reactions.[26] However, there are only a limited number of ligands which provide both excellent asymmetric induction and exceedingly high catalytic activity, We intended to synthesize a new useful ligand for catalytic asymmetric reactions. The target molecule selected is 1,4-bis(*o*-anisylphenylphosphino)butane (**14**). It is expected to exhibit similarly high asymmetric induction as diPAMP, In addition, the ligand, which forms a seven-membered chelate, may have catalytic activity higher than other ligands that form five- or six-membered chelates,[27]



Our initial trial to synthesize **14** was conducted with the reaction of *o*-anisylphenylphosphine–borane with (–)-menthyl chloroacetate in a manner similar to the preparation of ligand **13**. In this case, two diastereomers, **15** and **16**, were isolated as crystalline solids (Scheme VI),

The absolute configuration of the diastereomer **15** was determined by chemical correlations as shown in Scheme VII. Thus, **15** was converted to phosphine oxide **17** or phosphine–borane **18**, The former step provided **17** with high optical purity (92%), but in the latter, optical purity was unexpectedly low (41%). This unexpected result is ascribed to the partial racemization of the phosphine–borane at 130 °C, In order to confirm this, the same phosphine–borane with 71% optical purity was kept at the same temperature in xylene for 2 h, The optical purity of recovered phosphine–borane[28] was found to be 28%, These results can be explained by assuming the proximity effect of the *o*-methoxy group. Thus, the *o*-methoxy group abstracts the boranato group from the phosphorus atom to generate an intermediate phosphine which in turn racemizes under the conditions.[29] The process is an equilibrium, and the recovered phosphine–borane shows significant racemization.[30]

The diastereomer **16**, whose stereochemistry was established as described above, was converted to a new phosphine ligand (*S,S*)-1,4-bis(*o*-anisylphenylphosphino)butane (Scheme IX). Thus, reduction of **16** with $LiAlH_4$ afforded optically pure alcohol **19**,[31] which was derived to iodide **20** in the usual manner. The reductive dimerization of **20** by activated copper[32] afforded bis(phosphine–borane) **21**. The boranato groups of **21** were removed by treatment with a large excess of morpholine to furnish the desired ligand **22**,

Experimental Section

Synthesis of Phosphine–Boranes from Phosphine Oxides. The experimental procedure using $LiAlH_4$–$NaBH_4$–$CeCl_3$ as the reagent was described in a previous paper.[6]

Diphenylphosphine–Borane. A solution of chlorodiphenylphosphine (11.0 g, 50 mmol) in THF (20 mL) was cooled to 0 °C under argon. To this solution, borane–THF complex (38 mL of 1.7 M/L) was added, and then $LiAlH_4$ (2.3 g, 60 mmol) was added portionwise, After stirring at this temperature for 2 h, the reaction mixture was carefully poured with stirring into a mixture of concentrated HCl (20 mL) and ice (ca. 200 g). The product was extracted with benzene, and the combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was passed through a short column of silica gel eluting with benzene to give a crystalline solid (9.4 g, 94%); mp 43–44 °C (lit.[33] bp 148–150 °C/10 mmHg); IR (KBr) 2370, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.30 (dq, $^1J_{H-P}$ = 385 Hz, $^3J_{H-H}$ = 7 Hz, 1 H), 7.15–7.95 (m, 10 H). Anal. Calcd for $C_{12}H_{14}BP$: C, 72.06; H, 7.05. Found: C, 72,31; H, 7.06.

***tert*-Butylphenylphosphine–Borane.** In a 1-L, three-necked, round-bottomed flask equipped with a mechanical stirrer and a dropping funnel were placed 53.7 g (40.7 mL, 0.3 mol) of dichlorophenylphosphine and 80 mL of dry THF under argon. The flask was cooled to –78 °C, and a solution of *tert*-butylmagnesium chloride (220 mL of 1.36 M/L THF solution) was added with stirring from the dropping funnel during 1 h. After addition, the cooling bath was removed, and stirring was continued at ambient temperature for 1 h. The flask was then immersed in an ice bath, and $LiAlH_4$ (11.4 g, 0.3 mol) was added portionwise. Then, borane–THF complex (180 mL of 1.7 M/L) was added, and stirring was continued for an additional 1 h. The reaction mixture was carefully poured into a mixture of concentrated HCl (150 mL), ice (ca. 300 g), and CH_2Cl_2 (200 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The product was isolated by distillation under reduced pressure. The yield was 36.2 g (67%); bp 111–114 °C/0.4 mmHg; IR(neat) 2370, 1070 cm^{-1}; ^1H NMR (CCl_4) δ 1.18 (d, $^3J_{H-P}$ = 14 Hz, 9 H), 5.05 (dq, $^1J_{H-P}$ = 360 Hz, $^3J_{H-H}$ = 7 Hz, 1 H), 7.25–7.85 (m, 5 H). Anal. Calcd for $C_{10}H_{18}BP$: C, 66.71; H, 10.08. Found: C, 66.83; H, 10.15.

