JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Reduction of Functionalized Tertiary Phosphine Oxides with BH_3

Sylwia Sowa,[†] Marek Stankevič,[†] Anna Szmigielska,[†] Hanna Małuszyńska,[‡] Anna E. Kozioł,[§] and K. Michał Pietrusiewicz*,[†]

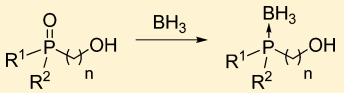
[†]Department of Organic Chemistry, Faculty of Chemistry, Maria Curie Sklodowska University, Gliniana Street 33, Lublin 20-614, Poland

[‡]Department of Radiospectroscopy, Faculty of Physics, Adam Mickiewicz University, Umultowska Street 85, 61-614 Poznań, Poland

[§]Department of Crystallography, Faculty of Chemistry, Maria Curie-Sklodowska University, Maria Curie Sklodowska Square 3, Lublin 20-031, Poland

Supporting Information

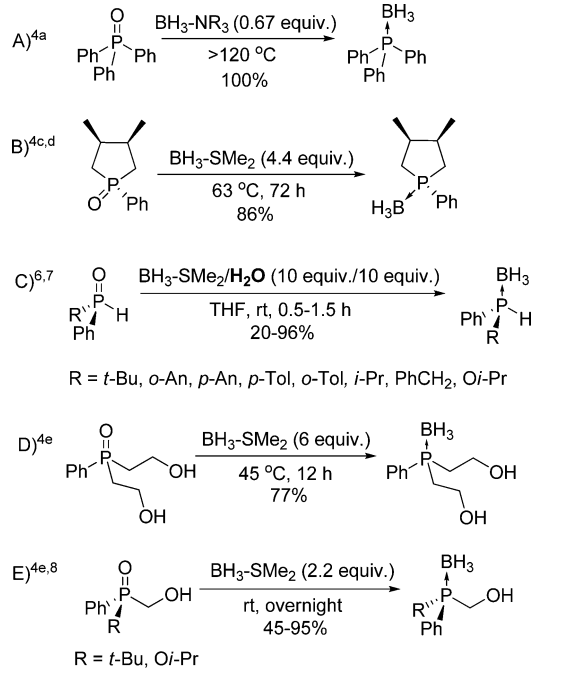
ABSTRACT: A direct stereoselective conversion of tertiary hydroxyalkylphosphine oxides to the corresponding tertiary hydroxyalkylphosphine−boranes involving facile reduction of the P═O bond by BH_3 under mild conditions has been developed. The unprecedented facility of reduction of the strong P═O bond by BH_3, a mild reducing agent, has been achieved through an intramolecular P═O···B complexation directed by proximal α- or β-hydroxy groups present in the phosphine oxide structures. As established by two chemical correlations, the developed transformation of hydroxyalkylphosphine oxides into hydroxyalkylphosphine−boranes takes place with complete inversion of configuration at P.



INTRODUCTION

Difficulties in reduction of the strong P═O bond or its conversion into a P−BH_3 bond still continue to cause numerous problems in syntheses of organophosphorus compounds utilizing robust phosphine oxides as intermediates. Although several useful reagents based on metal hydrides[1] and hydrosilanes[2] have been developed for reduction of the P═O bond, their use typically requires harsh reaction conditions which are not always compatible with functionalized and/or nonracemic P-stereogenic substrates. New milder methods for efficient and operationally simple reduction of P═O are thus in constant demand, and those which could allow for the direct transformation of P═O into an easily handled and storable borane-protected phosphine without isolation of the intermediate phosphine would be of high practical value. Conversions of phosphine oxides into phosphine−boranes are usually conducted by a two-step reduction−complexation sequence which involves reduction of the P═O bond with a strong reducing agent followed by complexation of the resulting phosphine with borane.[3] A more straightforward approach would be to apply borane reducing agent which could secure both the reduction of P═O and the complexation of the intermediate phosphine. To date, the number of precedents concerning the use of borane as an effective reducing agent for this transformation are very low in number and are of very limited scope.[4,5] The pertinent examples are displayed in Scheme 1. Recently, we reported that BH_3·SMe_2 could be used to effectively reduce secondary phosphine oxides to provide the corresponding secondary phosphine−boranes directly and under mild conditions.[6,7] We also observed that this conversion was facilitated by the addition of a small amount of water to the reaction mixture. Herein, we report that similarly straightforward conversion of tertiary phosphine oxides into the corresponding tertiary phosphine−boranes can be also acomplished by using commercially available BH_3 complexes under mild conditions.

Scheme 1. Previous Attempts at Phosphine Oxide Reduction with BH_3



Received: November 17, 2014
Published: January 12, 2015

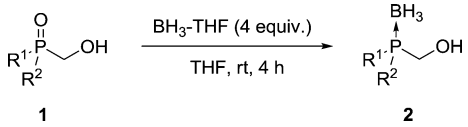
DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

RESULTS AND DISCUSSION

The observed beneficial effect of added water in the reduction of secondary phosphine oxides by BH_3·SMe_2 prompted us to hypothesize that placement of a hydroxyl group in the vicinity of the P═O function could bring similar activating effect intramolecularly. Singular examples of successful reductions of tertiary hydroxyalkyl phosphine oxides by BH_3 described by Kiełbasiński et al.[4e,8] (Scheme 1D,E) corroborated this hypothesis further. To check its generality, we synthesized four sets of tertiary hydroxyalkylphosphine oxides, i.e., hydroxymethylphosphine oxides >P(O)CH_2OH **1**, (1-hydroxyethyl)phosphine oxides >P(O)CH(Me)OH **4**, ((1-hydroxy)phenylmethyl)phosphine oxides >P(O)CH(Ph)OH **6**, and (2-(2-hydroxy)propyl)phosphine oxides >P(O)C-$(CH_3)_2$OH **10** and subjected them to reduction by borane complexes.

The validity of the concept was first tested by reactions of (hydroxymethyl)phosphine oxides **1** with BH_3·THF at room temperature. We were pleased to find that, under these mild conditions, the phosphine oxides were readily reduced and directly provided the corresponding phosphine–boranes in high to excellent yields within 3–4 h of reaction time (Table 1).

Table 1. Reaction of Phosphine Oxides 1 with BH_3·THF



1 **2**

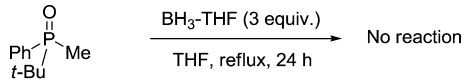
		substituents		
entry	compd	R^1	R^2	isolated yield of **2** (%)
1	**1a**	Ph	*o*-An	100
2	**1b**	Ph	1-Nphth[a]	86
3	**1c**	*p*-An	*p*-An	90
4	**1d**	*p*-F-C_6H_4	*p*-F-C_6H_4	72
5	**1e**	3,5-Me_2-C_6H_3	3,5-Me_2-C_6H_3	57
6	**1f**	Ph	*t*-Bu	98
7	**1g**	Ph	$PhCH_2$	99
8	**1h**	Ph	*i*-Pr	85(90)[b]
9	**1i**	Ph	*c*-Hex	80(93)[b]
10	**1j**	Ph	Me	72
11	**1k**	*c*-Hex	*c*-Hex	69(89)[c]
12	**1l**	*n*-Hex	*n*-Hex	76(87)[b]

[a]Nphth = naphthyl. [b]5 equiv of BH_3·SMe_2 was used. [c]Reaction run for 16 h.

The results collected in Table 1 reveal that either diaryl-, dialkyl-, or alkylaryl(hydroxymethyl)phosphine oxides **1**, including also sterically crowded ones (entries 1, 2, and 6), can be reduced under these conditions with equal facility. As demonstrated in entries 8, 9, and 12, replacement of BH_3·THF by BH_3·SMe_2, or use of a longer reaction time in some more difficult reductions (entry 11), may lead to a marked improvement of the overall yields.

To confirm the promoting effect of the α-hydroxyl group in the studied reductions, a reduction of *tert*-butylmethylphenylphosphine oxide (**3f**) devoid of the α-hydroxyl group was attempted. As shown in Scheme 2, no reaction was observed and the starting oxide **3f** was recovered unchanged. This result underscores the key role of the α-hydroxy group in the studied reduction process since *tert*-butyl(hydroxymethyl)phenylphosphine oxide (**1f**) underwent clean and nearly quantitative reduction under even milder conditions (Table 1, entry 6).

Scheme 2



3

A short series of α-monosubstituted (hydroxymethyl)-phosphine oxides >P(O)CH(R^3)OH **4**–**6** was screened next (Table 2). For the purpose of this study, the unsymmetrically P-substituted phosphine oxides **4**–**6** were used in the form of diastereoisomeric mixtures as indicated.

As found above for phosphine oxides **1**, phosphine oxides **4**–**6** showed similar propensity to reduction by BH_3·THF and yielded the corresponding tertiary phosphine–boranes **7**–**9** with comparable efficiency. This time, however, prolonged reaction times and increased reaction temperatures were sometimes required to drive the reaction to completion. Also, changing BH_3·THF to BH_3·SMe_2 resulted in improvement of yields of boranes **7** and **9** (cf., entries 1, 6, and 7, Table 2).

A short series of α,α-disubstituted (hydroxymethyl)-phosphine oxides **10** was also subjected to the reaction with BH_3 complexes, and the obtained results are listed in Table 3. In most cases the main or even the only product isolated from the reaction mixture was the desired phosphine borane **12**. However, in the case of a more crowded phosphine oxide **10b**, phosphinous acid–borane **14b** was found as the major component of the product mixture. In turn, treatment of **10d** with BH_3·SMe_2 led to the formation of phosphinous acid–borane **14d**, secondary phosphine–borane **15d**, and tertiary phosphine borane **12d**. These two results suggest that an excessive sterical crowding as well as electron-withdrawing nature of P-substituents can cause pronounced instability of the starting phosphine oxides, e.g., **10b** and **10d**, resulting in their partial decomposition to acetone and the corresponding secondary phosphine oxide. Reduction of the latter by BH_3 led to the formation of the observed side products **14** and **15** according to the complexation vs reduction pattern described previously.[6,7]

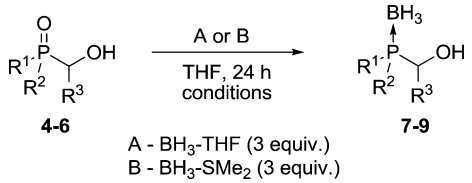
The activating effect of the OH group was also observed in reductions of phosphine oxides possessing that group in the β position. The results of the studied reductions of a series of β-hydroxyethyl phosphine oxides **16** and β-substituted-β-hydroxyethyl phosphine oxides **17** by BH_3·SMe_2 are shown in Table 4. As indicated above, for the purpose of this study, the unsymmetrically P-substituted β-substituted-β-hydroxyethyl phosphine oxides **17** were used in the form of diastereoisomeric mixtures.

The data collected in Table 4 reveal that also β-hydroxyethyl phosphine oxides **16** and **17** were reactive enough to undergo reduction by BH_3·SMe_2 and gave the corresponding phosphine–boranes **18** and **19**, respectively, although a replacement of THF by toluene and increasing the reaction temperature to 80 °C was needed to accomplish this conversion effectively. By the same token, reduction of *o*-hydroxyphenyl(diphenyl)phosphine oxide (**20**) afforded *o*-hydroxyphenyl(diphenyl)phosphine–borane (**21**) in 67% yield (Scheme 3).

To check whether a γ-hydroxyl group could also exert similar activating effect, a γ-hydroxy phosphine oxide **23** (prepared readily form *tert*-butylphenylphoshine oxide and acetone

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672–1688

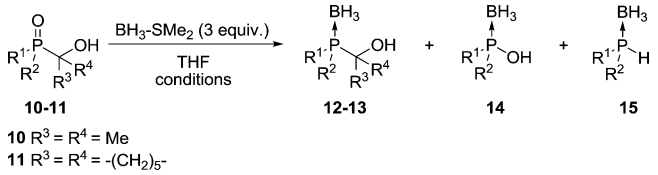
Table 2. Reaction of Phosphine Oxides 4−6 with BH_3 Complexes



		substituents				isolated yields (%)	
entry	compd	R^1	R^2	R^3	conditions	**7−9**	
1	**4a** (1:0.9)[a]	Ph	*o*-An	Me	B, 60 °C	**7a** (1:0.9)[a]	96
2	**4f** (1:0.6)[a]	Ph	*t*-Bu	Me	A, 60 °C	**7f** (1:0.5)[a]	69(74)[b]
3	**4j** (1:0.9)[a]	Ph	Me	Me	A, rt	7j (1:1)[a]	72[c]
4	**4k**	*c*-Hex	*c*-Hex	Me	A, rt	**7k**	95
5	**5m**	Ph	Ph	*i*-Pr	B, rt	**8m**	93
6	**6a** (1 dia)	Ph	*o*-An	Ph	B, rt	**9a** (1 dia)	41(72)[b,c]
7	**6f** (1 dia)	Ph	*t*-Bu	Ph	B, 60 °C	**9f** (1 dia)	47(54)[b,c]
8	**6j** (1:0.6)[a]	Ph	Me	Ph	B, 60 °C	**9j** (1:0.6)[a]	69[c]
9	**6k**	*c*-Hex	*c*-Hex	Ph	B, 60 °C	**9k**	93
10	**6m**	Ph	Ph	Ph	B, 60 °C	**9m**	63[c]

[a]Ratio of diastereoisomers. [b]Using 5 equiv of BH_3·SMe_2. [c]Formation of small amounts (less than 10%) of a secondary phosphine−borane was also observed.

Table 3. Reaction of 10 and 11 with BH_3 Complexes



		substituents			isolated yields (%)[a]		
entry	compd	R^1	R^2	conditions	**12** or **13**	**14**	**15**
1	**10a**	Ph	*o*-An	rt, 3 h	46(63)[b]	0	0
2	**10b**	Ph	1-Nphth[c]	rt,3 h	20(22)[d]	67(72)	0
3	**10c**	*p*-An	*p*-An	rt, 3 h	71(90)	traces	traces
4	**10d**	*p*-F-C_6H_4	*p*-F-C_6H_4	rt, 3 h	23(25)	30(38)	17(34)
5	**10j**	Ph	Me	rt, 2 h	87(100)	0	0
6	**10n**	Ph	*p*-An	rt, 3 h	87(100)[e]	0	0
7	**10o**	*p*-Tol	*p*-Tol	rt, 3 h	72(90)	traces	traces
8	**11m**	Ph	Ph	60 °C, 24 h	67(90)	traces	0

[a]^{31}P NMR yields in parentheses. [b]A secondary phosphine oxide was isolated as a side-product in 12% yield. [c]Nphth = naphthyl. [d]During column chromatography partial deboranation occurred and the isolated product was contaminated with a small amount of the corresponding phosphine. [e]Reaction was carried out with 3 equiv of BH_3·THF.

according to Scheme 4) was subjected to reduction by BH_3·SMe_2 in toluene at 80 °C for 4 days. However, as indicated in Scheme 4, no reaction was observed.

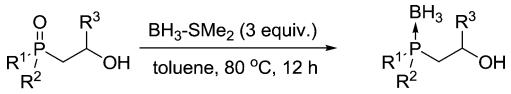
In fact, the observed lack of reactivity of hydroxyphosphine oxide **23** possessing a OH group in the distant γ-position toward BH_3 stays in line with the assumed intramolecular mode of activation expected to result from the intramolecular coordinative capping of P═O by the neighboring O-BH_2 unit. The plausible mechanistic picture for the studied reductions of hydroxyphosphine oxides is presented in Scheme 5.

According to this picture, the reduction process commences with a reaction of BH_3 with the OH group followed by intramolecular coordination of the resulting proximal boron functionality to phosphoryl oxygen and the formation of a cyclic zwitterionic intermediate. It seems also quite possible that it may be the other way around, i.e., a precoordination of BH_3 to phosphoryl oxygen facilitates its reaction with the proximal OH group, leading to the formation of the cyclic intermediate. Nonetheless, immediate liberation of hydrogen has always been observed upon adding borane to a solution of a hydroxyalkyl phosphine oxide at room temperature. The intramolecular coordination process is effective for α-hydroxy and β-hydroxy phosphine oxides where formation of a five- or a six-membered ring intermediate is possible but becomes ineffective for γ-hydroxy phosphine oxides calling for the formation of a seven-membered ring intermediate which is less favored.

In the next step, an intermolecular hydride transfer from external borane to phosphorus atom causes cleavage of the activated P−O bond in a S_N2 type process. The resulting protonated phosphine liberates another hydrogen molecule to give a free phosphine which finally undergoes complexation by

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

Table 4. Reactions of Phosphine Oxides 16 and 17 with BH_3·SMe_2

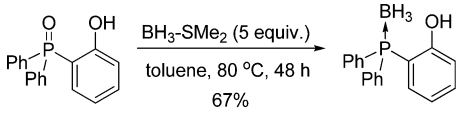


16-17 18-19

		substituents				
entry	compd	R^1	R^2	R^3	product	isolated yields (%) **18** and **19**
1	**16a**	Ph	*o*-An	H	**18a**	26(62)[a]
2	**16b**	Ph	1-Nphth[b]	H	**18b**	55(64)[a]
3	**16m**	Ph	Ph	H	**18m**	84
4	**17a** (1:0.9)[c]	Ph	*o*-An	Me	**19a** (1:0.9)[c]	90
5	**17b** (1:0.8)[c]	Ph	1-Nphth[b]	Me	**19b** (1:0.9)[c]	85
6	**17f** (1:0.9)[c]	Ph	*t*-Bu	Me	**19f** (1:1)[c]	29

[a]Reaction carried out for 24 h using 10 equiv of BH_3·SMe_2. [b]Nphth = naphthyl. [c]Ratio of diastereoisomers.

Scheme 3



20 21

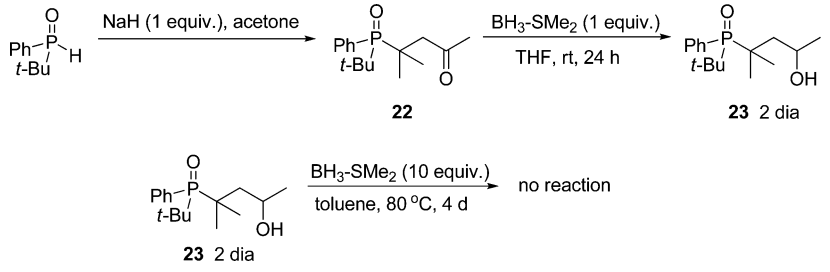
BH_3 and hydrolytic deprotection of the hydroxyl group to give hydroxyalkylphosphine–borane.

The mechanism presented above implies that inversion of configuration at phosphorus has to take place in the reduction step. While this would be in accordance with the recent observation that hydroxymethylphosphinates (as well as **1f**) are reduced by BH_3 with inversion of configuration,[8] it would still remain in contrast with earlier reports that five-membered tertiary phosphine oxides[4c,d] as well as secondary phosphine oxides[6] are reduced by BH_3 with retention of configuration. To get an insight into the stereochemistry of the studied reduction of the P=O bond by BH_3, we decided to check it again in a process utilizing optically active *tert*-butyl(hydroxymethyl)-phenylphosphine oxide (*R*)-**1f** as the starting material. In view of some earlier confusions in assignment of the absolute configuration to enantiomers of **1f**,[9] and to make our stereochemical assignments fully unequivocal, we confirmed the R_P absolute configuration of the starting optically active **1f** crystallographically. Reduction of (*R*)-**1f** by BH_3·SMe_2 under the conditions described above gave optically active **2f** in 99% yield. Preliminary attempts to directly correlate the obtained **2f** back to its precursor **1f** via a simple deboranation–reoxidation sequence failed due to instability of **2f** in the deboranation step. Use of DABCO led to racemized phosphine–borane **2f** probably due to reversible deformylation–formylation process. Similarly, in attempted deboranation under acidic condition (HBF_4) an extensive racemization of **2f** was also observed and was accompanied by formation of oligomeric side-products resulting from the liberated formaldehyde. These problems were finally overcome when the hydroxyl group in **2f** was protected as a methyl ether (Scheme 6).

Thus, part of the starting (*R*)-**1f** was converted into ether (*R*)-**24f**, and the rest of it was reduced by BH_3·SMe_2 to give **2f** in 99% isolated yield and without any loss of the enantiomeric purity (HPLC). Then the hydroxyl group in **2f** was protected to form **25f**. During this step, formation of a small amount of *tert*-butylmethylphenylphoshine–borane (**26f**) as a byproduct was also observed. The resulting ether **25f** was subjected to P-deprotection in the presence of DABCO at 40 °C for 5 h followed by oxidation of the resulting phosphine by H_2O_2 to afford optically active **24f**. Comparison of the signs of specific rotations of ether (*R*)-**24f** formed directly from (*R*)-**1f** and the second one that was obtained in the correlation process revealed that the two compounds were of the opposite configuration. Hence, the absolute configurations of the newly formed oxide **24f** was assigned as *S*. These results indicated that the studied reduction had to occur with inversion of configuration at phosphorus since the next two steps in the correlation i.e., deboranation of phosphine–borane by DABCO[10] and oxidation of phosphine by H_2O_2,[11] were known to proceed with retention of configuration at phosphorus. Moreover, as evidenced by HPLC analysis of (*S*)-(−)-**24f** on a chiral stationary phase, the reduction of the P=O bond by BH_3·SMe_2 took place under this condition without any detectable loss of enantiomeric purity. This result fully corroborates the earlier assignments of stereochemistry of the reduction of P=O bonds flanked by an *α*-hydroxyl functionality[8] and supports the conclusion that the stereochemical course of BH_3 reductions of phosphine oxides bearing *α*-hydroxyl functions take a stereocourse different from those of unfunctionalized phosphine oxides.

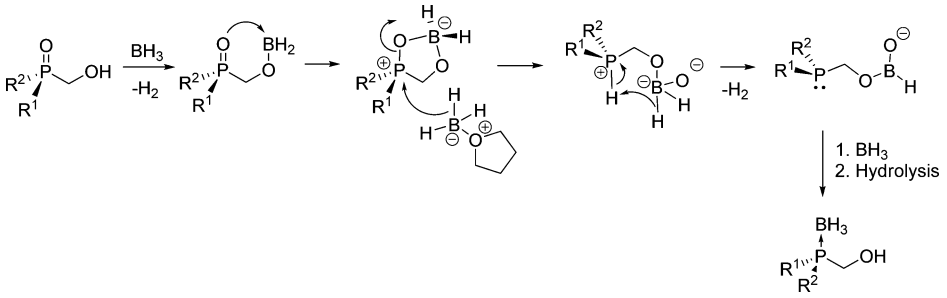
Similar chemical correlation was also carried out for *β*-hydroxyethylphosphine oxide **16a** (Scheme 7). In this case no protection of the hydroxyl group was needed. Compound **16a** that was enriched in the *R* enatiomer was reacted with BH_3·SMe_2 and yielded borane **18a** in 90% yield. Then BH_3 moiety was removed under acidic conditions (HBF_4), and the resulting phosphine was oxidized with H_2O_2 to phosphine oxide **16a**. The resulting **16a** showed a sign of specific rotation opposite to that of the starting material as well as reversed peak order in the HPLC analysis on a chiral stationary phase, attesting to the overall inversion of configuration at phosphorus. As above, in

Scheme 4

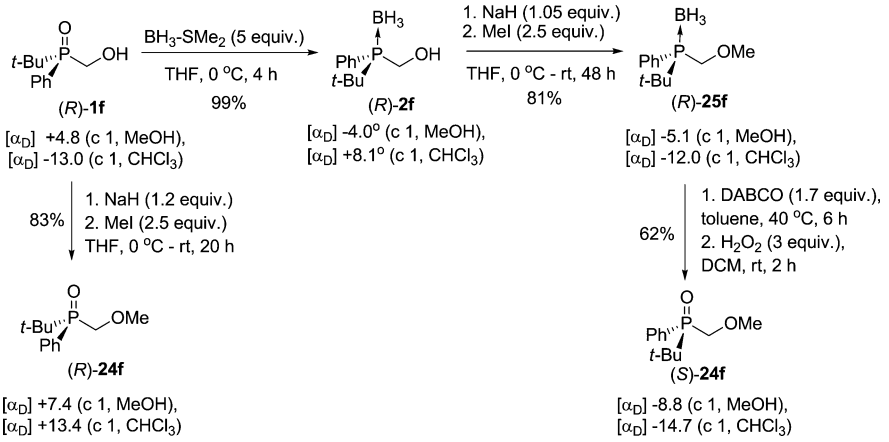


DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672–1688

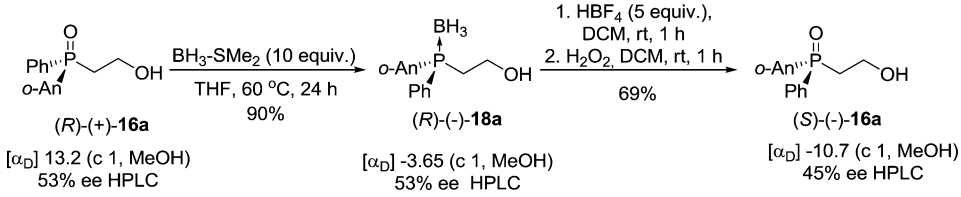
Scheme 5



Scheme 6



Scheme 7



this correlation only the reduction step could occur with inversion of configuration. In this correlation, some loss of enantiomeric purity of (*S*)-(−)-**16a** during the deboranation step under acidic conditions was observed.

CONCLUSION

A general and efficient method for reduction of the P═O bond in tertiary phosphine oxides possessing hydroxyalkyl substituents at phosphorus has been developed wherein a commercially available BH_3 complex acts as both the reducing and complexing agent. The key factor which enables the reduction process is the presence of a neighboring α or β hydroxyl group in the molecule, the lack of which or its longer distance from phosphorus causes inertness of the P═O bond toward BH_3. Lengthening of the distance between the P═O bond and the OH group from α to β leads to a noticeable lowering of the propensity of the P═O toward reduction by BH_3, and elevation of the reaction temperature from room temperature to 60 °C or even 80 °C is required to make the reduction effective. Stereochemical corelations performed on optically active (hydroxymethyl)phosphine oxide (*R*)-**1f** and (2-hydroxyethyl)phosphine oxide (*R*)-**16a** revealed that the reduction is completely stereoselective and takes place with inversion of configuration at the phosphorus center.

EXPERIMENTAL SECTION

General. All reactions were performed under an argon atmosphere using Schlenk techniques. Only dry solvents were used, and glassware was heated under vacuum prior to use. All chemicals were used as received unless noted otherwise. Solvents for chromatography and crystallization were distilled once before use, and solvents for extraction were used as received. THF, diethyl ether, and toluene were distilled from sodium/benzophenone ketyl under nitrogen.

Analytics and Instruments. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on 500, 400, or 300 MHz spectrometers at ambient temperature in $CDCl_3$ unless otherwise noted. Chemical shifts (δ) are reported in ppm relative to the residual solvent peak (7.26 ppm for ^{1}H and 77 ppm for ^{13}C). Mass spectra were recorded in electron ionization (EI) mode, and GC was recorded using the following parameters: pressure, 65 kPa; total flow, 33.9 mL/min; column flow, 1.0 mL/min; linear velocity, 36.8 cm/s; split, 30; temperature program (80 °C, hold 1 min; 80−300 °C/12 °C/min, hold 5 min; 300−340 °C/10 °C/min, hold 6.67 min; total 35 min) or 57.5 kPa; total flow, 24 mL/min; column flow, 1.0 mL/min; linear velocity, 36.5 cm/s; split, 20; temperature program (60 °C, hold 1 min; 60−220 °C/13 °C/min, hold 5 min; 220−250 °C/10 °C/min, hold 4.67 min; total 25 min). Thin-layer chromatography (TLC) was performed with precoated silica gel plates and visualized by UV light or $KMnO_4$

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

solution or iodide on silica gel. The reaction mixtures were purified by column chromatography over silica gel (60−240 mesh). Melting points were determined in a capillary tube and were uncorrected. HPLC-HRMS was performed using reversed phase stationary phase with water/methanol 80:20 as eluent, electronspray ionization (ESI), and IT-TOF detector. The X-ray diffraction data for compound (*R*)-**1f** were collected at room temperature using Cu Kα radiation (λ = 1.54178 Å). Structure was solved by the SHELXS-97 program and refined by full-matrix least-squares on F2 using the SHELXL-97 program.

The starting compounds: *o*-anisylphenylphosphine oxide,[12] (1-naphthyl)phenylphosphine oxide,[13] di-*p*-anisylphosphine oxide,[14] di-*p*-fluorophenylphosphine oxide,[1e] di-*p*-tolylphosphine oxide,[1e] di(3,5-dimethylphenyl)phosphine oxide,[15] *tert*-butylphenylphosphine oxide,[16] benzylphenylphosphine oxide,[17] phenyl(isopropyl)phosphine oxide,[1e] cyclohexylphenylphosphine oxide,[18] di-*c*-hexylphosphine oxide,[19] di-*n*-hexylphosphine oxide,[20] methylphenylphosphine oxide,[21] diphenylphosphine oxide,[1e] *tert*-butylmethylphenylphosphine oxide,[22] and optically active *tert*-butylphenylphosphine oxide[16] were prepared according to reported methods. Optically active *o*-anisyl(2-hydroxyethyl)phenylphosphine oxide was available from another studies.[23]

General Procedure for the Synthesis of Hydroxymethylphosphine Oxides 1. In a two-necked round-bottom flask (100 mL) equipped with a magnetic stirrer and an argon inlet was placed a catalytic amount of sodium in anhydrous ethanol (40 mL). Then a secondary phosphine oxide (2 mmol) and paraformaldehyde (0.18 g, 6 mmol) were added, and the mixture was heated at reflux for 24 h. Then the mixture was allowed to cool to room temperature, and ethanol was evaporated. The residue was dissolved in DCM (20 mL), acidified with 1 M HCl (10 mL), and extracted with DCM (3 × 50 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and evaporated. The residue was crystallized from methanol or purified by column chromatography using ethyl acetate/methanol (v/v = 20:1) as eluent.

*o-Anisyl(hydroxymethyl)phenylphosphine Oxide (**1a**).* According to the general procedure, *o*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) afforded product **1a** (0.257 g, 49%) as a solid; mp = 181.4−182.2 °C; R_f = 0.32 (ethyl acetate/methanol = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.96 (bs, 1H), 4.45−4.49 (dd, J_{H-P} = 14.19 Hz, J_{H-H} = 1.91 Hz, 1H), 4.44−4.61 (d, J_{P-C} = 14.19 Hz, 1H), 6.89−6.93 (m, 1H), 7.08−7.13 (m, 1H), 7.35−7.55 (m, 4H), 7.01−8.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.4, 60.9 (d, J_{P-C} = 81.3 Hz), 110.7 (d, J_{P-C} = 6.8 Hz), 118.4 (d, J_{P-C} = 95.0 Hz), 121.4 (d, J_{P-C} = 10.6 Hz), 128.2 (d, J_{P-C} = 11.9 Hz), 130.9 (d, J_{P-C} = 9.7 Hz), 131.6 (d, J_{P-C} = 2.8 Hz), 131.8 (d, J_{P-C} = 98.8 Hz), 134.2 (d, J_{P-C} = 1.8 Hz), 134.7 (d, J_{P-C} = 5.0 Hz), 160.1 (d, J_{P-C} = 5.1 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 30.96 (s). Anal. Calcd for $C_{14}H_{15}O_3P$: C, 64.12; H, 5.77. Found: C, 63.72; H 5.88.

*(Hydroxymethyl)-1-naphthylphenylphosphine Oxide (**1b**).* According to the general procedure, 1-naphthylphenylphosphine oxide (0.504 g, 2.0 mmol) afforded product **1b** (0.558 g, 99%) as a solid; mp = 149−150 °C; R_f = 0.7 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.53 (d, J_{P-H} = 14.54 Hz, 1H), 4.57 (d, J_{H-P} = 14.54 Hz, 1H), 5.94 (bs, 1H), 7.38 (m, 3H), 7.44−7.53 (m, 3H), 7.68−7.72 (m, 2H), 7.85−7.86 (m, 1H), 8.01−8.02 (m, 1H), 8.08−8.11 (m, 1H), 8.38−8.37 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 61.8 (d, J_{P-C} = 82.5 Hz), 124.5 (d, J_{P-C} = 13.5 Hz), 126.7 (d, J_{P-C} = 94.6 Hz), 126.36 126.56 (d, J_{P-C} = 5.3 Hz), 127.3, 128.6 (d, J_{P-C} = 11.69 Hz), 128.9, 131.6 (d, J_{P-C} = 96.0 Hz), 131.2 (d, J_{P-C} = 11.7 Hz), 131.9 (d, J_{P-C} = 2.8 Hz), 132.6 (d, J_{P-C} = 10.21 Hz), 133.4 (d, J_{P-C} = 7.6 Hz), 133.4 (d, J_{P-C} = 2.9 Hz), 133.8 (d, J_{P-C} = 8.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 33.58 (s). Anal. Calcd for $C_{17}H_{15}O_2P$: C, 72.33; H, 5.36. Found: C, 71.98; H, 5.47.

*(Hydroxymethyl)-di-p-anisylphosphine Oxide (**1c**).*[24] According to the general procedure, di-*p*-anisylphosphine oxide (0.524 g, 2.0 mmol) afforded product **1c** (0.426 g, 73%) as a yellow oil; R_f = 0.36 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 6H), 4.31 (d, J_{H-P} = 3.8 Hz, 2H), 5.92 (bs, 1H), 6.92−6.91 (m, 4H), 7.62−7.66 (m, 4H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.2, 61.4 (d, J_{P-C} = 83.6 Hz), 114.1 (d, J_{P-C} = 12.7 Hz), 121.9 (d, J_{P-C} = 103.54 Hz), 133.1 (d, J_{P-C} = 10.9 Hz), 162.4 (d, J_{P-C} = 2.72 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 31.02 (s); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{15}H_{18}O_4P$ 293.0943; found 293.0937. Anal. Calcd for $C_{15}H_{17}O_4P$: C, 61.64; H, 5.86. Found: C, 61.50; H, 5.80.