***o*-Anisylphenylphosphine–Borane.** Freshly distilled dichlorophenylphosphine (0.89 g, 5 mmol) was dissolved in dry THF (20 mL) under argon, and the solution was cooled to –78 °C. *o*-Anisylmagnesium bromide (20 mL of 0.25 M/L THF solution) was added dropwise over a period of 30 min to the solution with vigorous stirring. $LiAlH_4$ (0.188 g, 5 mmol) was added portionwise with stirring, and the mixture was warmed to ambient temperature. After stirring for an additional 2 h, borane–THF complex (6 mL of 1.0 M/L) was added at 0 °C. The reaction mixture was poured into a vigorously stirred mixture of 1 N HCl (20 mL), ice (ca. 5 g), and benzene. The organic layer was separated, and the aqueous layer was extracted with benzene. The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residual oil was dissolved in CH_2Cl_2, and the solution was passed

(26) For representative reviews, see: (a) Caplar, V.; Comisso, G.; Sujic, V. *Synthesis* **1981**, 85. (b) Hayashi, T.; Kumada, M. *Acc. Chem. Res.* **1982**, *15*, 395. (c) Kagan, H. B. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, pp 463–498. (d) Knowles, W. S. *Acc. Chem, Res.* **1983**, *16*, 106. (e) Tolman, C. A.; Faller, J. W. In *Homogeneous Catalysis with Metal Phosphine Complexes*; L. H. Pignolet, Ed.; Plenum: New York, 1983; pp 13–109. (f) Brown, J. M.; Chaloner, P. A. In *Homogeneous Catalysis with Metal Phosphine Complexes*; Fackler, J. P., Jr., Ed.; Plenum: New York, 1983; pp 137–165. (g) Ojima, I. *Pure Appl. Chem.* **1984**, *56*, 99. (h) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 5, Chapters 1–6. (i) *Asymmetric Catalysis*; Bosnich, B., Ed.; Nato ASI Series, Martinus Nijhoff: Dordrecht, 1986; Chapters 1–2. (j) Brunner, H. *J. Organomet. Chem.* **1986**, *300*, 39. (k) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books; Mill Valley, CA, 1987; Chapter 10. (l) Nogradi, M. In *Stereoselective Synthesis*; VCH: Weinheim, 1987, pp 53–87. (m) Kagan, H. B. *Bull. Soc. Chim. Fr.* **1988**, 846. (n) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581. (o) Blystone, S. L. *Chem. Rev.* **1989**, *89*, 1663. (p) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901.

(27) (a) Tanaka, M.; Hayashi, T.; Ogata, I. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2351. (b) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158.

(28) The phosphine–borane was recovered in 62% yield. The major by-product was *o*-anisylmethylphenylphosphine.

(29) (a) Munro, H. D.; Horner, L. *Tetrahedron* **1970**, *26*, 4621. (b) Baechler, R. D.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 3090.

(30) A few other phosphine–boranes were also examined for racemization under the similar conditions (*o*-xylene, 130 °C or 140 °C, 2 h). *p*-Anisylmethylphenylphosphine–borane did not readily racemize (95% ee → 93% ee at 130 °C; 95% ee → 82% ee at 140 °C), and *tert*-butylmethylphenylphosphine–borane was subjected to no racemization at 140 °C. Contrary to these results, *m*-anisylmethylphenylphosphine–borane racemized readily at 140 °C (82% ee → 75% ee at 130 °C; 82% ee → 7% ee at 140 °C). The ready racemization of *m*-anisyl derivative at 140 °C may be ascribed to the electron-attracting nature of *m*-anisyl group which decreases the electron density at the phosphorus atom. The borane complex of *m*-anisylmethylphenylphosphine, that is less stable than the corresponding *p*-anisyl derivative, reversibly dissociates to the parent phosphine and borane at elevated temperature to result in racemization.

(31) It is noted that no stereomutation of the phosphine–borane occurred under these conditions. This result is in sharp contrast to the reaction of phosphine oxides with $LiAlH_4$ which accompanies stereomutation prior to reduction.[10a]

(32) Ebert, G. W.; Reike, R. D. *J. Org. Chem.* **1984**, *49*, 5280.

(33) Hofmann, E. Brit. Patent 941, 558 (*Chem. Abstr.* **1963**, *60*, p 4185b),

through a short column of silica gel. The filtrate was concentrated to give a white solid (0.69 g, 60%).[34] Recrystallization from hexane provided a pure sample for elemental analysis; mp 95–96 °C; IR (KBr) 2380, 1585, 1475, 1255, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.75 (s, 3 H), 6.40 (dd, $^1J_{H-P}$ = 390 Hz, $^3J_{H-B}$ = 7 Hz, 1 H), 6.7–7.8 (m, 9 H). Anal. Calcd for $C_{13}H_{16}BOP$: C, 67.87 H, 7.01. Found: C, 67.84; H, 6.92.

Preparation of Phosphine–Borane Derivatives from Methyldiphenylphosphine–Borane (Ph_2MePBH_3)(General Procedure). A solution of Ph_2MePBH_3 (214 mg, 1 mmol) in dry THF (3 mL) was cooled to −78 °C under argon, and *sec*-butyllithium (1.1 mL of 1.0 M/L pentane solution) was added to the solution. After keeping the temperature for 2 h, 1.1 mmol of an electrophile (allyl bromide, trimethylsilyl chloride, or carbonyl compound) was added, and the mixture was stirred for 0.5 h. The reaction mixture was treated with 0.5 N HCl and extracted with ether. The combined extracts were washed with aqueous $NaHCO_3$ and brine and dried ($MgSO_4$). The product was obtained by preparative TLC on silica gel.

Alkylation of Diphenylphosphine–Borane ($Ph_2(H)PBH_3$) (General Procedure). A solution of KOH or MeONa (1.1 mL of 1 N solution in MeOH) was added to a mixture of $Ph_2(H)PBH_3$ (200 mg, 1 mmol) and alkyl halide (1.1 mmol) in MeOH (3 mL) at 0 °C, and the mixture was stirred until the reaction was complete. The mixture was treated with diluted HCl and extracted with ether. The product was isolated by preparative TLC.

Reaction of Diphenylphosphine–Borane with Carbonyl Compounds or Activated Olefins (General Procedure). To a mixture of $Ph_2(H)PBH_3$ (200 mg, 1 mmol) and substrate (carbonyl compound or activated olefin) (1.1 mmol) in MeOH (3 mL) was added 50 μL of 1 N KOH in MeOH under argon at 0 °C, The mixture was stirred at ambient temperature until the reaction was complete. The mixture was worked up in the usual manner, and the product was isolated by preparative TLC on silica gel.

Synthesis of $[Ph_2P(BH_3)CH_2CH_2]_3PBH_3$. A mixture of trivinylphosphine–borane[35] (63 mg, 0,5 mmol), $Ph_2(H)PBH_3$ (500 mg, 2.5 mmol), and 1 mL of 2 N KOH in MeOH was stirred under argon at room temperature for 12 h. To the mixture was added 0.1 mL of 30% H_2O_2,[36] and it was stirred for 15 min. Water was added, and the mixture was extracted with benzene. The extract was washed with aqueous $Na_2S_2O_3$ and brine, and dried (Na_2SO_4). The product was isolated by preparative TLC on silica gel (benzene). Yield was 236 mg (65%): mp 72–74 °C; IR (KBr) 3040, 2890, 2370, 1435, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45–1.90 (m, 6 H), 1.90–2.40 (m, 6 H), 7.05–7.60 (m, 30 H); MS (70 eV), *m/e* 684 (M − $3BH_3$), 670 (M−$4BH_3$). Anal. Calcd for $C_{42}H_{54}B_4P_4$: C, 69.48; H, 7.50. Found: C, 69.60; H, 7.35.

Reaction of Methylphenylphosphine–Borane with *o*-Iodoanisole in the Presence of $(Ph_3P)_4Pd$. A mixture of $PhMe(H)PBH_3$ (276 mg, 2 mmol), *o*-iodoanisole (234 mg, 1 mmol), $(Ph_3P)_4Pd$ (58 mg, 0,05 mmol), and anhydrous potassium carbonate (140 mg) in dry toluene (2 mL) was stirred at 70–80 °C under argon for 3 h. The mixture was cooled to room temperature, and water (5 mL) and a few drops of 30% H_2O_2 were added. After stirring for 15 min, the organic layer was separated, washed with aqueous $Na_2S_2O_3$ and brine, and dried (Na_2SO_4). The product *o*-anisylmethylphenylphosphine–borane (223 mg, 91% based on *o*-iodoanisole) was isolated by preparative TLC on silica gel,

(*S*)-*o*-Anisylmethylphenylphosphine–Borane (1). (*S*)-*o*-Anisylmethylphenylphosphine oxide ($[\alpha]^{25}_D$ −24.2° (*c* 1.3, MeOH) (93% ee))(1.10 g, 4.47 mmol) was reduced with $HSiCl_3$–NEt_3 according to a published procedure.[37] The crude product was allowed to react with borane–THF complex (5.6 mL of 1.2 M/L) at room temperature for 2 h. The solvent was evaporated in vacuo, and the residue was subjected to preparative TLC on silica gel (AcOEt/hexane, 1:5) to afford **1** (780 mg, 67%); mp 66.5–67.5 °C; $[\alpha]^{25}_D$ +24.1° (*c* 1.5, MeOH) (89% ee); IR (KBr) 2340, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.94 (d, $^2J_{H-P}$ = 10.5 Hz, 3 H), 3.69 (s, 3 H), 6.8–7.9 (m, 9 H). Anal. Calcd for $C_{14}H_{18}BOP$: C, 68.89; H, 7.43. Found: C, 68.81; H, 7.47. Enantiomeric excess of this compound was determined to be 89% by HPLC analysis with "CHIRALCEL OK" prepared by Daicel Chemical Industries, Ltd.

Reaction of 1 with Diethylamine. A solution of **1** (100 mg) in 1 mL of degassed diethylamine was kept under argon at 50 °C for 8 h. Excess diethylamine was removed in vacuo, and the residual oil was passed through a short column of basic alumina under argon. The solvent was evaporated in vacuo to leave (*S*)-*o*-anisylmethylphenylphosphine ($[\alpha]^{25}_D$−38.3° (*c* 1.7 MeOH)). This phosphine was oxidized by H_2O_2 to (*R*)-*o*-anisylmethylphenylphosphine oxide ($[\alpha]^{25}_D$ +23.2° (*c* 1.3, MeOH) (89% ee)).[19]

(*S*,*S*)-1,2-Bis(*o*-anisylboranatophenylphosphino)ethane (2). Optically active phosphine–borane **1** (89% ee) (488 mg, 2 mmol) was dissolvd in dry THF (6 mL) under argon, and the solution was cooled to −78 °C. To this solution *sec*-BuLi (2.2 mL of 1.0 M/L pentane solution) was added, and stirring was continued for 2 h. Anhydrous copper(II) chloride (404 mg, 3 mmol) was added with vigorous stirring. The temperature was elevated during 1.5 h to room temperature and kept at this level for 1 h. The reaction was quenched with diluted HCl, and the mixture was extracted with $CHCl_3$. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was subjected to preparative TLC on silica gel (AcOEt/hexane/CH_2Cl_2 1:4:1) to afford **2** (316 mg, 65%): mp 162.5–163.0 °C, $[\alpha]^{25}_D$−70.2° (*c* 1.3, $CHCl_3$); IR (KBr) 2370, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.58 (br s, 4 H), 3.62 (s, 6 H), 6.81 (d, *J* = 7.6 Hz, 2 H), 7.03 (t, *J* = 7.6 Hz, 2 H), 7.34–7.49 (m, 8 H), 7,63–7.70 (m, 4 H), 7.83–7.91 (m, 2 H). Anal. Calcd for $C_{28}H_{34}B_2O_2P_2$: C, 69.18; H, 7.05. Found; C, 69.23; H, 6.91.