*Di-p-fluorophenyl(hydroxymethyl)phosphine Oxide (**1d**).* According to the general procedure, di-*p*-fluorophenylphosphine oxide (0.476 g, 2.0 mmol) afforded product **1d** (0.413 g, 77%) as a yellow solid; mp = 109.7−100.2 °C; R_f = 0.36 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.36 (d, J_{P-H} = 5.9 Hz, 2H), 6.05 (bs, 1H), 7.11−7.15 (m, 4H), 7.71−7.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.3 (d, J_{C-P} = 84.5 Hz), 116.2 (dd, J_{C-P} = 21.8 Hz, J_{C-F} = 12.7 Hz), 126.1 (dd, J_{C-P} = 99.9 Hz, J_{C-F} = 3.6 Hz), 133.9 (dd, J_{C-P} = 9.1 Hz, J_{C-F} = 10.9 Hz), 165.3 (dd, J_{C-P} = 3.6 Hz, J_{C-F} = 254.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 30.11 (s). Anal. Calcd for $C_{13}H_{11}F_2O_2P$: C, 58.22; H, 4.13. Found: C, 57.82; H, 4.20.

*Di(3,5-dimethylphenyl)hydroxymethylphosphine Oxide (**1e**).* According to the general procedure, di(3,5-dimethylphenyl)phosphine oxide (0.516 g, 2.0 mmol) afforded product **1e** (0.374 g, 65%) as a light yellow solid; mp = 219.4−220.3 °C; R_f = 0.49 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 12H), 4.37 (s, 2H), 4.92 (bs, 1H), 7.14 (s, 1H), 7.34−7.37 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 61.1 (d, J_{P-C} = 80.8 Hz), 128.8 (d, J_{P-C} = 10.0 Hz), 130.3 (d, J_{P-C} = 96.3 Hz), 133.9 (d, J_{P-C} = 2.7 Hz), 138.4 (d, J_{P-C} = 12.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 31.16 (s). Anal. Calcd for $C_{17}H_{21}O_2P$: C, 70.82; H, 7.34. Found: C, 70.78; H, 7.30.

*tert-Butyl(hydroxymethyl)phenylphosphine Oxide (**1f**).*[24] According to the general procedure, *tert*-butylphenylphosphine oxide (0.364 g, 2.0 mmol) afforded product **1f** (0.331 g, 78%) as a solid; mp = 153.7−154.7 °C; R_f = 0.47 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (d, J_{H-P} = 14.19 Hz, 9H), 4.24 (dd, J_{P-H} = 14.19 Hz, J_{H-H} = 6.31 Hz, 1H), 4.44 (dd, J_{P-H} = 14.5 Hz, J_{H-H} = 6.94 Hz, 1H), 5.47 (bs, 1H), 7.40−7.44 (m, 2H), 7.48−7.50 (m, 1H), 7.66−7.69 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6, 32.5 (d, J_{P-C} = 64.5 Hz), 57.4 (d, J_{P-C} = 71.8 Hz), 128.2 (d, J_{P-C} = 10.9 Hz), 128.7 (d, J_{P-C} = 85.4 Hz), 131.5 (d, J_{P-C} = 7.3 Hz), 131.6 (d, J_{P-C} = 2.73 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 46.39 (s). Anal. Calcd for $C_{11}H_{17}O_2P$: C, 62.25; H, 8.07. Found: C, 62.40; H, 8.11.

*Benzyl(hydroxymethyl)phenylphosphine Oxide (**1g**).* According to the general procedure, benzylphenylphosphine oxide (0.432 g, 2.0 mmol) afforded product **1g** (0.226 g, 46%) as a solid; mp = 127.1−127.9 °C; R_f = 0.41 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.46−3.49 (m, 2H), 4.11−4.12 (m, 2H), 5.65 (bs, 1H), 7.10−7.11 (m, 2H), 7.15−7.21 (m, 3H), 7.38−7.41 (m, 2H), 7.48−7.51 (m, 3H), 7.54−7.57 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.9 (d, J_{P-C} = 60.9 Hz), 59.6 (d, J_{P-C} = 80.8 Hz), 126.8 (d, J_{P-C} = 2.7 Hz), 128.4 (d, J_{P-C} = 13.6 Hz), 128.5 (d, J_{P-C} = 5.5 Hz), 129.4 (d, J_{P-C} = 90.8 Hz); 129.9 (d, J_{P-C} = 4.5 Hz), 130.9 (d, J_{P-C} = 8.2 Hz), 131.0 (d, J_{P-C} = 9.1 Hz), 132.0 (d, J_{P-C} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 37.20 (s). Anal. Calcd for $C_{14}H_{15}O_2P$: C, 68.29; H, 6.14. Found: C, 68.04; H, 6.28.

*(Hydroxymethyl)phenyl-isopropylphosphine Oxide (**1h**).*[25] According to the general procedure, phenyl-isopropylphosphine oxide (0.336 g, 2.0 mmol) afforded product **1h** (0.317 g, 80%) as an oil; R_f = 0.28 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 16.08 Hz, 3H), 1.25 (dd, J_{H-H} = 6.94 Hz, J_{P-H} = 14.50 Hz, 3H), 2.14−2.34 (m, 1H), 4.20 (m, 2H), 4.85 (bs, 1H), 7.44−7.49 (m, 2H), 7.50−7.55 (m, 1H), 7.69−7.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0 (d, J_{C-P} = 2.7 Hz), 15.5 (d, J_{C-P} = 1.8 Hz), 26.1 (d, J_{C-P} = 67.2 Hz), 59.2 (d, J_{C-P} = 76.3 Hz), 128.6 (d, J_{C-P} = 10.9 Hz), 129.2 (d, J_{C-P} = 88.1 Hz), 131.0 (d, J_{C-P} = 8.2 Hz), 132.9 (d, J_{C-P} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 40.08 (s). Anal. Calcd for $C_{10}H_{15}O_2P$: C, 60.60; H, 7.63. Found: C, 60.44; H, 7.48.

*Cyclohexyl(hydroxymethyl)phenylphosphine Oxide (**1i**).*[26] According to the general procedure, cyclohexylphenylphosphine oxide (0.416 g, 2.0 mmol) afforded product **1i** (0.447 g, 94%) as a solid; mp = 115.7−116.7 °C; R_f = 0.33 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.10−1.39 (m, 5H), 1.56−1.78 (m, 4H), 2.00−2.05 (m, 2H), 4.13 (m, 2H), 5.73 (bs, 1H), 7.40−7.43 (m, 2H),

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

7.47−7.50 (m, 1H), 7.67−7.70 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6 (d, J_{P-C} = 2.7 Hz), 24.7 (d, J_{P-C} = 2.7 Hz), 25.6, 26.1 (d, J_{P-C} = 8.2 Hz), 26.1 (d, J_{P-C} = 8.2 Hz), 35.7 (d, J_{P-C} = 67.2 Hz), 58.8 (d, J_{P-C} = 79.0 Hz), 128.4 (d, J_{P-C} = 10.9 Hz), 129.4 (d, J_{P-C} = 88.1 Hz), 130.9 (d, J_{P-C} = 8.2 Hz), 131.7 (d, J_{P-C} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 42.03 (s). Anal. Calcd for $C_{13}H_{19}O_2P$: C, 65.53; H, 8.04. Found: C, 65.85; H, 8.03.

*Hydroxymethyl(methyl)phenylphosphine Oxide (**1j**).* According to the general procedure, methylphenylphosphine oxide (0.28 g, 2.0 mmol) afforded product **1j** (0.204 g, 60%) as a solid; mp = 62.8−63.5 °C; R_f = 0.27 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.77 (d, J_{H-H} = 11.66 Hz, 3H), 3.95−4.14 (m, 2H), 5.22 (bs, 1H), 7.46−7.48 (m, 2H), 7.52−7.54 (m, 1H), 7.69−7.76 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.8 (d, J_{P-C} = 68.2 Hz), 62.3 (d, J_{P-C} = 81.7 Hz), 128.7 (d, J_{P-C} = 10.0 Hz), 130.4 (d, J_{P-C} = 8.2 Hz), 131.0 (d, J_{P-C} = 93.6 Hz), 132.1; ^{31}P NMR (202 MHz, $CDCl_3$) δ 38.03 (s). Anal. Calcd for $C_8H_{11}O_2P$: C, 56.47; H, 6.52. Found: C, 56.82; H, 6.66.

*Dicyclohexyl(hydroxymethyl)phosphine Oxide (**1k**).*[27] According to the general procedure, dicyclohexylphosphine oxide (0.428 g, 2.0 mmol) afforded product **1k** (0.478 g, 98%) as a light yellow solid; mp = 154.7−155.7 °C; R_f = 0.21 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17−1.28 (m, 6H), 1.39−1.51 (m, 4H), 1.64−1.70 (m, 2H), 1.71−1.97 (m, 10H), 3.94 (s, 2H), 5. Twenty-five (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.0, 24.4, 25.8, 26.70, 26.5 (d, J_{P-C} = 8.2 Hz), 34.3 (d, J_{P-C} = 60.9 Hz), 56.1 (d, J_{P-C} = 71.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 50.65 (s). Anal. Calcd for $C_{13}H_{25}O_2P$: C, 63.91; H, 10.31. Found: C, 63.85; H, 9. 94.

*Di-n-hexyl(hydroxymethyl)phosphine Oxide (**1l**).*[28] According to the general procedure di-*n*-hexylphosphine oxide (0.38 g, 2.0 mmol) afforded product **1l** (0.483 g, 97%) as an oil; R_f = 0.67 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, J_{H-H} = 6.94 Hz, 6H), 1.28−1.31 (m, 8H), 1.37−1.41 (m, 4H), 1.54−1.60 (m, 4H), 1.70−1.78 (m, 4H), 3.86 (bs, 2H), 5.11 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 21.3 (d, J_{P-C} = 3.6 Hz), 22.4, 25.7 (d, J_{P-C} = 63.6 Hz), 30.8 (d, J_{P-C} = 13.6 Hz), 31.3, 58.9 (d, J_{P-C} = 76.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 49.53 (s); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{30}O_2P$ 249.1983; found 249.1978. Anal. Calcd for $C_{13}H_{29}O_2P$: C, 62.87; H, 11.77. Found: C, 62.50; H, 11.50.

General Procedure for the Synthesis of Phosphine Oxides 4 and 6. To a solution of a secondary phosphine oxide (2 mmol) in THF (10 mL) was added DBU (30 μL, 0.2 mmol) at room temperature followed by an aldehyde (2−3 mmol), and the reaction mixture was stirred for 24 h. The reaction was quenched by saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The crude reaction mixture was analyzed by NMR and then purified by column chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) as eluent.

*o-Anisyl-(1-hydroxyethyl)phenylphosphine Oxide (**4a**).* According to the general procedure, *o*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) and acetaldehyde (112 μL, 3.0 mmol) afforded product **4a** (0.496 g, 95%) as two diastereomers isolated as a mixture (dr = 53:47). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (dd, J_{H-H} = 7.25 Hz, J_{H-P} = 16.39 Hz, 3H, major), 1.45 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 15.76 Hz, 3H, minor), 3.75 (s, 3H, major), 3.83 (s, 3H, minor), 4.29 (bs, 2H), 4.79−4.87 (m, 2H), 6.87−6.90 (m, 1H, major), 6.92−6.95 (m, 1H, minor), 7.07−7.11 (m, 2H), 7.36−7.41 (m, 4H), 7.43−7.46 (m, 2H), 7.48−7.51 (m, 2H), 7.78−7.82 (m, 2H), 7.83−7.87 (m, 2H), 7.97−8.04 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.9 (d, J_{C-P} = 24.5 Hz, minor), 17.1 (d, J_{C-P} = 24.5 Hz, major), 55.3 (major), 55.5 (minor), 66.1 (d, J_{C-P} = 81.7 Hz, minor), 66.5 (d, J_{C-P} = 80.8 Hz, major), 110.6 (d, J_{C-P} = 6.4 Hz, major), 111.2 (d, J_{C-P} = 7.3 Hz, minor), 118.9 (d, J_{C-P} = 93.6 Hz, major), 119.2 (d, J_{C-P} = 90.8 Hz, minor), 121.3 (d, J_{C-P} = 10.0 Hz) and 121.4 (d, J_{C-P} = 10.0 Hz), 128.0 (d, J_{C-P} = 11.8 Hz, major), 128.2 (d, J_{C-P} = 11.8 Hz, minor), 131.1 (d, J_{C-P} = 9.1 Hz, minor), 131.3 (d, J_{C-P} = 9.1 Hz, major), 131.4 (d, J_{C-P} = 1.8 Hz, major), 131.5 (d, J_{C-P} = 1.8 Hz, minor), 131.6 (d, J_{C-P} = 34.5 Hz) and 133.9 (minor), 134.0 (major), 134.7 (d, J_{C-P} = 4.5 Hz, major), 135.1 (d, J_{C-P} = 4.5 Hz, major), 159.5 (d, J_{C-P} = 4.5 Hz) and 159.6 (d, J_{C-P} = 4.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 33.64 (s, minor) and 34.62 (s, major). Anal. Calcd for $C_{15}H_{17}O_3P$: C, 65.21; H, 6.20. Found: C, 64.82; H, 6.25.

*tert-Butyl(1-hydroxyethyl)phenylphosphine Oxide (**4f**).*[29] According to the general procedure, *tert*-butylphenylphosphine oxide (0.364 g, 2.0 mmol) and acetaldehyde (112 μL, 3.0 mmol) afforded product **4f** (0.227 g, 50%) as two diastereomers isolated as a mixture (dr = 63:37). Major diastereoisomer: R_f = 0.28 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (d, J_{H-P} = 13.87 Hz, 9H), 1.32 (dd, J_{H-H} = 6.97 Hz, J_{H-P} = 13.56 Hz, 3H), 4.59 (m, 1H), 5.09 (bs, 1H), 7.42−7.45 (m, 3H), 7.66−7.69 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.8, 25.3, 33.2 (d, J_{C-P} = 64.5 Hz), 64.7 (d, J_{C-P} = 72.7 Hz), 128.2 (d, J_{C-P} = 9.9 Hz), 130.0 (d, J_{C-P} = 80,8 Hz), 131.4 (d, J_{C-P} = 7.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 47.94 (s). Anal. Calcd for $C_{12}H_{19}O_2P$: C, 63.70; H, 8.46. Found: C, 63.54; H, 8.42. Minor diastereoisomer: R_f = 0.15 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (d, J_{H-P} = 13.87 Hz, 9H), 1.46 (dd, J_{H-H} = 6.62 Hz, J_{H-P} = 13.56 Hz, 3H), 4.63 (m, 1H), 5.09 (bs, 1H), 7.48−7.51 (m, 3H), 7.94−7.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.5, 25.0, 32.9 (d, J_{C-P} = 62.7 Hz), 65.3 (d, J_{C-P} = 80.8 Hz,), 127.8 (d, J_{C-P} = 9.9 Hz), 128.2 (d, J_{C-P} = 82.6 Hz), 131.4 (d, J_{C-P} = 4.5 Hz), 132.6 (d, J_{C-P} = 7.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 48.35 (s). Anal. Calcd for $C_{12}H_{19}O_2P$: C, 63.70; H, 8.46. Found: C, 63.54; H, 8.42.

*1-Hydroxyethyl(methyl)phenylphosphine Oxide (**4j**).* According to the general procedure, methylphenylphosphine oxide (0.28 g, 2.0 mmol) and acetaldehyde (112 μL, 3.0 mmol) afforded product **4j** (0.151 g, 41%) as two diastereomers isolated as a mixture (dr = 53:47); R_f = 0.22 (chloroform/ethyl acetate/methanol = 30:5:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (dd, J_{H-H} = 6.62 Hz, J_{H-P} = 15.76 Hz, 3H, minor), 1.34 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 15.45 Hz, 3H, major), 1.75 (d, J_{H-P} = 12.61 Hz, 3H, major), 1.78 (d, J_{H-P} = 12.30 Hz, 3H, minor), 4.02−4.09 (m, 1H, minor), 4.16−4.22 (m, 1H, major), 4.87 (bs, 2H), 7.45−7.48 (m, 4H), 7.51−7.55 (m, 2H), 7.70−7.77 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.1 (d, J_{C-P} = 86.3 Hz) and 11.6 (d, J_{C-P} = 85.4 Hz), 16.3 (s, major), 16.7 (s, minor), 66.9 (d, J_{C-P} = 84.5 Hz) and 67.3 (d, J_{C-P} = 82.7 Hz), 128.5 (d, J_{C-P} = 11.8 Hz) and 126.27 (d, J_{C-P} = 11.8 Hz), 130.6 (d, J_{C-P} = 8.2 Hz) and 131.0 (d, J_{C-P} = 8.2 Hz), 131.9 (d, J_{C-P} = 3.6 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 40.90 (s) and 41.85 (s). Anal. Calcd for $C_9H_{13}O_2P$: C, 58.69; H, 7.11. Found: C, 58.67; H, 7.17.