(*S*,*S*)-1,2-Bis(*o*-anisylphenylphosphino)ethane (diPAMP). Bis(phosphine–borane) **2** (100 mg, 0.21 mmol) was dissolved in 2 mL of degassed diethylamine, and the solution was kept at 50 °C for 10 h under argon. Excess diethylamine was removed in vacuo, and the residue was passed through a short column of basic alumina eluting with degassed benzene under argon to give practically pure diPAMP (81 mg, 84%). The product was recrystallized from hot methanol under argon to give a pure product: mp 102–103 °C; $[\alpha]^{24}_D$ +87.0° (*c* 1.0, $CHCl_3$)(lit.[19] mp 102–104 °C; $[\alpha]^{25}_D$ −85.0° (*c* 1.0, $CHCl_3$)).

(S_P,1′*R*,2′*S*,5′R)-Anisyl((2′-isopropyl-5′-methylcyclohexyl)oxy)phenylphosphine–Borane (3) and (R_P,1′*R*,2′*S*,5′*R*)-Anisyl((2′-isopropyl-5′-methylcyclohexyl)oxy)phenylphosphine–Borane (4). *o*-Anisylmagnesium bromide (40 mL of 0.25 M/L THF solution) was added dropwise during 50 min into a solution of dichlorophenylphosphine (1.1 mL, 8.1 mmol) in dry THF (40 mL) with vigorous stirring at −78 °C under argon. After addition, (−)-menthol (1.56 g, 10 mmol) and pyridine (0,8 mL, 10 mmol) were added at the same temperature. The cooling bath was removed, and the mixture was allowed to stir overnight at ambient temperature. The reaction mixture was filtered quickly to remove pyridinium salt, and the filtrate was cooled to 0 °C. Then, borane–THF complex (30 mL of 1.0 M/L) was added. After stirring at room temperature for 1 h, the reaction mixture was quenched with 1 N HCl (100 mL). The product was extracted with ether. The combined extracts were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residual oil was subjected to column chromatography on silica gel (Wakogel C-200) with benzene/hexane (1:1) as the eluent. The product, which was obtained as a pasty mass, was triturated with hexane to give a mixture of **3** and **4** as white powder (2.83 g).

Each diastereomer was separated by preparative TLC on silica gel with toluene/cyclohexane (1:4) as the developing solvent.

3: oil; $[\alpha]^{25}_D$ −75.6° (*c* 0.9, C_6H_6); IR (neat) 2950, 2390, 1590, 1480, 1280 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0.49 (d, *J* = 6.9 Hz, 3 H), 0.80–1.64 (m, 13 H), 1.92–1.96 (m, 1 H), 2.09 (m, 1 H), 3.53 (s, 3 H), 4.23–4.25 (m, 1 H), 6.80–7.96 (m, 9 H). Anal. Calcd for $C_{23}H_{34}BO_2P$: C, 71.88; H, 8.92. Found: C, 71.49; H, 8.63. Diastereomeric excess of this compound was determined to be 100% by ^1H NMR (500 MHz).

4: mp 85.0–87.5 °C; $[\alpha]^{25}_D$ −49.0° (*c* 1.0, C_6H_6); IR (KBr) 2940, 2390, 1480, 1280, 1015, 765 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0,55 (d, *J* = 6.9 Hz, 3 H), 0.79–1.64 (m, 13 H), 1.87–1.91 (m, 1 H), 2.06 (m, 1 H), 3.55 (s, 3 H), 4.26–4.29 (m, 1 H), 6.82–7.93 (m, 9 H). Anal. Calcd for $C_{23}H_{34}BO_2P$: C, 71.88; H, 8.92. Found; C, 71.85; H, 8,80. Diastereomeric excess of this compound was determined to be 93% by ^1H NMR (500 MHz).

Reaction of 3 and 4 with Methyllithium. Methyllithium (0,5 mL of 1.3 M/L ether solution) was added to a solution of **3** (83 mg, 0.2 mmol) in dry benzene (3 mL) at room temperature. After stirring for 3 h, the reaction was quenched with diluted HCl. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was subjected to preparative TLC on silica gel (benzene/hexane 2:1) to give *o*-anisylmethylphenylphosphine–borane (50 mg, 95%): oil; $[\alpha]^{25}_D$ −27.0° (*c* 1.5, MeOH). Enantiomeric excess of this compound was determined to be 100% by HPLC analysis with "CHIRALCEL OK" prepared by Daicel Chemical Industries, Ltd.

In a similar manner, compound **4** was converted to other enantiomer; $[\alpha]^{25}_D$ +25.2° (*c* 1.6, MeOH) (93% ee).

(S_P,1′*R*,2′*S*,5′*R*)-((2′-Isopropyl-5′-methylcyclohexyl)oxy)phenylphosphine–Borane (5) and (R_P,1′*R*,2′*S*,5′*R*)-((2′-Isopropyl-5′-methylcyclohexyl)oxy)phenylphosphine–Borane (6). A mixture of (−)-menthol (28.8 g, 0.185 mol) and pyridine (15 mL, 0.185 mol) in 100 mL of dry

(34) Experiment with 50 mmol scale provided lower yield (30–40%).

(35) Trivinylphosphine–borane was prepared by the addition of 1 equiv of borane–THF complex to trivinylphosphine prepared from phosphorus trichloride and vinylmagnesium bromide.

(36) For easier separation by preparative TLC, the starting phosphine–borane was oxidized with H_2O_2.

(37) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D. *Adv. Chem. Ser.* **1974**, *132*, 274.

benzene was added during 2 h dropwise into a stirred dichlorophenylphosphine (25 mL, 0.185 mol) in 100 mL of dry benzene at room temperature under argon, The reaction mixture was stirred for 12 h, and it was filtered quickly to remove the pyridinium salt. The filtrate was added slowly to a solution of $LiAlH_4$ (8.42 g, 0.222 mol) and borane–THF complex (225 mL of 1.0 M/L) in dry THF (100 mL) at 0 °C. After stirring at room temperature for 30 min, the reaction mixture was poured into a vigorously stirred mixture of concentrated HCl (40 mL), ice (ca. 200 g), and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed with brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel (benzene/hexane 1:2) to give a mixture of **5** and **6** as a white powder. It was recrystallized from hexane 3 times to give a pure diastereomer **5** (5.7 g). Another diastereomer **6** (ca. 0.6 g) was obtained from the mother solution.

5: colorless needles; mp 94–96 °C; $[\alpha]^{25}_D$ −117.6° (*c* 1.0, $ClCH_2CH_2Cl$); IR (KBr) 2900, 2375, 1445, 1135, 1060, 970 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0.6–1.7 (m, 7 H), 0.63 (d, *J* = 7.2 Hz, 3 H), 0.888 (d, *J* = 6.60 Hz, 3 H), 0.893 (d, *J* = 6.88 Hz, 3 H), 2.01–2.08 (m, 2 H), 3.85–3.94 (m, 1 H), 7.48–7.60 (m, 3 H), 7.77–7.82 (m, 2 H); ^{11}B NMR (96 MHz) ($CDCl_3$) δ (relative to external $(CH_3O)_3B$) −58.9 (d, J_{B-P} = 59,0 Hz); MS (70 eV), *m/e* 264 ($M^+ - BH_3$). Anal. Calcd for $C_{16}H_{28}OBP$: C, 69.08; H, 10.14. Found: C, 69.03; H, 9.93.

6: colorless cubes; mp 81–82 °C; $[\alpha]^{25}_D$ −62.8° (*c* 1.0, $ClCH_2CH_2Cl$); IR (KBr) 2900, 2390, 1435, 1130, 1060, 970 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0.6–1.8 (m, 7 H), 0.70 (d, *J* = 6.87 Hz, 3H), 0.85 (d, *J* = 6.87 Hz, 3 H), 0.91 (d, *J* = 6.32 Hz, 3 H), 1.92–1.96 (m, 1 H), 2.04–2.09 (m, 1 H), 3.97–4.04 (m, 1 H), 7.49–7.60 (m, 3 H), 7.77–7.82 (m, 2 H); ^{11}B NMR (96 MHz) ($CDCl_3$) δ (relative to external $(CH_3O)_3B$) −59.1 (d, J_{B-P} = 59.0 Hz). Anal. Calcd for $C_{16}H_{28}OBP$: C, 69.08; H, 10.14. Found: C, 68.87; H, 9.90.

(R_P,1′*R*,2′*S*,5′*R*)-((2′-Isopropyl-5′-methylcyclohexyl)oxy)methylphenylphosphine–Borane (7) and (S_P,1′*R*,2′*S*,5′*R*)-((2′-Isopropyl-5′-methylcyclohexyl)oxy)methylphenylphosphine–Borane (8), Sodium hydride (92 mg of 40% oil dispersion, 2.3 mmol) was added to a mixture of **5** (167 mg, 0.60 mmol) and iodomethane 48 μL, 0.77 mmol) in 3 mL of THF at 0 °C under argon. After stirring at room temperature for 1 h, the reaction mixture was treated with 1 N HCl. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed with aqueous $Na_2S_2O_3$ and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residual oil was subjected to preparative TLC on silica gel (benzene/hexane 1:4) to give **7** as a white crystalline solid (175 mg, 100%). In a similar manner the other diastereomer **8** was obtained in quantitative yield.

7: mp 65,0–66,0 °C; $[\alpha]^{26}_D$ −6.0° (*c* 1.03, C_6H_6); IR (KBr) 2910, 2350, 1440, 1020, 1000, 910 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0.77 (d, *J* = 6.60 Hz, 3 H), 0.86 (d, *J* = 7.14 Hz, 3 H), 0.94 (d, *J* = 7.15 Hz, 3 H), 1.64 (d, $^3J_{H-P}$ = 9.07 Hz, 3 H), 2.06–2.17 (m, 1 H), 4.09–4.17 (m, 1 H), 0.40–1.80 (m, 8 H), 7.44–7.84 (m, 5 H); MS (70 eV), *m/e* 278 ($M - BH_3$). Anal. Calcd for $C_{17}H_{30}OBP$: C, 69.88; H, 10.35. Found: C, 69.82; H, 10.07. This compound was treated successively with morpholine and H_2O_2 in order to determine the abolute configuration at phosphorus. The product (mp 88–89 °C; $[\alpha]^{26}_D$ −17.3° (*c* 1.0, C_6H_6) was identified as (*R*P̂)-menthyl methylphenylphosphinate (lit.[38] mp 89 °C; $[\alpha]_D$ −16° (C_6H_6)).

8: oil; $[\alpha]^{26}_D$ −119.1° (*c* 1.03, C_6H_6); IR (neat) 2900, 2350, 1440, 1010, 990, 910 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0.41 (d, *J* = 7.14 Hz, 3 H), 0.77 (d, *J* = 7.15 Hz, 3 H), 0.93 (d, *J* = 6.60 Hz, 3 H), 1.72 (d, $^3J_{H-P}$ = 9.07 Hz, 3 H), 2.21–2.26 (m, 1 H), 3.95–4.02 (m, 1 H), 0.40–1.77 (m, 8 H), 7.44–7.84 (m, 5 H); MS (70 eV), *m/e* 278 ($M - BH_3$). Anal. Calcd for $C_{17}H_{30}OBP$: C, 69.88; H, 10.35. Found: C, 69.93; H, 10.21.