*Di-c-hexyl-(1-hydroxyethyl)phosphine Oxide (**4k**).* According to the general procedure, dicyclohexylphosphine oxide (0.428 g, 2.0 mmol) and acetaldehyde (112 μL, 3.0 mmol) afforded product **1k** (0.309 g, 60%) as a solid; mp = 135.9−136.4 °C; R_f = 0.22 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16−1.26 (m, 6H), 1.37−1.42 (m, 4H), 1.44 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 12.93 Hz, 3H), 1.62−1.92 (m, 12H), 4.16 (q, J_{H-H} = 6.94 Hz, 1H), 5.07 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.9, 25.7, 25.8, 25.9, 26.0, 26.6 (d, J_{C-P} = 2.7 Hz), 26.7, 26.8 (d, J_{C-P} = 4.5 Hz), 26.9, 34.3 (d, J_{C-P} = 58.1 Hz), 34.6 (d, J_{C-P} = 59.9 Hz), 63.5 (d, J_{C-P} = 71.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 51.73 (s). Anal. Calcd for $C_{14}H_{27}O_2P$: C, 65.09; H, 10.53. Found: C, 64.96; H, 10.74.

*o-Anisyl-((1-hydroxy)phenylmethyl)phenylphosphine Oxide (**6a**).* According to the general procedure, *o*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) and benzaldehyde (203 μL, 2.0 mmol) afforded product **6a** (0.466 g, 69%) as two diastereomers (dr = 67:33). Crystallization from ethyl acetate/methanol mixture allowed to obtain major diastereoisomer (0.203 g, 30%) as a solid; mp = 159.1−160.0 °C; R_f = 0.35 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, CD_3OD) δ 3.84 (s, 3H), 5.92 (d, J_{H-P} = 3.47 Hz, 1H), 6.93−6.96 (m, 1H), 7.03−7.16 (m, 1H), 7.12−7.14 (m, 3H), 7.29−7.30 (m, 3H), 7.45−7.60 (m, 5H), 7.85−7.89 (m, 2H); ^{13}C NMR (125 MHz, CD_3OD) δ 56.1, 73.4 (d, J_{C-P} = 88.1 Hz), 112.5 (d, J_{C-P} = 7.3 Hz), 119.8 (d, J_{C-P} = 96.3 Hz), 122.1 (d, J_{C-P} = 10.9 Hz), 128.9 (d, J_{C-P} = 2.7 Hz), 128.9, 128.9 (d, J_{C-P} = 2.7 Hz), 129.3 (d, J_{C-P} = 11.8 Hz), 132.2 (d, J_{C-P} = 99.0 Hz), 133.1 (d, J_{C-P} = 2.7 Hz), 133.2, 133.3, 135.1 (d, J_{C-P} = 5.5 Hz), 135.9 (d, J_{C-P} = 1.8 Hz), 161.9 (d, J_{C-P} = 3.6 Hz; ^{31}P NMR (202 MHz, CD_3OD) δ 34.67 (s). Anal. Calcd for $C_{20}H_{19}O_3P$: C, 71.00; H, 5.66. Found: C, 70.91; H, 6.00.

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

*tert-Butyl((1-hydroxy)phenylmethyl)phenylphosphine Oxide (**6f**).*[29] According to the general procedure, *tert*-butylphenylphosphine oxide (0.364 g, 2.0 mmol) and benzaldehyde (203 μL, 3.0 mmol) afforded product **6f** (0.227 g, 50%) as two diastereomers (dr = 53:47). Crystallization from ethyl acetate/methanol mixture allowed to obtain major diastereoisomer (0.0903 g, 20%) as a solid; mp = 144.5−145.0 °C; R_f = 0.34 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, CD_3OD) δ 1.26 (d, J_{H-P} = 14.50 Hz, 9H), 5.59 (bs, 1H), 7.11−7.19 (m, 3H), 7.36−7.52 (m, 5H), 7.75−7.78 (m, 2H); ^{13}C NMR (125 MHz, CD_3OD) δ 26.1, 35.3 (d, J_{C-P} = 63.6 Hz), 73.8 (d, J_{C-P} = 78.1 Hz), 128.9, 129.4 (d, J_{C-P} = 10.9 Hz), 129.6 (d, J_{C-P} = 4.5 Hz), 130.7 (d, J_{C-P} = 84.5 Hz), 133.1 (d, J_{C-P} = 2.7 Hz), 133.2 (d, J_{C-P} = 7.3 Hz), 139.2 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, CD_3OD) δ 51.67 (s). Anal. Calcd for $C_{17}H_{21}O_2P$: C, 70.82; H, 7.34. Found: C, 70.61; H, 7.39.

*((1-Hydroxy)phenylmethyl)(methyl)phenylphosphine Oxide (**6j**).* According to the general procedure, methylphenylphosphine oxide (0.28 g, 2.0 mmol) and benzaldehyde (203 μL, 3.0 mmol) afforded product **6j** (0.241 g, 49%) as two diastereomers isolated as a mixture (dr = 63:37). R_f = 0.22 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.54 (d, J_{H-P} = 12.93 Hz, 3H, minor), 1.69 (d, J_{H-P} = 12.93 Hz, 3H, major), 4.97 (dd, J_{H-P} = 7.88 Hz, J_{H-H} = 5.67 Hz, 1H, minor), 5.10 (dd, J_{H-P} = 7.88 Hz, J_{H-H} = 5.04 Hz, 1H, major), 6.30−6.36 (m, 2H), 7.13−7.15 (m, 2H), 7.18−7.22 (m, 3H), 7.23−7.27 (m, 2H), 7.29−7.30 (m, 2H), 7.40−7.43 (m, 3H), 7.47−7.52 (m, 3H), 7.53−7.58 (m, 3H), 7.73−7.77 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 10.4 (d, J_{C-P} = 67.2 Hz, minor) and 13.0 (d, J_{C-P} = 67.2 Hz, major), 72.4 (d, J_{C-P} = 83.6 Hz), 72.8 (d, J_{C-P} = 83.6 Hz), 127.0 (d, J_{C-P} = 3.6 Hz), 127.08 (d, J_{C-P} = 4.5 Hz), 127.1 and 127.3 (d, J_{C-P} = 2.7 Hz), 127.4 and 127.6 (d, J_{C-P} = 1.8 Hz), 127.8 and 128.1 (d, J_{C-P} = 10.9 Hz), 128.9 (d, J_{C-P} = 86.3 Hz), 131.1 and 131.2 (d, J_{C-P} = 8.2 Hz), 131.3 (d, J_{C-P} = 1.8 Hz) and 131.34, 131.9, and 132.3 (d, J_{C-P} = 90.8 Hz), 138.26 (major) and 138.31 (minor); ^{31}P NMR (202 MHz, DMSO-d_6) δ 36.33 (s, minor); 36.55 (s, major). Anal. Calcd for $C_{14}H_{15}O_2P$: C, 68.29; H, 6.14. Found: C, 67.92; H, 6.05.

*Di-c-hexyl((1-hydroxy)phenylmethyl)phosphine Oxide (**6k**).* According to the general procedure, cyclohexylphosphine oxide (0.428 g, 2.0 mmol) and benzaldehyde (203 μL, 3.0 mmol) afforded product **6k** (0.371 g, 58%) as a solid; mp = 161.9−162.0 °C; R_f = 0.34 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05−1.35 (m, 9H), 1.41−1.51 (m, 1H), 1.54−1.99 (m, 12H), 4.85 (bs, 1H), 5.13 (d, J_{H-P} = 6.31 Hz, 1H), 7.27−7.35 (m, 3H), 7.44−7.47 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.3 (d, J_{C-P} = 3.6 Hz), 25.6 (d, J_{C-P} = 2.7 Hz), 25.7 (d, J_{C-P} = 2.7 Hz), 25.8 (d, J_{C-P} = 3.6 Hz), 25.9 (d, J_{C-P} = 9.1 Hz), 26.5, 26.6 (d, J_{C-P} = 3.6 Hz), 26.7, 26.8, 26.9 (d, J_{C-P} = 4.5 Hz), 34.3 (d, J_{C-P} = 59.0 Hz), 34.8 (d, J_{C-P} = 58.1 Hz), 70.0 (d, J_{C-P} = 67.2 Hz), 126.5 (d, J_{C-P} = 4.5 Hz), 127.6 (d, J_{C-P} = 1.8 Hz), 128.3, 138.3;^{31}P NMR (202 MHz, $CDCl_3$) δ 51.38 (s). Anal. Calcd for $C_{19}H_{29}O_2P$: C, 71.22; H, 9.12. Found: C, 70.91; H, 9.25.

General Procedure for the Synthesis of Phosphine Oxides 5m and 6m. To a solution of a secondary phosphine oxide (2 mmol) in THF (10 mL) was added *n*-butyllithium (1.5 mL, 1.6 M in hexanes, 2.4 mmol) at −78 °C, and the reaction mixture was stirred at −78 °C for 15 min. Subsequently, an aldehyde was added, and the reaction mixture was allowed to warm to room temperature and stirred for 40 h. The reaction was then quenched by saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. Product was crystallized from ethyl acetate or ethyl acetate/methanol mixture.

*(1-Hydroxy-2-methylpropyl)diphenylphosphine Oxide (**5m**).* According to the general procedure, diphenylphosphine oxide (0.404 g, 2.0 mmol) and isobutyraldehyde (200 μL, 2.2 mmol) afforded product **5m** as a solid; mp = 134−134.4 °C; R_f = 0.4 (chloroform/ethyl acetate/methanol = 30:5:1); yield 0.378 g (69%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (d, J_{H-P} = 6.31 Hz, 3H), 1.00 (d, J_{H-P} = 6.62 Hz, 3H), 2.08 (sept, 1H), 3.40 (bs, 1H), 4.24 (bs, 1H), 7.41−7.50 (m, 6H), 7.77−7.82 (m, 2H), 7.89−7.94 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.4, 20.7 (d, J_{C-P} = 9.1 Hz), 29.9, 75.0 (d, J_{C-P} = 82.7 Hz), 128.4 (d, J_{C-P} = 13.6 Hz), 128.5 (d, J_{C-P} = 11.8 Hz), 131.1 (d, J_{C-P} = 92.6 Hz), 131.2 (d, J_{C-P} = 9.1 Hz), 131.7, 131.8; ^{31}P NMR (202 MHz, $CDCl_3$) δ 31.06 (s). Anal. Calcd for $C_{16}H_{19}O_2P$: C, 70.06; H, 6.98. Found: C, 69.66; H, 6.92.

*((1-Hydroxy)phenylmethyl)(diphenyl)phosphine Oxide (**6m**).*[30] According to the general procedure, diphenylphosphine oxide (0.404 g, 2.0 mmol) and benzaldehyde (304 μL, 3.0 mmol) afforded product **6m** (0.376 g, 61%) as a solid; mp = 162.6−163.1 °C; R_f = 0.30 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.61−5.65 (m, 1H), 6.52 (m, 1H), 7.18−7.25 (m, 5H), 7.45−7.57 (m, 6H), 7.79−7.84 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 72.4 (d, J_{C-P} = 86.3 Hz), 127.3 (d, J_{C-P} = 1.8 Hz), 127.4 (d, J_{C-P} = 1.8 Hz), 127.7 (d, J_{C-P} = 4.5 Hz), 128.1 (d, J_{C-P} = 10.9 Hz), 128.3 (d, J_{C-P} = 10.9 Hz), 131.0 (d, J_{C-P} = 92.6 Hz), 131.3 (d, J_{C-P} = 8.2 Hz), 131.5 and 131.6 (d, J_{C-P} = 2.7 Hz), 131.9 (d, J_{C-P} = 8.2 Hz), 132.9 (d, J_{C-P} = 93.6 Hz), 138.1; ^{31}P NMR (202 MHz, DMSO-d_6) δ 27.75 (s). Anal. Calcd for $C_{19}H_{17}O_2P$: C, 74.02; H, 5.56. Found: C, 73.72; H, 5.41.

General Procedure for the Synthesis of (2-(2-Hydroxy)-propyl)phosphine Oxide 10. A solution of a secondary phosphine oxide (2 mmol) in acetone (20 mL) was refluxed and stirred for 72 h. The crude reaction mixture was analyzed by TLC and NMR. Product was purified by crystallization from acetone or by flash chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) or chloroform/acetone (v/v = 2:1) as eluent.

*o-Anisyl-(1-hydroxy-1-methylethyl)phenylphosphine Oxide (**10a**).* According to the general procedure, *o*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) afforded product **10a** (0.249 g, 43%) as a solid; mp = 95.3−96 °C; R_f = 0.26 (chloroform/acetone = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (d, J_{H-P} = 14.50 Hz, 3H), 1.48 (d, J_{H-P} = 13.56 Hz, 3H), 3.84 (s, 3H), 4.12 (bs, 1H), 6.98−7.01 (m, 1H), 7.17−7.20 (m, 1H), 7.37−7.41 (m, 2H), 7.46−7.49 (m, 1H), 7.54−7.57 (m, 1H), 7.86−7.90 (m, 2H), 8.17−8.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.0 (d, J_{C-P} = 6.4 Hz), 26.1 (d, J_{C-P} = 10.0 Hz), 55.5, 71.9 (d, J_{C-P} = 79.9 Hz), 111.0 (d, J_{C-P} = 7.3 Hz), 119.3 (d, J_{C-P} = 85.4 Hz), 122.1 (d, J_{C-P} = 10.0 Hz), 128.1 (d, J_{C-P} = 11.8 Hz), 131.3 (d, J_{C-P} = 93.6 Hz), 131.5 (d, J_{C-P} = 7.3 Hz), 131.7 (d, J_{C-P} = 9.1 Hz), 134.1 (d, J_{C-P} = 2.7 Hz), 135.9 (d, J_{C-P} = 4.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 39.99 (s). Anal. Calcd for $C_{16}H_{19}O_3P$: C, 66.20; H, 6.60. Found: C, 65.80; H, 6.23.

*(1-Hydroxy-1-methylethyl)(1-naphthyl)phenylphosphine Oxide (**10b**).* According to the general procedure, 1-naphthylphenylphosphine oxide (0.504 g, 2.0 mmol) afforded product **10b** (0.248 g, 40%) as a solid; mp = 134.3−134.5 °C; R_f = 0.52 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, CD_3OD) δ 1.46 (dd, J_{P-H} = 14.19 Hz, J_{H-H} = 1.26 Hz, 3H), 1.52 (dd, J_{P-H} = 13.56 Hz, J_{H-H} = 1.26 Hz, 3H), 2.12 (s, 1H), 7.38−7.47 (m, 4H), 7.48−7.55 (m, 2H), 7.88−7.91 (m, 3H), 8.05−8.06 (m, 1H), 8.46−8.52 (m, 1H), 8.72−8.73 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 26.34 (d, J_{C-P} = 17.3 Hz), 26.4 (d, J_{C-P} = 18.2 Hz), 73.7 (d, J_{C-P} = 89.9 Hz), 125.7 (d, J_{C-P} = 13.6 Hz), 129.5 (d, J_{C-P} = 10.9 Hz), 130.3, 133.2 (d, J_{C-P} = 2.7 Hz), 133.7 (d, J_{C-P} = 9.1 Hz), 134.5 (d, J_{C-P} = 2.7 Hz), 135.1 (d, J_{C-P} = 10.0 Hz), 135.7 (d, J_{C-P} = 6.3 Hz), 135.8 (d, J_{C-P} = 8.2 Hz); ^{31}P NMR (202 MHz, CD_3OD): δ 41.39 (s). Anal. Calcd for $C_{19}H_{19}O_2P$: C, 73.54; H, 6.17. Found: C, 73.75; H, 6.24.

*Di-p-anisyl-(1-hydroxy-1-methylethyl)phosphine Oxide (**10c**).* According to the general procedure, di-*p*-anisylphosphine oxide (0.524 g, 2.0 mmol) afforded product **10c** (0.384 g, 60%) as a solid; mp = 134.4−134.6 °C (acetone); R_f = 0.27 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (d, J_{P-H} = 13.24 Hz, 6H), 2.64 (bs, 1H), 3.84 (s, 3H), 6.96−6.98 (m, 4H), 7.88−7.92 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.1 (d, J_{C-P} = 7.3 Hz), 55.2, 72.3 (d, J_{C-P} = 87.2 Hz), 114.0 (d, J_{C-P} = 11.8 Hz), 121.2 (d, J_{C-P} = 98.1 Hz), 134.2 (d, J_{C-P} = 10.0 Hz), 162.3 (d, J_{C-P} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 34.87 (s). Anal. Calcd for $C_{17}H_{21}O_4P$: C, 63.74; H, 6.61. Found: C, 63.71; H, 6.63.

*Di-p-fluorophenyl-(1-hydroxy-1-methylethyl)phosphine Oxide (**10d**).* According to the general procedure, di-*p*-fluorophenylphosphine oxide (0.476 g, 2.0 mmol) afforded product **10d** (0.225 g, 38%)

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

as a solid; mp = 124.7−125.6 °C (acetone); R_f = 0.49 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (d, J_{P-H} = 13.87 Hz, 6H), 3.47 (bs, 1H), 7.13−7.17 (m, 4H), 7.97−8.01 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.06 (d, J_{C-P} = 6.4 Hz), 72.3 (d, J_{C-P} = 88.1 Hz), 115.8 (dd, J_{C-P} = 20.9 Hz, J_{C-F} = 12.7 Hz), 126.5 (d, J_{C-P} = 93.6 Hz), 134.8 (t, J_{C-F} = 9.1 Hz), 165.3 (d, J_{C-F} = 253.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 30.90 (s). Anal. Calcd for $C_{15}H_{15}F_2O_2P$: C, 60.81; H, 5.10. Found: C, 60.41; H, 4.73.