(R_P,1′*R*,2′*S*,5′*R*)-*tert*-Butyl[[((2′-isopropyl-5′-methylcyclohexyl)oxy)carbonyl]methyl]phenylphosphine–Borane (9). A mixture of *tert*-butylphenylphosphine–borane (18.5 g, 0.103 mol) and (−)-menthyl chloroacetate[39] (24 g, 0.103 mol) in 30 mL of dry THF was added dropwise to a stirred slurry of NaH (0.25 mol) in dry THF (20 mL) at 0 °C during 0.5 h. After addition, the mixture was gradually warmed to 40 °C and kept at this temperature for 1 h, The reaction mixture was cooled to room temperature and diluted with hexane (150 mL); then it was poured into ice–water (ca. 300 g) containing acetic acid (15 mL). The organic layer was separated, and the aqueous layer was extracted with hexane. The combined extracts were washed with aqueous $NaHCO_3$ and brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the residue was dissolved in 30 mL of hexane. The solution was kept in a refrigerator at 5 °C for 3 days. A crystalline solid (12.3 g) was collected, and it was further recrystallized from hexane 4 times to give a pure diastereomer **9** (8.2 g): mp 106.5–107.5 °C; $[\alpha]^{25}_D$ +20.6° (*c* 0.9, MeOH); IR (KBr) 2930, 2380, 1725, 1275, 1125, cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.45–2.00 (m, 18 H), 1.13 (d, $^3J_{H-P}$ = 15 Hz, 9 H), 2.8–3.4 (m, 2 H), 4.3–4.7 (m, 1 H), 7.2–7.9 (m, 5 H); MS (70 eV), *m/e* 376 ($M - BH_3$), 237, 225, 210, 169, 168, 139. Anal. Calcd for $C_{22}H_{38}BO_2P$: C, 70.22; H, 10.18. Found: C, 70.41; H, 9.99.

(*R*)-*tert*-Butyl(carboxylmethyl)phenylphosphine–Borane (10). A solution of KOH (3.8 g) in MeOH (22 mL) was added to a solution of phosphine–borane **9** (8.11 g, 21.6 mmol) in THF (15 mL). The mixture was stirred at room temperature for 2 h, whereupon a large amount of precipitate appeared. Water (5 mL) was added to dissolve the precipitate, and the mixture was allowed to stand at room temperature overnight. The mixture was diluted with water and extracted with ether twice. The aqueous layer was acidified with concentrated HCl and extracted with CH_2Cl_2. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to leave **10** (5.13 g, 99%): mp 124,5–125.5 °C; $[\alpha]^{25}_D$ + 84.5° (*c* 1.0, MeOH); IR (KBr) 2940, 2390, 1705, 1300, 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (d, $^3J_{H-P}$ = 15 Hz, 9 H), 2.95–3.25 (m, 2 H), 7.3–7.9 (m, 5 H). Anal. Calcd for $C_{12}H_{20}BO_2P$: C, 60.54; H, 8.47. Found: C, 60.57; H, 8.22.

(*R*)-*tert*-Butylmethylphenylphosphine–Borane (11). A solution of **10** (1.5 g, 6.3 mmol) in pure anisole (45 mL) was heated at 110 °C for 2.5 h under argon. The solvent was removed in vacuo, the residue was passed through a short column of silica gel eluting with benzene, and the filtrate was concentrated. The residue was subjected to preparative TLC on silica gel (benzene/hexane 2:1) to give **11** (620–920 mg, 51–75%). Recrystallization from hexane afforded a pure product: mp 52.5–53.0 °C; $[\alpha]^{25}_D$ −8.2° (*c* 1.0, MeOH); IR (KBr) 2950, 2370, 1440, 1370, 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (d, $^3J_{H-P}$ = 15 Hz, 9 H), 1.55 (d, $^2J_{H-P}$ = 10 Hz, 3 H), 7.3–7.8 (m, 5 H). Anal. Calcd for $C_{11}H_{20}BP$: C, 68.08; H, 10.39. Found: C, 68.13; H, 10.17. Enantiomeric excess of this compound was determined to be 100% ee by HPLC analysis with "CHIRALPAK OT".

(*R*,*R*)-1,2-Bis(boranato-*tert*-butylphenylphosphino)ethane (12). This compound was prepared in 76% yield from **11** in a similar procedure as the preparation of **2**: mp 154–156 °C (hexane); $[\alpha]^{25}_D$ −51.2° (*c* 0.9, MeOH); IR (KBr) 2960, 2370, 1460, 1370, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, $^3J_{H-P}$ = 13.9 Hz, 18 H), 1.98–2.06 (m, 2 H), 2.26–2.33 (m, 2 H), 7.41–7.61 (m, 10 H). Anal. Calcd for $C_{22}H_{38}B_2P_2$: C, 68.44; H, 9.92. Found: C, 68.41; H, 9.74.

(*R*,*R*)-1,2-Bis(*tert*-butylphenylphosphino)ethane (13). Bis(phosphine–borane) **12** (130 mg, 0.34 mmol) was dissolved in degassed morpholine (2 mL) under argon. The solution was kept at 70 °C for 2 h. Unreacted morpholine was removed in vacuo, and the residue was washed with degassed methanol under argon to give practically pure **13** (112 mg, 92%). A pure compound was obtained by recrystallization from hot methanol under an atmosphere of high grade argon: mp 110.5–111.5 °C; $[\alpha]^{25}_D$ +78.7° (*c* 0.9, C_6H_6); IR (KBr) 2920, 1430, 1360, 755, 705 cm^{-1}; ^1H NMR (C_6D_6) δ 0.84 (d, $^3J_{H-P}$ = 11.6 Hz, 18 H), 1.86–1.96 (m, 2 H), 2.02–2.10 (m, 2 H), 7.03–7.71 (m, 10 H); HRMS calcd for $C_{14}H_{14}P_2$ 301.1277 ($M - t\text{-}C_4H_9$), found 301.1298.

(R_P,1′*R*,2′*S*,5′*R*)-*o*-Anisyl[[((2′-isopropyl-5′-methylcyclohexyl)oxy)carbonyl]methyl]phenylphosphine–Boranes (15) and (S_P,1*R*,2′*S*,5′*R*)-*o*-Anisyl[[((2′-isopropyl-5′-methylcyclohexyl)oxy)carbonyl]methyl]phenylphosphine–Boranes (16). A mixture of *o*-anisylphenylphosphine–borane (4.6 g, 20 mmol) and (−)-menthyl chloroacetate (5.6 g, 24 mmol) in dry THF (20 mL) was added dropwise during 30 min to a stirred suspension of oil-free NaH (30 mmol) in THF (30 mL) at 0–5 °C under argon. After addition, the mixture was heated 40 °C for 1 h. The reaction mixture was slowly added to a mixture of 0.5 N HCl (100 mL) and benzene (50 mL). The organic layer was separated, and the aqueous layer was extracted with benzene. The combined extracts were washed with aqueous $NaHCO_3$ and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residual oil was chromatographed on silica gel (benzene/hexane 1:2) to give a mixture of two diastereomers as a pasty oil. Trituration of the oil with hexane afforded a white powder (6.3 g). Fractional crystallization of the powder from hexane afforded **15** (2.6 g) and **16** (1.7 g).

15: colorless plates; mp 100–101 °C; $[\alpha]^{25}_D$ −8.1° (*c* 1.0, $ClCH_2CH_2Cl$); IR (KBr) 2920, 2370, 1720, 1475, 1260 cm^{-1}; ^1H NMR (500 MHz) ($CDCl_3$) δ 0.62–1.85 (m, 18 H), 3.36–3.72 (m, 2 H), 3.75 (s, 3 H), 4.52–4.57 (m, 1 H), 6.89–7.90 (m, 9 H). Anal. Calcd for $C_{25}H_{36}BO_3P$: C, 70.43; H, 8.51. Found: C, 70.25; H, 8.28.

16: colorless needles; mp 120–121 °C; $[\alpha]^{25}_D$ −41.7° (*c* 1.0, $ClCH_2CH_2Cl$); IR (KBr) 2920, 2370, 1690, 1475, 1250 cm^{-1}; ^1H NMR

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(40) In a similar manner, another diastereomer **15** was converted to the corresponding alcohol whose rotation was $[\alpha]^{25}_D$ −4.5° (*c* 1.0, $ClCH_2CH_2Cl$).

(41) Major byproduct was (*S*)-*o*-anisylethylphenylphosphine–borane.

(500 MHz) ($CDCl_3$) δ 0.64-1.78 (m, 18 H), 3.43-3.65 (m, 2 H), 3.76 (s, 3 H), 4.54-4.59 (m, 1 H), 6.90-7.88 (m, 9 H). Anal. Calcd for $C_{25}H_{36}BO_3P$: C, 70.43; H, 8.51. Found: C, 70.59; H, 8.48.

(*S*)-*o*-Anisyl(2-hydroxyethyl)phenylphosphine-Borane (19). A solution of **16** (2.13 g, 5 mmol) in dry ether (10 mL) was added to a slurry of $LiAlH_4$ (190 mg, 5 mmol) in ether (10 mL) at 0-10 °C under argon. The mixture was stirred at ambient temperature for 2 h, and the reaction was quenched with diluted HCl. The product was extracted with ether, the combined extracts were washed and dried ($MgSO_4$), and the solvent was evaporated. The residual oil was purified by column chromatography on silica gel eluting with AcOEt/hexane (1:1) to give **19** as a colorless oil (1.20 g, 87%). Enantiomeric excess of this compound was determined to be 100% by HPLC analysis with "CHIRALPAK OP": $[\alpha]^{25}_D$ +4.6° (*c* 1.0, $ClCH_2CH_2Cl$);[40] IR (neat) 3360, 2930, 2370, 1590, 1480, 1255 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.2 (br s, 1 H), 2.5-3.0 (m, 2 H), 3.58 (s, 3 H), 3.6-4.0 (m, 2 H), 6.6-7.9 (m, 9 H). Anal. Calcd for $C_{15}H_{20}BO_2P$: C, 65.73; H, 7.35. Found: C, 65.70; H, 7.53.