*(1-Hydroxy-1-methylethyl)(methyl)phenylphosphine Oxide (**10j**).* According to the general procedure, methylphenylphosphine oxide (0.28 g, 2.0 mmol) afforded product **10j** (0.119 g, 30%) as a solid; mp = 141.4−141.7 °C (acetone); R_f = 0.19 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (d, J_{H-P} = 13.87 Hz, 3H), 1.41 (d, J_{H-P} = 12.93 Hz, 3H), 1.78 (d, J_{H-P} = 12.61 Hz, 3H), 4.23 (bs, 1H), 7.43−7.48 (m, 2H), 7.50−7.54 (m, 1H), 7.75−7.80 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.1 (d, J_{P-C} = 66.3 Hz), 23.9 (d, J_{P-C} = 7.3 Hz), 24.4 (d, J_{P-C} = 7.3 Hz), 70.4 (d, J_{P-C} = 85.4 Hz), 128.3 (d, J_{P-C} = 10.9 Hz), 130.8 (d, J_{P-C} = 88.1 Hz), 131.4 (d, J_{P-C} = 8.2 Hz), 131.8 (d, J_{P-C} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 44.56 (s). Anal. Calcd for $C_{10}H_{15}O_2P$: C, 60.60; H, 7.63. Found: C, 60.59; H, 7.76.

*p-Anisyl-(1-hydroxy-1-methylethyl)phenylphosphine Oxide (**10n**).* According to the general procedure, *p*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) afforded product **10n** (0.384 g, 60%) as a solid; mp = 94.4−94.6 °C; R_f = 0.52 (chloroform/acetone = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (d, J_{P-H} = 14.50 Hz, 3H), 1.47 (d, J_{P-H} = 13.56 Hz, 3H), 3.84 (s, 3H), 4.13 (bs, 1H), 6.98−7.02 (m, 1H), 7.16−7.19 (m, 1H), 7.38−7.41 (m, 2H), 7.45−7.48 (m, 1H), 7.52−7.58 (m, 1H), 7.86−7.90 (m, 2H), 8.17−8.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.0 (d, J_{C-P} = 6.4 Hz), 26.1 (d, J_{C-P} = 10.0 Hz), 55.5, 71.9 (d, J_{C-P} = 79.9 Hz), 111.0 (d, J_{C-P} = 7.3 Hz), 119.4 (d, J_{C-P} = 85.4 Hz), 122.0 (d, J_{C-P} = 10.0 Hz), 128.0 (d, J_{C-P} = 11.8 Hz), 131.2 (d, J_{C-P} = 93.6 Hz), 131.5 (d, J_{C-P} = 2.7 Hz), 131.7 (d, J_{C-P} = 9.1 Hz), 134.0 (d, J_{C-P} = 1.8 Hz), 135.9 (d, J_{C-P} = 4.5 Hz), 158.0 (d, J_{C-P} = 4.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 39.32 (s). Anal. Calcd for $C_{16}H_{19}O_3P$: C, 66.20; H, 6.60. Found: C, 65.81; H, 6.39.

*Di-p-tolyl(1-hydroxy-1-methylethyl)phosphine Oxide (**10o**).* According to the general procedure, di-*p*-tolylphosphine oxide (0.46 g, 2.0 mmol) afforded product **10o** (0.184 g, 32%) as a solid; mp = 125.2−125.6 °C; R_f = 0.36 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (d, J_{P-H} = 13.24 Hz, 6H), 2.39 (bs, 3H), 2.77 (bs, 1H), 7.26−7.28 (m, 4H), 7.85−7.89 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 25.1 (d, J_{C-P} = 6.4 Hz), 72.2 (d, J_{C-P} = 85.4 Hz), 126.5 (d, J_{C-P} = 93.6 Hz), 129.1 (d, J_{C-P} = 10.9 Hz), 132.4 (d, J_{C-P} = 8.2 Hz), 142.3; ^{31}P NMR (202 MHz, $CDCl_3$): δ 34.97 (s). Anal. Calcd for $C_{17}H_{21}O_2P$: C, 70.82; H, 7.34. Found: C, 70.47; H, 7.17.

*Synthesis of Diphenyl(1-hydroxycyclohexyl)phosphine Oxide (**11m**).*[31] To a solution of diphenylphosphine oxide (1 g, 4.95 mmol) in anhydrous THF (20 mL) was added triethylamine (0.76 mL, 5.45 mmol), and the reaction mixture was cooled to 0 °C. Then trimethylsilane chloride (0.69 mL, 5.45 mmol) was added dropwise, and the mixture was stirred at this temperature for 1.5 h. Then anhydrous THF (10 mL) was added, and the solution was filtered. Subsequently, the filtrate was concentrated on a vacuum pump, and a solution of cyclohexanone (2.05 mL, 19.8 mmol) in anhydrous toluene (15 mL) was added to the crude reaction mixture. The resulting mixture was stirred overnight at 100 °C. Then the mixture was allowed to cool to room tempetature, and the crystallization of product was observed. Crystals were filtered and washed with cold toluene and diethyl ether (0.747 g, 49%). The filtrate was concentrated and then diluted with chloroform (50 mL), and saturated solution of NH_4Cl (10 mL) was added. After extraction with chloroform (3 × 40 mL), organic phases were dried over Na_2SO_4 and concentrated. Product was purified by crystallization from toluene. Product **11m** (0.895 g, 60%) was obtained as a solid; mp = 154.9−155.1 °C; R_f = 0.38 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.08−1.17 (m, 11H), 5.41−5.42 (m, 1H), 7.48−7.56 (m, 6H), 7.95−7.98 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 19.6, 19.7, 24.8, 30.4, 30.5, 72.5 (d, J_{P-C} = 91.7 Hz), 128.1 (d, J_{P-C} = 10.0 Hz), 131.0, 128.56, 131.2 (d, J_{P-C} = 2.7 Hz), 131.3 (d, J_{P-C} = 88.1 Hz), 132.2 (d, J_{P-C} = 7.3 Hz); ^{31}P NMR (202 MHz, DMSO-d_6): δ 29.99 (s). Anal. Calcd for $C_{18}H_{21}O_2P$: C, 71.98; H, 7.05. Found: C, 72.00; H, 6.81.

General Procedure for the Synthesis of Hydroxyethylphosphine Oxide 16 and 17. To a solution of a secondaryphosphine oxide (2.0 mmol) in THF (5 mL) was added sodium hydride (84 mg, 60% dispersion in mineral oil, 2.1 mmol) at 0 °C, and the mixture was stirred for 15 min. Then epoxide (3.0 mmol) was added, and the reaction mixture was allowed to warm to room temperature and stirred for 24 h. The reaction was quenched by saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The crude reaction mixture was analyzed by NMR and purified by column chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) as eluent.

*o-Anisyl-(2-hydroxyethyl)phenylphosphine Oxide (**16a**).* According to the general procedure, *o*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) and ethylene oxide (150 μL, 3.0 mmol) afforded product **16a** (0.464 g, 84%) as a solid; mp = 118−119 °C; R_f = 0.7 (ethyl acetate/methanol = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.68−2.72 (m, 2H), 3.75 (s, 3H), 3.69−3.96 (m, 1H), 3.97−4.00 (m, 1H), 6.88−6.91 (m, 1H), 6.96−7.03 (m, 1H), 7.10−7.13 (m, 1H), 7.40−7.43 (m, 2H), 7.46−7.53 (m, 2H), 7.74−7.78 (m, 2H), 7.96−8.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.6 (d, J_{C-P} = 72.7 Hz), 55.3, 57.3 (d, J_{C-P} = 5.5 Hz), 110.8 (d, J_{C-P} = 6.4 Hz), 119.4 (d, J_{C-P} = 98.1 Hz), 121.3 (d, J_{C-P} = 10.9 Hz), 128.3 (d, J_{C-P} = 11.8 Hz), 130.5 (d, J_{C-P} = 10.0 Hz), 131.6 (d, J_{C-P} = 2.7 Hz), 133.4 (d, J_{C-P} = 101.7 Hz), 134.2 (d, J_{C-P} = 2.7 Hz), 134.3, 159.6 (d, J_{C-P} = 4.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 34.01 (s). Anal. Calcd for $C_{15}H_{17}O_3P$: C, 65.21; H, 6.20. Found: C, 64.96; H, 6.34.

*(2-Hydroxyethyl)(1-naphthyl)phenylphosphine Oxide (**16b**).* According to the general procedure, 1-naphthylphenylphosphine oxide (0.504 g, 2.0 mmol) and ethylene oxide (150 μL, 3.0 mmol) afforded product **16b** (0.242 g, 41%) as an yellow solid; mp = 118.2−119.0 °C; R_f = 0.24 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.60−2.67 (m, 2H), 2.82−2.90 (m, 2H), 3.90 (bs, 1H), 4.03−4.07 (m, 2H), 7.45−7.56 (m, 6H), 7.71−7.75 (m, 2H), 7.88−7.96 (m, 2H), 8.04−8.05 (m, 1H), 8.38−8.40 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.1 (d, J_{C-P} = 69.9 Hz), 57.3, 124.4 (d, J_{C-P} = 12.7 Hz), 126.2 (d, J_{C-P} = 5.5 Hz), 126.5, 127.5, 127.9 (d, J_{C-P} = 97.2 Hz), 128.8 (d, J_{C-P} = 11.8 Hz), 129.1, 130.8 (d, J_{C-P} = 10.0 Hz), 132.0, 132.1, 132.9 (d, J_{C-P} = 100.0 Hz), 132.8 (d, J_{C-P} = 8.2 Hz), 133.5 (d, J_{C-P} = 1.8 Hz), 133.8 (d, J_{C-P} = 9.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 37.13 (s). Anal. Calcd for $C_{18}H_{17}O_2P$: C, 72.96; H, 5.78. Found: C, 72.58; H, 5.78.

*o-Anisyl-(2-hydroxypropyl)phenylphosphine Oxide (**17a**).* According to the general procedure, *o*-anisylphenylphosphine oxide (0.464 g, 2.0 mmol) and propylene oxide (210 μL, 3.0 mmol) afforded product **17a** (0.284 g, 49%) as two diastereomers isolated as a mixture (dr = 53:47). R_f = 0.29 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 and 1.26 (d, J_{H-H} = 6.22 and 6.31 Hz, 6H), 2.41−2.50 (m, 2H), 2.59−2.67 (m, 2H), 3.71 (s, 3H), 3.80 (s, 3H), 4.16−4.17(m, 1H), 4.27−4.28 (m, 1H), 4.40 (bs, 1H), 6.90−6.93 (m, 2H), 7.05−7.10 (m, 1H), 7.12−7.17 (m, 1H), 7.41−7.54 (m, 8H), 7.70−7.73 (m, 2H), 7.78−7.82 (m, 2H), 7.88−7.92 (m, 1H), 8.06−8.10 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.7 (d, J_{C-P} = 15.4 Hz), 37.0 (d, J_{C-P} = 72.7 Hz) and 37.7 (d, J_{C-P} = 71.5 Hz), 55.2, 55.3, 63.4 (d, J_{C-P} = 3.6 Hz) and 63.5 (d, J_{C-P} = 4.5 Hz), 110.8 (d, J_{C-P} = 5.5 Hz), 119.1 (d, J_{C-P} = 98.1 Hz) and 120.9 (d, J_{C-P} = 98.1 Hz), 121.1 (d, J_{C-P} = 10.9 Hz) and 121.3 (d, J_{C-P} = 10.0 Hz), 128.2 (d, J_{C-P} = 12.7 Hz) and 128.3 (d, J_{C-P} = 11.8 Hz), 130.1 (d, J_{C-P} = 10.0 Hz) and 130.6 (d, J_{C-P} = 10.0 Hz), 131.5 (d, J_{C-P} = 2.7 Hz), 133.3 (d, J_{C-P} = 5.5 Hz), 133.4 (d, J_{C-P} = 12.7 Hz), 134.1 (d, J_{C-P} = 1.8 Hz) and 134.2, 134.7 (d, J_{C-P} = 5.5 Hz), 159.4 (d, J_{C-P} = 4.5 Hz) and 159.6 (d, J_{C-P} = 4.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 33.22 (s) and 33.62 (s). Anal. Calcd for $C_{16}H_{19}O_3P$: C, 66.20; H, 6.60. Found: C, 66.48, H, 6.48.

*tert-Butyl(hydroxypropyl)phenylphosphine Oxide (**17f**).* According to the general procedure, *tert*-butylphenylphosphine oxide (0.364 g, 2.0 mmol) and propylene oxide (210 μL, 3.0 mmol) afforded

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

product **17f** (0.211 g, 44%) as two diastereomers isolated as a mixture (dr = 53:47). Major diastereoisomer: R_f = 0.38 (ethyl acetate/methanol = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (d, J_{H-P} = 15.13 Hz, 9H), 1.26 (d, J_{H-P} = 5.99 Hz, 3H), 2.16−2.20 (m, 2H), 4.35−4.41 (m, 1H), 4.58 (bs, 1H), 7.43−7.48 (m, 3H), 7.68−7.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1, 24.87 (d, J_{C-P} = 10.9 Hz), 32.4 (d, J_{C-P} = 63.6 Hz), 33.1 (d, J_{C-P} = 68.1 Hz), 64.6 (d, J_{C-P} = 5.5 Hz), 128.2 (d, J_{C-P} = 10.9 Hz), 129.2 (d, J_{C-P} = 86.3 Hz), 131.3, (d, J_{C-P} = 8.2 Hz), 131.6 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 49.49 (s). Anal. Calcd for $C_{13}H_{21}O_2P$: C, 64.98; H, 8.81. Found: C, 64.64; H, 8.72. Minor diastereoisomer: R_f = 0.25 (ethyl acetate/methanol = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (d, J_{H-P} = 14.82 Hz, 9H), 1.23 (d, J_{H-P} = 5.99 Hz, 3H), 2.07−2.10 (m, 2H), 3.96−4.06 (m, 1H), 4.58 (bs, 1H), 7.49−7.51 (m, 3H), 7.73−7.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.9, 24.86 (d, J_{C-P} = 14.5 Hz), 31.1 (d, J_{C-P} = 63.6 Hz), 32.7 (d, J_{C-P} = 69.0 Hz), 63.2 (d, J_{C-P} = 5.5 Hz), 128.4 (d, J_{C-P} = 10.0 Hz), 129.2 (d, J_{C-P} = 86.3 Hz), 131.8 (d, J_{C-P} = 7.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 53.07 (s). Anal. Calcd for $C_{13}H_{21}O_2P$: C, 64.98; H, 8.81. Found: C, 64.64; H, 8.72.

General Procedure for the Synthesis of Hydroxyethylphosphine Oxide 16 and 17. To a solution of a secondary phosphine oxide (2 mmol) in THF (10 mL) was added *n*-butyllithium (1.38 mL, 1.6 M in hexanes, 2.2 mmol) at −78 °C, and the reaction mixture was stirred at −78 °C for 15 min. Subsequently, epoxide (3 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 24 h. The reaction was then quenched by addition of saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 50 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. Product was purified by column chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) as eluent.

*(2-Hydroxyethyl)diphenylphosphine Oxide (**16m**).*[32] According to the general procedure, diphenylphosphine oxide (0.404 g, 2.0 mmol) and ethylene oxide (150 μL, 3.0 mmol) afforded **16m** (0.315 g, 64%) as a solid; mp = 93.9−94.5 °C; R_f = 0.28 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.55−2.60 (m, 2H), 3.73 (bs, 1H), 3.96−4.02 (m, 2H), 7.46−7.54 (m, 6H), 7.70−7.74 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.2 (d, J_{C-P} = 70.8 Hz), 56.8 (d, J_{C-P} = 3.6 Hz), 128.7 (d, J_{C-P} = 11.8 Hz), 130.6 (d, J_{C-P} = 9.1 Hz), 131.9 (d, J_{C-P} = 2.7 Hz), 132.8; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 34.22 (s). Anal. Calcd for $C_{14}H_{15}O_2P$: C, 68.29; H, 6.14. Found: C, 68.33; H, 6.18.