(*S*)-*o*-Anisyl-(2-iodoethyl)phenylphosphine-Borane (20). Methanesulfonyl chloride (0.40 g, 3.5 mmol) was added to a solution of **19** (0.79 g, 2.9 mmol) in dry pyridine (1 mL) at 0 °C, and the mixture was stirred at this temperature for 2 h. Water was added, and the product was extracted with ether. The combined extracts were washed with diluted HCl, brine, aqueous $NaHCO_3$, and brine and dried ($MgSO_4$). The solvent was evaporated, and the residue was chromatographed on silica gel with AcOEt/hexane (1:1) as the eluent to give the corresponding methanesulfonate as a pasty oil (0.98 g, 96%). This product was stirred with NaI (8 mmol) in dry acetone (8 mL) at 40 °C for 20 h. Water was added, and the product was extracted with ether. The combined extracts were washed with brine and dried ($MgSO_4$), and the solvent was evaporated. The residue was chromatographed on silica gel with AcOEt/hexane (1:5) to afford **20** (0.79 g, 71% from **19**). Recrystallization from hexane provided a sample for elemental analysis; mp 74-75 °C; $[\alpha]^{25}_D$ +6.7° (*c* 1.0, C_6H_6); IR (KBr) 2350, 1580, 1475, 1240, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80-3.40 (m, 4 H), 3.74 (s, 3 H), 6.8-8.0 (m, 9 H). Anal. Calcd for $C_{15}H_{19}BIOP$: C, 46.92; H, 4.99. Found: C, 46.99; H, 5.03.

(*S,S*)-1,4-Bis(*o*-anisylboranatophenylphosphino)butane (21). A solution of activated copper (4 mg atom) in dry THF was prepared according to the Rieke method,[32] and it was cooled to 0 °C. To this solution, **20** (384 mg, 1 mmol) was added in one portion with vigorous stirring. After 30 min, the reaction mixture was passed through a short column of silica gel eluting with CH_2Cl_2. The filtrate was concentrated in vacuo, and the residue was subjected to preparative TLC with AcOEt/hexane (1:2) as the developing solvent to give **21** (51-70%):[41] mp 156-158 °C; $[\alpha]^{25}_D$ +11.8° (*c* 1.0, C_6H_6); IR (KBr) 2350, 1580, 1475, 1250, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2-1.9 (m, 4 H), 1.9-2.6 (m, 4 H), 3.58 (s, 6 H), 6.65-7.90 (m, 18 H); ^{31}P NMR (121 MHz) ($CDCl_3$) δ (relative to external $(PhO)_3PO$) 25.2 (br s), 25.8 (br s); ^{11}B NMR (96 MHz) ($CDCl_3$) δ (relative to external $(CH_3O)_3B$) -57.3 (br s). Anal. Calcd for $C_{30}H_{38}B_2O_2P_2$: C, 70.08; H, 7.45. Found: C, 69.73; H, 7.35.

(*S,S*)-1,4-Bis(*o*-anisylphenylphosphino)butane (22). Bis(phosphine-borane) **21** (200 mg, 0.39 mmol) was dissolved in degassed morpholine (2 mL) under argon, and the solution was kept at 70 °C for 2 h. The solvent was removed in vacuo, and the residue was subjected to preparative TLC (benzene) under argon to give **22** (161 mg, 85%): mp 99.0-101.5 °C; $[\alpha]^{25}_D$ -18.2° (*c* 1.0, C_6H_6); IR (KBr) 2920, 1570, 1460, 1435, 1245, 1025 cm^{-1}; ^1H NMR (C_6D_6) δ 1.59-1.70 (m, 4 H), 1.88-1.94 (m, 2 H), 2.08-2.12 (m, 2 H), 3.18 (s, 6 H), 6.43-7.54 (m, 18 H); ^{31}P NMR (121 MHz) ($CDCl_3$) δ (relative to external $(PhO)_3PO$) 58.1 (s), 58.3 (s); HRMS calcd for $C_{30}H_{32}O_2P_2$ 486.1880, found 486.1886.

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Specific Detection of C-4′ Hydroxylated Abasic Sites Generated by Bleomycin and Neocarzinostatin in DNA

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Abstract: A new, general method for detection and quantitation of C-4′ hydroxylated abasic sites generated by bleomycin and neocarzinostatin in DNA was described. The specific detection method was based on a chemical and enzymatic transformation of C-4′ hydroxylated abasic sites to deoxynucleoside 3′-(3-pyridazinylmethyl) phosphates. Enzymatic digestion of 3′-(3-pyridazinylmethyl) 2′-deoxycytidylyl-(3′-5′)-2′-deoxy-3′-guanylate (**7**) with snake venom phosphodiesterase (s.v. PDE) and alkaline phosphatase (AP) gave 2′-deoxycytidine and 3′-(3-pyridazinylmethyl) 2′-deoxyguanylate (**4**) in high yields, indicating that a pyridazine-substituted phosphodiester bond at the 3′-end resists digestion with s.v. PDE. Enzymatic digestion of d(CGCGAATTCGCG) treated with photoactivated green cobalt-peplomycin (Co·PEM) with s.v. PDE and AP following treatment with aqueous hydrazine was examined. Consistent with the previous results on the cleavage of this dodecanucleotide, **4** was obtained as a major product. Photoactivated Co·PEM also mediated spontaneous thymine release from poly(dA-dT) with formation of **5** and **6**. Digestion of Co·PEM-treated calf thymus DNA having a C-4′ hydroxylated abasic site gave pyridazine derivatives **3**–**6** and the total amount of **3**–**6** corresponded well to the sum of spontaneously released free bases. Also investigated was the formation of **3**–**6** in Fe·PEM- and neocarzinostatin- (NCS-) mediated degradation of calf thymus DNA. Hydrazine treatment of their reaction mixtures followed by enzymatic digestion produced pyridazine derivatives **3**–**6**, indicating that C-4′ hydroxylated abasic sites are actually produced in calf thymus DNA. Quantitative analysis indicated that C-4′ hydroxylation is estimated to be a minimum of 17% of the total event caused by the action of NCS on calf thymus DNA.

The chemistry of DNA backbone oxidation mediated by naturally occurring antitumor antibiotics[1] and designed DNA-cleaving molecules[2] is a topic of intense current interest. Such DNA cleavers usually oxidize the deoxyribose moiety via hydrogen

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