*(2-Hydroxypropyl)(1-naphthyl)phenylphosphine Oxide (**17b**).* According to the general procedure, 1-naphthylphenylphosphine oxide (0.504 g, 2.0 mmol) and propylene oxide (210 μL, 3.0 mmol) afforded product **17b** (0.422 g, 68%) as two diastereomers isolated as a mixture (dr = 56:44). Major diastereoisomer: R_f = 0.4 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (dd, J_{H-H} = 1.89 Hz J_{H-P} = 6.31 Hz, 3H), 2.58−2.69 (m, 2H), 4.22 (bs, 1H), 4.27−4.56 (m, 1H), 7.41−7.45 (m, 3H), 7.50−7.52 (m, 2H), 7.58−7.62 (m, 1H), 7.68−7.72 (m, 2H), 7.90−7.92 (m, 1H), 8.07−8.16 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.8 (d, J_{C-P} = 14.5 Hz), 37.8 (d, J_{C-P} = 72.5 Hz), 63.7 (d, J_{C-P} = 4.5 Hz), 124.2 (d, J_{C-P} = 13.6 Hz), 126.0 (d, J_{C-P} = 5.5 Hz), 126.4, 127.1 (d, J_{C-P} = 95.4 Hz), 127.3, 128.79 (d, J_{C-P} = 11.8 Hz), 128.97, 130.4 (d, J_{C-P} = 10.0 Hz), 131.1, 132.1 (d, J_{C-P} = 2.7 Hz), 132.6, 132.8 (d, J_{C-P} = 8.2 Hz), 133.1, 133.5 (d, J_{C-P} = 3.6 Hz), 133.8 (d, J_{C-P} = 9.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 36.28 (s); GC t_R = 22.58 min; GC−MS (EI, 70 eV) *m*/*z* = 310 (M^+) (28), 309 (48), 295 (17), 293 (12), 291 (17), 278 (8), 277 (40), 266 (25), 265 (100), 252 (29), 251 (85), 250 (19), 249 (90), 233 (19), 203 (20), 202 (32), 200 (6), 173 (69), 144 (10), 141 (33), 133 (11), 128 (63), 127 (63), 126 (29), 1125 (12), 112 (24), 101 (14); HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{19}H_{19}O_2PNa$ 333.1020; found 333.1015. Anal. Calcd for $C_{19}H_{19}O_2P$: C, 73.54; H, 6.17. Found: C, 73.40; H, 6.25. Minor diastereoisomer: R_f = 0.4 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (dd, J_{H-H} = 1.58 Hz and J_{H-P} = 5.99 Hz, 3H), 2.39−2.43 (m, 1H), 2.72−2.80 (m, 1H), 4.22 (bs, 1H), 4.28−4.38 (m, 1H), 7.49−7.51 (m, 6H), 7.74−7.78 (m, 3H), 7.87−7.79 (m, 1H), 8.02−8.04 (m, 1H), 8.56−8.58 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.9 (d, J_{C-P} = 15.5 Hz), 37.9 (d, J_{C-P} = 72.7 Hz), 63.2 (d, J_{C-P} = 63.6 Hz), 124.5 (d, J_{C-P} = 13.6 Hz), 126.0 (d, J_{C-P} = 5.5 Hz), 126.3 (d, J_{C-P} = 6.4 Hz), 126.4, 127.6, 128.6 (d, J_{C-P} = 98.1 Hz), 128.8 (d, J_{C-P} = 11.8 Hz), 129.2, 131.0 (d, J_{C-P} = 9.1 Hz), 131.2, 131.8, 132.0 (d, J_{C-P} = 2.7 Hz), 132.9 (d, J_{C-P} = 8.2 Hz), 133.2, 133.6 (d, J_{C-P} = 2.7 Hz), 133.9 (d, J_{C-P} = 9.9 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 37.23 (s); GC t_R = 22.58 min; GC−MS (EI, 70 eV) *m*/*z* = 310 (M^+) (28), 309 (48), 295 (17), 293 (12), 291 (17), 278 (8), 277 (40), 266 (25), 265 (100), 252 (29), 251 (85), 250 (19), 249 (90), 233 (19), 203 (20), 202 (32), 200 (6), 173 (69), 144 (10), 141 (33), 133 (11), 128 (63), 127 (63), 126 (29), 1125 (12), 112 (24), 101 (14); HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{19}H_{19}O_2PNa$ 333.1020; found 333.1015. Anal. Calcd for $C_{19}H_{19}O_2P$: C, 73.54; H, 6.17. Found: C, 73.40; H, 6.25.

*Diphenyl(o-hydroxyphenyl)phosphine Oxide (**20**).*[33] Prepared according to reported procedure.[19] Crystallization from methanol afforded product **20** (0.398 g, 55%) as a solid; mp = 229.6−230.6 °C; R_f = 0.64 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81−6.85 (m, 1H), 6.97−7.01 (m, 2H), 7.39−7.42 (m, 1H), 7.47−7.52 (m, 4H), 7.57−7.7.60 (m, 2H), 7.67−7.71 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 111.6 (d, J_{C-P} = 103.8 Hz), 118.6 (d, J_{C-P} = 8.2 Hz), 119.0 (d, J_{C-P} = 12.7 Hz), 128.7 (d, J_{C-P} = 12.7 Hz), 131.6 (d, J_{C-P} = 79.1 Hz), 132.0 (d, J_{C-P} = 10.0 Hz), 132.5 (d, J_{C-P} = 2.7 Hz), 134.4 (d, J_{C-P} = 2.7 Hz), 163.9 (d, J_{C-P} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ39.55 (s); GC t_R = 19.62 min; 295 (14), 294 (M, 81) 293 (100), 277 (8), 214 (24), 198 (35), 183 (11), 152 (27), 141 (7), 115 (12). Anal. Calcd for $C_{18}H_{15}O_2P$: C, 73.46; H, 5.14. Found: C, 73.48; H, 4.84.

*Synthesis of tert-Butylphenyl(2-(2-methyl-3-oxopentyl))phosphine Oxide (**22**).* A solution of *tert*-butylphenylphosphine oxide (0.364 g, 2 mmol) in acetone (40 mL) was treated with NaH (80 mg, 60% dispersion in mineral oil, 2 mmol). The reaction mixture was stirred for 24 h at 60 °C and then was quenched by saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 50 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. Product was purified by column chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) as eluent. Product **22** (0.448 g, 80%) was isolated as a solid; mp = 87.5−88.4 °C; R_f = 0.35 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 1.22 (d, J_{H-P} = 13.56 Hz, 9H), 1.29 and 1.39 (d, J_{H-H} = 14.50 Hz, 3H), 2.07 (s, 3H), 2.62−2.87 (m, 2H), 7.51−7.58 (m, 3H), 7.83−7.87 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6, 80 °C) δ 22.2 (d, J_{C-P} = 20.0 Hz), 26.5, 33.1 (d, J_{C-P} = 1.8 Hz), 35.2 (d, J_{C-P} = 59.9 Hz), 38.1 (d, J_{C-P} = 59.0 Hz), 47.7, 127.5 (d, J_{C-P} = 9.1 Hz), 130.4 (d, J_{C-P} = 76.3 Hz), 130.7 (d, J_{C-P} = 2.7 Hz), 131.3 (d, J_{C-P} = 6.4 Hz), 206.0 (d, J_{C-P} = 12.7 Hz); ^{31}P NMR (202 MHz, DMSO-d_6) δ 50.55 (s). Anal. Calcd for $C_{16}H_{25}O_2P$: C, 68.55; H, 8.99. Found: C, 68.20; H, 8.94.

*Synthesis of tert-Butylphenyl(2-(2-methyl-3-hydroxypentyl))phosphine Oxide (**23**).* A solution of phosphine oxide **22** (0.124 g, 0.44 mmol) in THF (5 mL) was treated with $BH_3{\cdot}SMe_2$ complex (42 μL, 0.44 mmol), and the reaction was stirred for 24 h at room temperature. Then the reaction mixture was quenched by saturated Na_2CO_3 solution (5 mL) and extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. Product was purified by column chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) as eluent. The compound **23** (0.114 g, 91%) was isolated as a mixture of diastereoisomers (dr = 56:44). R_f = 0.3 (chloroform/ethyl acetate/methanol = 30:5:1). ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 1.00 and 1.02 (d, J_{H-P} = 4.1 Hz, 3H), 1.20 (d, J_{H-P} = 14.82 Hz, 3H), 1.21 (d, J_{H-P} = 13.24 Hz, 9H), 1.22 (d, J_{H-P} = 13.56 Hz, 9H), 1.24 (d, J_{H-P} = 14.19 Hz, 3H), 1.34 (d, J_{H-P} = 14.19 Hz, 3H), 1.40 (d, J_{H-P} = 14.50 Hz, 3H), 1.48−1.69 (m, 3H), 1.80−1.86 (m, 1H), 3.82−3.91 (m, 2H), 4.89 (bs, 2H), 7.50−7.58 (m, 6H), 7.81−7.89 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6, 80 °C) δ 23.8, 24.6, 25.0 (d, J_{C-P} = 10.0 Hz), 26.0 (d, J_{C-P} = 7.3 Hz), 26.5, 35.1 (d, J_{C-P} = 59.9 Hz), 35.3 (d, J_{C-P} = 59.0 Hz), 38.3 (d, J_{C-P} = 59.0 Hz), 38.4 (d, J_{C-P} = 58.1 Hz), 47.4, 47.8, 61.9 (d, J_{C-P} = 7.3 Hz), 62.0 (d, J_{C-P} = 7.3 Hz), 128.3 (d,

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

J_{C-P} = 10.0 Hz), 128.4 (d, J_{C-P} = 10.0 Hz), 131.4 (d, J_{C-P} = 2.7 Hz), 131.5 (d, J_{C-P} = 2.7 Hz), 131.6 (d, J_{C-P} = 76.3 Hz), 131.7 (d, J_{C-P} = 76.3 Hz), 132.7 (d, J_{C-P} = 6.4 Hz), 132.8 (d, J_{C-P} = 7.3 Hz); ^{31}P NMR (202 MHz, DMSO-d_6, 80 °C) δ 52.92 (s) and 53.33 (s); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{28}O_2P$ 283.1821; found 283.1775. Anal. Calcd for $C_{16}H_{27}O_2P$: C, 68.06; H, 9.64. Found: C, 68.00; H, 9.60.

General Procedure for the Reaction of Hydroxymethylphosphine Oxides with BH_3·THF. In a two-necked round-bottom flask (25 mL) equipped with magnetic stirrer and argon inlet was placed hydroxymethylphosphine oxide **1** (0.5 mmol) in anhydrous THF (2 mL). Then BH_3·THF complex (1.5 mL, 1.5 mmol, 1 M solution in THF) was added via syringe over a period of 2 min to avoid uncontrolled bubbling. After addition of BH_3 complex, the reaction mixture was stirred for an indicated time at room temperature or 60 °C. Then the reaction mixture was evaporated to dryness, and the residue was purified by column chromatography using hexane/ethyl acetate (v/v = 4:1) as eluent.

General Procedure for the Reaction of α-Hydroxyphosphine Oxides with BH_3 Complexes. In a two-necked round-bottom flask (25 mL) equipped with magnetic stirrer and argon inlet was dissolved hydroxymethylphosphine oxide (0.5 mmol) in anhydrous THF (2 mL). Then BH_3·THF complex (1.5 mL, 1.5 mmol, 1 M solution in THF) or BH_3·SMe_2 (142 μL, 1.5 mmol) was added via syringe over a period of 2 min to avoid uncontrolled bubbling. After addition of BH_3 complex, the reaction mixture was stirred for an indicated time at room temperature or 60 °C. Then the reaction mixture was evaporated to dryness, and the residue was purified by column chromatography using hexane/ethyl acetate (v/v = 4:1) or hexane/ethyl acetate (v/v = 2:1) as eluent.

*o-Anisyl(hydroxymethyl)phenylphosphine−Borane (**2a**).* According to the general procedure, **1a** (0.131 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2a** (0.13 g, 100%) as a greasy oil; R_f = 0.68 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.57−1.34 (bm, 3H), 2.54 (bs, 1H), 4.75 (s, 3H), 4.58 (m, 2H), 6.94−6.96 (m, 1H), 7.07−7.11 (m, 1H), 7.39−7.42 (m, 2H), 7.44−7,47 (m, 1H), 7.52−7.55 (m, 1H), 7.64−7.66 (m, 1H), 7.82−7.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.7, 59.9 (d, J_{P-C} = 41.8 Hz), 111.3 (d, J_{P-C} = 4.5 Hz), 114.3 (d, J_{P-C} = 53.6 Hz), 121.5 (d, J_{P-C} = 10.9 Hz), 127.9 (d, J_{P-C} = 56.3 Hz), 128.5 (d, J_{P-C} = 10.9 Hz), 130.9 (d, J_{P-C} = 2.7 Hz), 131.9 (d, J_{P-C} = 9.1 Hz), 134.1, 134.3 (d, J_{P-C} = 12.7 Hz), 161.1; ^{31}P NMR (202 MHz, $CDCl_3$) δ 17.47 (m). Anal. Calcd for $C_{14}H_{18}BO_2P$: C, 64.65; H, 6.98. Found: C, 64.25; H, 7.20.

*(Hydroxymethyl)-1-naphthylphenylphosphine−Borane (**2b**).* According to the general procedure, **1b** (0.141 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2b** (0.120 g, 86%) as a thick oil; R_f = 0.74 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82−1.50 (bm, 3H), 2.38 (bs, 1H), 4.59 (m, 2H), 7.36−7.50 (m, 5H), 7.58−7.67 (m, 3H), 7.89−8.06 (m, 3H), 8.14−8.18 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 60.9 (d, J_{P-C} = 41.8 Hz), 122.7 (d, J_{P-C} = 51.8 Hz), 125.0 (d, J_{P-C} = 10.9 Hz), 126.4, 126.5, 126.9, 127.4 (d, J_{P-C} = 53.9 Hz), 129.0 (d, J_{P-C} = 10.0 Hz), 129.2, 131.6 (d, J_{P-C} = 2.7 Hz), 132.3 (d, J_{P-C} = 9.1 Hz), 133.0 (d, J_{P-C} = 2.7 Hz), 133.2 (d, J_{P-C} = 8.2 Hz), 133.5 (d, J_{P-C} = 8.2 Hz), 133.9 (d, J_{P-C} = 7.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 17.02 (m). Anal. Calcd for $C_{17}H_{18}BOP$: C, 72.89; H, 6.49. Found: C, 73.27; H, 6.89.

*(Hydroxymethyl)-di-p-anisylphosphine−Borane (**2c**).* According to the general procedure, **1c** (0.146 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2c** (0.129 g, 90%) as a thick oil; R_f = 0.62 (hexane/ethyl acetate = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.23−1.49 (bm, 3H), 2.16 (bs, 1H), 3.83 (s, 6H), 4.34 (s, 2H), 6.95−7.00 (m, 4H), 7.61−7.67 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.3, 60.6 (d, J_{C-P} = 42.53 Hz), 114.6 (d, J_{C-P} = 10.63 Hz), 117.6 (d, J_{C-P} = 60.4 Hz), 134.3 (d, J_{C-P} = 10.4 Hz), 162.2 (d, J_{C-P} = 2.3 Hz); ^{31}P NMR (122 MHz, $CDCl_3$) δ 14.68 (m). Anal. Calcd for $C_{15}H_{20}BO_3P$: C, 62.10; H 6.95. Found: C, 62.33; H, 7.15.

*Di-p-fluorophenyl(hydroxymethyl)phosphine−Borane (**2d**).* According to the general procedure, **1d** (0.134 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2d** (0.096 g, 72%) as a thick oil; R_f = 0.73 (hexane/ethyl acetate = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.33−1.47 (bm, 3H), 2.27 (bs, 1H), 4.41 (s, 2H), 7.15−7.20 (m, 4H), 7.69−7.77 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 60.5 (d, J_{C-P} = 42.2 Hz), 116.5 (dd, J_{C-P} = 10.4 Hz, J_{C-F} = 21.6 Hz), 122.3 (dd, J_{C-P} = 57.2 Hz, J_{C-F} = 3.5 Hz), 135.1 (dd, J_{C-P} = 10.4 Hz, J_{C-F} = 8.6 Hz), 165.0 (dd, J_{C-P} = 2.9 Hz, J_{C-F} = 254.3 Hz); ^{31}P NMR (122 MHz, $CDCl_3$) δ 16.58 (m). Anal. Calcd for $C_{13}H_{14}BF_2OP$: Calc: C, 58.69; H, 5.30. Found: C, 58.30; H, 5.14.

*Di(3,5-dimethylphenyl)hydroxymethylphosphine−Borane (**2e**).* According to the general procedure, **1e** (0.144 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2e** (0.0815 g, 57%) as a thick oil; R_f = 0.89 (hexane/ethyl acetate = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.5−1.44 (bm, 3H), 2.13 (bs, 1H), 2.34 (s, 12H), 4.41 (s, 2H), 7.1−14−7.16 (m, 2H), 7.29−7.35 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 60.3 (d, J_{P-C} = 41.4 Hz), 126.4 (d, J_{P-C} = 54.6 Hz), 130.1 (d, J_{P-C} = 9.2 Hz), 133.4 (d, J_{P-C} = 2.9 Hz), 138.6 (d, J_{P-C} = 10.3 Hz); ^{31}P NMR (122 MHz, $CDCl_3$) δ 17.01 (m). Anal. Calcd for $C_{17}H_{24}BOP$: C, 71.35; H, 8.45. Found: C, 71.04; H, 8.26.

*tert-Butyl(hydroxymethyl)phenylphosphine−Borane (**2f**).*[4e] According to the general procedure, **1f** (0.106 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2f** (0.103 g, 98%) as a solid; mp = 68.7−64.7 °C; R_f = 0.58 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.37−1.00 (bm, 3H), 1.18 (d, J_{P-H} = 13.87 Hz, 9H), 2.10 (bs, 1H), 4.39 (m, J_{H-P} = 13.24 Hz, J_{H-H} = 2.21 Hz, 2H), 7.45−7.55 (m, 3H), 7.70−7.73 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.8, 29.2 (d, J_{P-C} = 30.0 Hz), 55.9 (d, J_{P-C} = 39.1 Hz), 124.8 (d, J_{P-C} = 49.9 Hz), 128.5 (d, J_{P-C} = 9.1 Hz), 131.6 (d, J_{P-C} = 2.7 Hz), 133.5 (d, J_{P-C} = 7.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 31.45 (m). Anal. Calcd for $C_{11}H_{20}BOP$: C, 62.90; H, 9.60. Found: C, 62.61; H, 9.51.

*Benzyl(hydroxymethyl)phenylphosphine−Borane (**2g**).* According to the general procedure, **1g** (0.123 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2g** (0.121 g, 99%) as a thick oil; R_f = 0.73 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.35−1.03 (bm, 3H), 2.13 (bs, 1H), 3.39 (d, J_{P-H} = 12.30 Hz, 2H), 4.13 (m, 2H), 7.06−7.09 (m, 2H), 7.23−7.25 (m, 3H), 7.41−7.44 (m, 2H), 7.51−7.54 (m, 1H), 7.60−7.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.3 (d, J_{P-C} = 30.9 Hz), 58.1 (d, J_{P-C} = 40.9 Hz), 125.5 (d, J_{P-C} = 50.9 Hz), 127.1 (d, J_{P-C} = 2.7 Hz), 128.4 (d, J_{P-C} = 1.8 Hz), 128.7 (d, J_{P-C} = 9.1 Hz), 131.7 (d, J_{P-C} = 6.4 Hz), 131.9 (d, J_{P-C} = 2.7 Hz), 132.7 (d, J_{P-C} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 17.23 (m). Anal. Calcd for $C_{14}H_{18}BOP$: C, 68.89; H, 7.43. Found: C, 68.35; H, 7.24.

*(Hydroxymethyl)phenyl-isopropylphosphine−Borane (**2h**).* The reaction was performed analogously to that described above using **1h** (0.099 g, 0.5 mmol), BH_3·THF (2.5 mL, 2.5 mmol). The reaction afforded product **2h** (0.0882 g, 90%) as an oil; R_f = 0.73 (hexane/ethyl acetate = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.08−0.93 (bm, 3H), 1.04 (dd, J_{H-H} = 7.14 Hz, J_{P-H} = 15.73 Hz, 3H), 1.26 (dd, J_{H-H} = 7.14 Hz, J_{H-P} = 15.92 Hz, 3H), 2.21 (bs, 1H), 2.39−2.53 (m, 1H), 4.13 (m, 2H), 7.43−7.58 (m, 3H), 7.74−7.80 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 16.6 (d, J_{C-P} = 1.2 Hz), 21.7 (d, J_{C-P} = 35.1 Hz), 58.3 (d, J_{C-P} = 40.2 Hz), 125.8 (d, J_{C-P} = 51.2 Hz), 128.7 (d, J_{C-P} = 9.2 Hz), 131.7 (d, J_{C-P} = 2.3 Hz), 132.8 (d, J_{C-P} = 8.1 Hz); ^{31}P NMR (122 MHz, $CDCl_3$) δ 26.32 (m). Anal. Calcd for $C_{10}H_{18}BOP$: C, 61.27; H, 9.25. Found: C, 61.47; H, 9.14.

*Cyclohexyl(hydroxymethyl)phenylphosphine−Borane (**2i**).* The reaction was performed analogously to that described above using **1i** (0.119 g, 0.5 mmol), BH_3·THF (2.5 mL, 2.5 mmol). The reaction afforded product **2i** (0.109 g, 90%) as an oil; R_f = 0.83 (hexane/ethyl acetate = 2:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00−1.13 (bm, 3H), 1.16−1.97 (m, 10H), 2.05 (bs, 1H), 2.12−2.25 (m, 1H), 4.20 (m, 2H), 7.44−7.53 (m, 3H), 7.73−7.80 (m, 2H); ^{13}C NMR (75 MHz,

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

$CDCl_3$) δ 25.6 (d, J_{P-C} = 1.7 Hz), 26.1, 26.34, 26.4, 26.5 (d, J_{P-C} = 0.9 Hz), 31.7 (d, J_{P-C} = 33.9 Hz), 57.9 (d, J_{P-C} = 39.7 Hz), 125.6 (d, J_{P-C} = 51.2 Hz), 128.6 (d, J_{P-C} = 9.2 Hz), 131.6 (d, J_{P-C} = 2.9 Hz), 132.8 (d, J_{P-C} = 7.5 Hz); ^{31}P NMR (122 MHz, $CDCl_3$) δ 22.44 (m). Anal. Calcd for $C_{13}H_{22}BOP$: C, 66.13; H, 9.39. Found: C, 66.42; H, 9.42.

*Hydroxymethyl(methyl)phenylphosphine−Borane (**2j**).* According to the general procedure, **1j** (0.085 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 4 h. The reaction afforded product **2j** (0.0605 g, 99%) as an oil; R_f = 0.45 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.35−1.04 (bm, 3H), 1.64 (d, J_{H-P} = 10.40 Hz, 3H), 2.08 (bs, 1H), 4.07 (s, 2H), 7.46−7.50 (m, 2H), 7.52−7.56 (m, 1H), 7.73−7.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.9 (d, J_{P-C} = 39.1 Hz), 60.9 (d, J_{P-C} = 40.9 Hz), 127.0 (d, J_{P-C} = 53.6 Hz), 128.9 (d, J_{P-C} = 10.0 Hz), 131.8 (d, J_{P-C} = 2.7 Hz), 131.9 (d, J_{P-C} = 9.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 11.02 (m). Anal. Calcd for $C_8H_{14}BOP$: C, 57.20; H, 8.40. Found: C, 57.00; H, 8.20.

*Di-c-hexyl(hydroxymethyl)phosphine−Borane (**2k**).* According to the general procedure, **1k** (0.122 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 16 h. The reaction afforded product **2j** (0.108 g, 89%) as a solid; mp = 107.4−108.1 °C; R_f = 0.83 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.12−0.62 (bm, 3H), 1.20−1.59 (m, 10H), 1.72−1.91 (m, 12H), 4.01 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.8, 26.6, 26.7, 26.8, 26.9, 29.8 (d, J_{P-C} = 31.8 Hz), 55.5 (d, J_{P-C} = 37.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 27.51 (m). Anal. Calcd for $C_{13}H_{28}BOP$: C, 64.48; H, 11.66. Found: C, 64.26; H, 11.59.

*Di-n-hexyl(hydroxymethyl)phosphine−Borane (**2l**).* The reaction was performed analogously to that described above using **1l** (0.11 g, 0.5 mmol), BH_3·SMe_2 (237 μL, 2.5 mmol) at room temperature for 4 h. The reaction afforded product **2l** (0.095 g, 87%) as an oil; R_f = 0.65 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.04−0.69 (bm, 3H), 0.87 (t, J_{H-H} = 6.64 Hz, 6H), 1.23−1.28 (m, 8H), 1.33−1.43 (m, 4H), 1.46−1.56 (m, 4H), 1.582−1.61 (m, 4H), 2.20 (bs, 1H), 3.93 (bs, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 20.8 (d, J_{P-C} = 33.6 Hz), 22.4, 22.5, 30.8 (d, J_{P-C} = 12.7 Hz), 31.2, 57.3 (d, J_{P-C} = 39.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.36 (m). Anal. Calcd for $C_{13}H_{32}BOP$: C, 63.43; H, 13.10. Found: C, 63.03; H, 13.25.

*Attempted Reduction of tert-Butylmethylphenylphosphine Oxide (**3f**).* According to the general procedure, **3f** (0.098g, 0.5 mmol) was treated with BH_3·SMe_2 (0.142 mL, 1.5 mmol) and heated to reflux for 24 h. The analysis by NMR showed presence only of starting material. The starting material **3f** was recovered as a solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (d, J_{P-H} = 15.13 Hz, 9H), 1.76 (d, J_{P-H} = 11.98 Hz, 3H), 7.47−7.50 (m, 2H), 7.50−7.55 (m, 1H), 7.69−7.75 (m, 2H); ^{13}C NMR (75 MHz) δ 10.3 (d, J_{P-C} = 65.5 Hz), 12.2, 32.5 (d, J_{P-C} = 70.9 Hz), 128.1 (d, J_{P-C} = 11.0 Hz), 131.38, 131.4 (d, J_{P-C} = 8.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 49.98 ppm (s). Anal. Calcd for $C_{11}H_{17}OP$: C, 67.33; H, 8.73. Found: C, 67.45; H, 8.43.

*o-Anisyl(1-hydroxyethyl)phenylphosphine−Borane (**7a**).* According to the general procedure, **4a** (0.131 g, 0.5 mmol) was treated with BH_3·SMe_2 (0.142 mL, 1.5 mmol) and stirred at 60 °C for 24 h and afforded **7a** (0.119 g, 92%) as a mixture of two diastereoisomers (dr = 63:37). Both diastereoisomers were separated and characterized. Major diastereoisomer (0.048 g, 37%): solid; mp = 109.9−110 °C; R_f = 0.58 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.50−1.26 (bm, 3H), 1.34 (dd, J_{H-H} = 6.62 Hz, J_{H-P} = 15.13 Hz, 3H), 2.34 (bs, 1H), 3.76 (s, 3H), 5.16−5.21 (m, 1H), 6.91−6.94 (m, 1H), 7.06−7.10 (m, 1H), 7.37−7.47 (m, 3H), 7.51−7.54 (m, 1H), 7.73−7.76 (m, 2H), 7.83−7.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.9 (d, J_{C-P} = 9.1 Hz), 55.6, 64.9 (d, J_{C-P} = 41.8 Hz), 111.2 (d, J_{C-P} = 4.5 Hz), 115.5 (d, J_{C-P} = 50.9 Hz), 121.6 (d, J_{C-P} = 11.8 Hz), 128.3 (d, J_{C-P} = 10.0 Hz), 128.4 (d, J_{C-P} = 56.3 Hz), 130.8 (d, J_{C-P} = 2.7 Hz), 132.3 (d, J_{C-P} = 9.1 Hz), 133.9, 136.7 (d, J_{C-P} = 12.7 Hz), 160.8; ^{31}P NMR (202 MHz, $CDCl_3$) δ 25.28 (m, major). Anal. Calcd for $C_{15}H_{20}BO_2P$: C, 65.73; H, 7.35. Found: C, 65.35; H, 7.43. Minor diastereoisomer (0.044 g, 34%): oil; R_f = 0.52 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.53−1.26 (bm, 3H), 1.42 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 15.45 Hz, 3H), 2.78 (bs, 1H), 3.77 (s, 3H), 4.97−5.01 (m, 1H), 6.99−7.01 (m, 1H), 7.13−7.16 (m, 1H), 7.38−7.45 (m, 3H), 7.54−7.58 (m, 1H), 7.59−7.64 (m, 2H), 7.99−8.03 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1 (d, J_{C-P} = 8.2 Hz), 55.9, 65.3 (d, J_{C-P} = 37.2 Hz), 111.6 (d, J_{C-P} = 4.5 Hz), 114.2 (d, J_{C-P} = 50.0 Hz), 122.0 (d, J_{C-P} = 11.8 Hz), 128.1 (d, J_{C-P} = 55.4 Hz), 128.4 (d, J_{C-P} = 10.0 Hz), 130.8 (d, J_{C-P} = 1.8 Hz), 132.2 (d, J_{C-P} = 8.2 Hz), 134.0, 137.5 (d, J_{C-P} = 12.7 Hz), 160.6; ^{31}P NMR (202 MHz, $CDCl_3$) δ 27.76 (m). Anal. Calcd for $C_{15}H_{20}BO_2P$: C, 65.73; H, 7.35. Found: C, 65.45; H, 7.43.

*tert-Butyl(1-hydroxyethyl)phenylphosphine−Borane (**7f**).* According to the general procedure, **4f** (0.114 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at 60 °C for 18 h. The reaction afforded **7f** (0.083 g, 74%) as two diastereomers isolated as a mixture (dr = 67:33). Major diastereoisomer: R_f = 0.67 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.28−0.97 (bm, 3H), 1.22 (d, J_{H-P} = 13.56 Hz, 9H), 1.53 (dd, J_{H-H} = 6.62 Hz, J_{H-P} = 13.87 Hz, 3H), 2.06 (bs, 1H), 4.76 (m, 1H), 7.42−7.47 (m, 3H), 7.92−7.95 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.6 (d, J_{C-P} = 4.5 Hz), 26.7, 30.1 (d, J_{C-P} = 30.0 Hz), 64.9 (d, J_{C-P} = 37.2 Hz), 124.8 (d, J_{C-P} = 48.1 Hz), 128.2 (d, J_{C-P} = 9.1 Hz), 131.3 (d, J_{C-P} = 2.7 Hz), 134.7 (d, J_{C-P} = 7.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 38.85 (m). Anal. Calcd for $C_{12}H_{22}BOP$: C, 64.32; H, 9.90. Found:. C, 64.20; H, 9.86. Minor diastereoisomer: R_f = 0.67 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.28−0.97 (bm, 3H), 1.19 (d, J_{H-P} = 13.55 Hz, 9H), 1.31 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 12.93 Hz, 3H), 2.06 (bs, 1H), 4.86 (m, 1H), 7.49−7.54 (m, 3H), 7.64−7.67 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.0 (d, J_{C-P} = 7.3 Hz), 26.3, 29.3 (d, J_{C-P} = 30.0 Hz), 62.6 (d, J_{C-P} = 40.0 Hz), 126.2 (d, J_{C-P} = 47.2 Hz), 128.4 (d, J_{C-P} = 47.2 Hz), 131.4 (d, J_{C-P} = 2.7 Hz), 133.6 (d, J_{C-P} = 6.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 36.48 (m). Anal. Calcd for $C_{12}H_{22}BOP$: C, 64.32; H, 9.90. Found: C, 64.20; H, 9.86.

*(1-Hydroxyethyl)(methyl)phenylphosphine−Borane (**7j**).* According to the general procedure, **4j** (0.092 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at 60 °C for 24 h. The reaction afforded product **7j** (0.0655 g, 72%) as two diastereomers isolated as a mixture (dr = 50:50). R_f = 0.51 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.35−1.01 (bm, 6H), 1.31 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 14.19 Hz, 3H) and 1.33 (dd, J_{H-H} = 6.94 Hz, J_{H-P} = 14.50 Hz, 3H), 1.62 (d, J_{H-P} = 3.47 Hz, 3H) and 1.64 (d, J_{H-P} = 3.47 Hz, 3H), 1.99 (bs, 2H), 4.17−4.20 (m, 2H) and 4.18−4.22 (m, 2H), 7.46−7.50 (m, 4H), 7.51−7.57 (m, 2H), 7.71−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.7 and 6.0 (d, J_{C-P} = 38.3 Hz), 17.8 (d, J_{C-P} = 5.5 Hz), 17.8 (d, J_{C-P} = 3.6 Hz), 66.4 (d, J_{C-P} = 40.9 Hz), 66.5 (d, J_{C-P} = 41.8 Hz), 125.9 and 127.1 (d, J_{C-P} = 51.8 Hz), 128.7 and 128.9 (d, J_{C-P} = 10.0 Hz), 131.67 (d, J_{C-P} = 2.7 Hz), 131.7 (d, J_{C-P} = 1.8 Hz), 132.1 (d, J_{C-P} = 9.1 Hz), 132.6 (d, J_{C-P} = 9.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.14 (m). Anal. Calcd for $C_9H_{16}BOP$: C, 59.39; H, 8.86. Found: C, 59.22; H, 8.85.

*Di-c-hexyl(1-hydroxyethyl)phosphine−Borane (**7k**).* According to the general procedure, **4k** (0.129 g, 0.5 mmol) was treated with BH_3·THF (1.5 mL, 1.5 mmol) and stirred at room temperature for 24 h. The reaction afforded product **7k** (0.122 g, 95%) as a solid; mp = 77.9−79.1 °C; R_f = 0.60 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.06−0.64 (bm, 3H), 1.21−1.31 (m, 6H), 1.40−1.42 (m, 4H), 1.49 (dd, J_{H-H} = 7.25 Hz, J_{H-P} = 11.98 Hz, 3H), 1.69−2.08 (m, 12H), 4.22 (q, J_{H-H} = 6.94 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2, 26.0, 26.9, 27.0, 27.02 (d, J_{C-P} = 5.5 Hz), 27.1 (d, J_{C-P} = 5.5 Hz), 27.3 (d, J_{C-P} = 1.8 Hz), 27.5, 27.6 (d, J_{C-P} = 2.7 Hz), 27.8, 30.4 (d, J_{C-P} = 29.1 Hz), 30.61 (d, J_{C-P} = 29.1 Hz), 62.5 (d, J_{C-P} = 36.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 32.27 (m). Anal. Calcd for $C_{14}H_{30}BOP$: C, 65.64; H, 11.80. Found: C, 65.33; H, 12.00.

*(1-Hydroxy-2-methylpropyl)diphenylphosphine−Borane (**8m**).* According to the general procedure, **5m** (0.137 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 24 h. The reaction afforded product **8m** (0.126 g, 93%) as an oil; R_f = 0.84 (hexane/AcOEt = 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.70−1.30 (bm, 3H), 0.89 (d, J_{H-P} = 6.94 Hz, 3H), 0.96 (d, J_{H-P} = 6.62 Hz, 3H), 2.11 (bs, 1H), 2.20 (sept, 1H), 4.47 (ms, 1H), 7.43−7.50 (m, 6H), 7.74−7.78 (m, 2H), 7.87−7.91 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.0 (d, J_{C-P} = 4.5 Hz), 21.3 (d, J_{C-P} = 8.2 Hz), 30.8 (d, J_{C-P} = 7.3 Hz), 75.0 (d, J_{C-P} = 36.3 Hz), 127.7 (d, J_{C-P} =

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

53.6 Hz), 128.5 (d, J_{C-P} = 52.6 Hz), 128.6 (d, J_{C-P} = 9.1 Hz), 128.8 (d, J_{C-P} = 10.0 Hz), 131.3 (d, J_{C-P} = 1.8 Hz), 131.4 (d, J_{C-P} = 1.8 Hz), 132.7 (d, J_{C-P} = 8.2 Hz), 133.4 (d, J_{C-P} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 21.58 (m). Anal. Calcd for $C_{16}H_{22}BOP$: C, 70.62; H, 8.15. Found: C, 70.41; H, 8.22.

*o-Anisyl((1-hydroxy)phenylmethyl)phenylphosphine−Borane (**9a**).* The reaction was performed analogously to that described above using major diastereoisomer of **6a** (0.169 g, 0.5 mmol), $BH_3{\cdot}SMe_2$ (237 μL, 2.5 mmol) at room temperature for 24 h. The reaction afforded product **9a** (0.121 g, 72%) as a solid; mp = 114.3−114.5 °C; R_f = 0.66 (hexane/ethyl acetate = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.45−1.49 (bm, 3H), 3.83 (s, 3H), 4.70 (bs, 1H), 6.02 (d, J_{H-P} = 4.20 Hz, 1H), 7.03−7.09 (m, 2H), 7.13−7.19 (m, 5H), 7.27−7.41 (m, 5H), 7.54−7.58 (m, 1H), 7.75−7.81 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.0, 72.0 (d, J_{C-P} = 32.8 Hz), 111.6 (d, J_{C-P} = 4.6 Hz), 114.1 (d, J_{C-P} = 49.4 Hz), 122.1 (d, J_{C-P} = 12.1 Hz), 127.1 (d, J_{C-P} = 4.0 Hz), 126.8, 127.3 (d, J_{C-P} = 42.5 Hz), 127.7 (d, J_{C-P} = 2.3 Hz), 127.9 (d, J_{C-P} = 2.9 Hz), 128.1 (d, J_{C-P} = 10.4 Hz), 128.5, 130.8 (d, J_{C-P} = 2.9 Hz), 132.6 (d, J_{C-P} = 8.6 Hz), 134.1 (d, J_{C-P} = 2.3 Hz), 137.2 (d, J_{C-P} = 2.3 Hz), 137.4 (d, J_{C-P} = 12.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.34 (m). Anal. Calcd for $C_{20}H_{22}BO_2P$: C, 71.46; H 6.60. Found: C, 71.46; H, 6.50.

*tert-Butyl((1-hydroxy)phenylmethyl)phenylphosphine−Borane (**9f**).* The reaction was performed analogously to that described above using single diastereoisomer of **6f** (0.144 g, 0.5 mmol), $BH_3{\cdot}SMe_2$ (237 μL, 2.5 mmol) at 60 °C for 24 h. The reaction afforded product **9f** (0.078 g, 54%) as a solid; mp = 89.2−90.2 °C; R_f = 0.28 (hexane/ethyl acetate = 6:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.28−0.96 (bm, 3H), 1.15 (d, J_{H-P} = 13.56 Hz, 9H), 2.62 (bs, 1H), 5.64 (d, J_{H-P} = 4.41 Hz, 1H), 7.27−7.28 (m, 3H), 7.38−7.40 (m, 2H), 7.45−7.48 (m, 2H), 7.53−7.56 (m, 1H), 8.01−8.04 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.6, 31.0 (d, J_{C-P} = 28.2 Hz), 71.6 (d, J_{C-P} = 34.5 Hz), 124.6 (d, J_{C-P} = 46.3 Hz), 128.1, 128.2, 128.3 (d, J_{C-P} = 3.6 Hz), 128.8, 134.9 (d, J_{C-P} = 8.2 Hz), 138.2 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 39.81 (m). Anal. Calcd for $C_{17}H_{24}BOP$: C, 71.35; H, 8.45. Found: C, 71.01; H, 8.25.

*((1-Hydroxy)phenylmethyl)(methyl)phenylphosphine−Borane (**9j**).* According to the general procedure, **6j** (0.123 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at 60 °C for 24 h. The reaction afforded product **9j** (0.084 g, 69%) as two diastereomers isolated as a mixture (dr = 63:37). R_f = 0.57 (hexane/ethyl acetate = 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.41−1.17 (bm, 3H), 1.52 (d, J_{H-P} = 10.09 Hz, 3H, minor), 1.58 (d, J_{H-P} = 10.40 Hz, 3H, major), 2.66 (bs, 2H), 5.15 (bs, 2H), 6.96−7.98 (m, 2H, minor), 7.08−7.09 (m, 2H, major), 7.32−7.32 (m, 7H), 7.37−7.43 (m, 4H), 7.47−7.55 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.0 (d, J_{C-P} = 38.2 Hz, minor) and 5.6 (d, J_{C-P} = 39.1 Hz, major), 73.4 (d, J_{C-P} = 37.2 Hz, major) and 73.5 (d, J_{C-P} = 38.2 Hz, minor), 125.7 (d, J_{C-P} = 50.9 Hz), 126.6, 127.9 (d, J_{C-P} = 7.3 Hz), 128.3, 128.4 (d, J_{C-P} = 10.0 Hz), 131.7, 132.62 (d, J_{C-P} = 7.3 Hz) and 132.64 (d, J_{C-P} = 8.2 Hz), 135.8 (s, minor), 135.9 (s, major); ^{31}P NMR (202 MHz, $CDCl_3$) δ 19.98 (m) and 19.76 (m). Anal. Calcd for $C_{14}H_{18}BOP$: C, 68.89; H, 7.43. Found: C, 68.69; H, 7.07.

*Di-c-hexyl((1-hydroxy)phenylmethyl)phosphine−Borane (**9k**).* According to the general procedure, **6k** (0.16 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at 60 °C for 24 h. The reaction afforded product **9k** (0.184 g, 93%) as a solid, mp = 110−111 °C; R_f = 0.69 (hexane/ethyl acetate = 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.04−0.96 (bm, 3H), 1.03−1.56 (m, 11H), 1.60−1.99 (m, 11H), 2.81 (bs, 1H), 5.24 (d, J_{H-P} = 1.72 Hz, 1H), 7.27−7.44 (m, 5H); 13C NMR (75 MHz, $CDCl_3$) δ 25.8 (d, J_{C-P} = 6.3 Hz), 26.7, 26.8, 27.0, 27.1 (d, J_{C-P} = 9.2 Hz), 27.4 (d, J_{C-P} = 3.5 Hz), 29.9, 30.3, 30.5, 30.9 (d, J_{C-P} = 4.6 Hz), 69.4 (d, J_{C-P} = 33.3 Hz), 126.5 (d, J_{C-P} = 2.9 Hz), 128.2, 128.33, 136.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 36.00 (m). Anal. Calcd for $C_{19}H_{32}BOP$: C, 71.71; H, 10.14. Found: C, 71.65; H, 10.03.

*((1-Hydroxy)phenylmethyl)(diphenyl)phosphine−Borane (**9m**).*[34] According to the general procedure, **6m** (0.154 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at 60 °C for 24 h. The reaction afforded product **9m** (0.096 g, 63%) as a thick oil; R_f = 0.69 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.50−1.41 (bm, 3H), 2.69 (bs, 1H), 5.66 (d, J_{H-P} = 2.21 Hz), 7.03−7.05 (m, 2H), 7.17−7.21 (m, 2H), 7.23−7.25 (m, 1H), 7.35−7.40 (m, 2H), 7.45−7.50 (m, 3H), 7.54−7.58 (m, 3H), 7.78−7.83 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 73.3 (d, J_{C-P} = 37.2 Hz, major), 125.5 (d, J_{C-P} = 53.6 Hz), 126.6 (d, J_{C-P} = 53.6 Hz), 127.3 (d, J_{C-P} = 3.6 Hz), 127.8 (d, J_{C-P} = 1.8 Hz), 128.4 (d, J_{C-P} = 2.7 Hz), 128.5 (d, J_{C-P} = 10.0 Hz), 128.6 (d, J_{C-P} = 10.0 Hz), 131.4 (d, J_{C-P} = 2.7 Hz), 131.7 (d, J_{C-P} = 2.7 Hz), 133.3 (d, J_{C-P} = 9.1 Hz), 135.9 (d, J_{C-P} = 8.2 Hz), 136.2; ^{31}P NMR (202 MHz, $CDCl_3$) δ 27.45 (m). Anal. Calcd for $C_{19}H_{20}BOP$: C, 74.54; H, 6.58. Found: C, 74.45; H, 6.40.

*o-Anisyl(1-hydroxy-1-methylethyl)phenylphosphine−Borane (**12a**).* According to the general procedure, **10a** (0.145 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **12a** (0.0662 g, 46%) as a solid, mp = 87.2−87.6 °C; R_f = 0.32 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.59−1.30 (bm, 3H), 1.40 (d, J_{P-H} = 13.56 Hz, 3H), 1.63 (d, J_{P-H} = 14.19 Hz, 3H), 3.71 (s, 3H), 4.07 (bs, 1H), 6.99−7.01 (m, 1H), 7.14−7.17 (m, 1H), 7.35−7.44 (m, 3H), 7.54−7.57 (m, 1H), 7.74−7.78 (m, 2H), 8.12−8.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3 (d, J_{C-P} = 10.0 Hz), 28.3 (d, J_{C-P} = 11.3 Hz), 55.9, 72.2 (d, J_{C-P} = 31.8 Hz), 111.86 (d, J_{C-P} = 3.6 Hz), 116.0 (d, J_{C-P} = 46.3 Hz), 122.3 (d, J_{C-P} = 11.8 Hz), 128.1 (d, J_{C-P} = 10.0 Hz), 128.3 (d, J_{C-P} = 54.5 Hz), 130.5 (d, J_{C-P} = 2.7 Hz), 132.6 (d, J_{C-P} = 8.2 Hz), 133.9 (d, J_{C-P} = 1.8 Hz), 138.0 (d, J_{C-P} = 12.7 Hz), 159.8 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 36.08 (m). Anal. Calcd for $C_{16}H_{22}BO_2P$: C, 66.70; H, 7.70. Found: C, 66.70; H, 7.70.

o-Anisylphenylphosphine Oxide.[12] According to the general procedure, **10a** (0.145 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded **12a** and *o*-anisylphenylphosphine oxide (14 mg, 12%) as a solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.92 (s), 7.04−7.07 (m, 1H), 7.25−7.24 (m, 1H), 7.59−7.76 (m, 2H), 7.60−7.68 (m, 2H), 7.89−7.90 (m, 2H), 7.92−7.96 (m, 1H), 8.18 (d, J_{H-P} = 499.06 Hz); ^{31}P NMR (202 MHz) δ 14.29 (s). Anal. Calcd for $C_{13}H_{13}O_2P$: C, 67.24; H, 5.64. Found: C, 67.20; H, 5.68.

*(1-Hydroxy-1-methylethyl)(1-naphthyl)phenylphosphine−Borane (**12b**).* According to the general procedure, **10b** (0.155 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **12b** (0.0365 g, 25%) as a solid; R_f = 0.60 (hexane/ethyl acetate = 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.80−1.56 (bm, 3H), 1.59 (d, J_{P-H} = 12.30 Hz, 3H), 1.60 (d, J_{P-H} = 12.93 Hz, 3H), 2.35 (bs, 1H), 7.28−7.32 (m, 1H), 7.38−7.50 (m, 4H), 7.56−7.58 (m, 1H), 7.76−7.80 (m, 2H), 7.86−7.87 (m, 1H), 7.96−7.97 (m, 1H), 8.01−8.03 (m, 1H), 8.46−8.50 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.7 (d, J_{C-P} = 8.2 Hz), 27.5 (d, J_{C-P} = 9.1 Hz), 73.0 (d, J_{C-P} = 37.2 Hz), 123.4 (d, J_{C-P} = 47.3 Hz), 124.7 (d, J_{C-P} = 10.9 Hz), 126.1, 126.4, 127.7 (d, J_{C-P} = 4.5 Hz), 128.7 (d, J_{C-P} = 10.0 Hz), 128.8 (d, J_{C-P} = 50.86 Hz), 129.0 (d, J_{C-P} = 10.0 Hz), 129.1, 131.1 (d, J_{C-P} = 1.8 Hz), 132.6 (d, J_{C-P} = 10.0 Hz), 132.8 (d, J_{C-P} = 2.7 Hz), 133.2 (d, J_{C-P} = 8.2 Hz), 133.5 (d, J_{C-P} = 6.4 Hz), 134.2 (d, J_{C-P} = 7.2 Hz), 135.6 (d, J_{C-P} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 31.08 (m).

*1-Naphthylphenylphosphinous Acid−Borane (**14b**).*[35] According to the general procedure, **10b** (0.155 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **14b** as an oil (0.0851 g, 64%); R_f = 0.23 (hexane/ethyl acetate = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.34−1.83 (bm, 3H), 4.79 (bs, 1H), 7.32−7.51 (m, 5H), 7.55−7.77 (m, 3H), 7.83−7.99 (m, 1H), 8.09−8.20 (m, 2H), 8.26−8.48 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 124.62 (d, J_{C-P} = 13.51 Hz), 126.27, 126,50 (d, J_{C-P} = 5.64 Hz), 126.91; 128.49 (d, J_{C-P} = 10.49 Hz), 128.97, 130.63 (d, J_{C-P} = 11.70 Hz), 131.37 (d, J_{C-P} = 2.45 Hz), 133.39 (d, J_{C-P} = 2.61 Hz), 133.61 (d, J_{C-P} = 16.04 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 96.31 (m). Anal. Calcd for $C_{16}H_{16}BOP$: C, 72.22; H, 6.06. Found: C, 72.01; H, 6.24.

*Di-p-anisyl(1-hydroxy-1-methylethyl)phosphine−Borane (**12c**).* According to the general procedure, **10c** (0.16 g, 0.5 mmol) was treated with $BH_3{\cdot}SMe_2$ (142 μL, 1.5 mmol) and stirred at room

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

temperature for 3 h. The reaction afforded product **12c** (0.113 g, 71%) as a solid; mp = 102.7−103.5 °C; R_f = 0.28 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.59−1.30 (bm, 3H), 1.47 (d, J_{P-H} = 13.24 Hz, 3H), 2.01 (bs, 1H), 3.83 (s, 3H), 6.96−6.98 (m, 4H), 7.88−7.92 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.5 (d, J_{C-P} = 10.0 Hz), 55.3, 72.5 (d, J_{C-P} = 38.2 Hz), 114.2 (d, J_{C-P} = 10.9 Hz), 117.5 (d, J_{C-P} = 58.1 Hz), 135.6 (d, J_{C-P} = 9.1 Hz), 162.0 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 27.45 (m). Anal. Calcd for $C_{17}H_{24}BO_3P$: C, 64.18; H, 7.60. Found: C, 63.84; H, 7.64.

*Di-p-fluorophenyl-(1-hydroxy-1-methylethyl)phosphine−Borane (**12d**).* According to the general procedure, **10d** (0.148 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **12d** (0.034 g, 23%) as a solid; mp = 94.1−95.1 °C; R_f = 0.47 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.59−1.36 (bm, 3H), 1.48 (d, J_{P-H} = 13.87 Hz, 6H), 1.77 (bs, 1H), 7.15−7.17 (m, 4H), 7.97−8.02 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.7 (d, J_{C-P} = 10.0 Hz), 72.7 (d, J_{C-P} = 39.1 Hz), 116.1 (dd, J_{C-P} = 21.8 Hz, J_{C-F} = 10.9 Hz), 122.3 (dd, J_{C-P} = 54.5 Hz, J_{C-F} = 3.6 Hz), 136.4 (t, J_{C-F} = 9.1 Hz), 165.3 (dd, J_{C-F} = 253.4 Hz, J_{C-P} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 28.90 (m). Anal. Calcd for $C_{15}H_{18}BF_2OP$: C, 61.26; H, 6.17. Found: C, 61.41; H, 6.23.

*Di-p-fluorophenylphosphinous Acid−Borane (**14d**).* According to the general procedure, **10d** (0.148 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **14d** (0.038 g, 30%) as an oil; R_f = 0.27 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.80−1.55 (bm, 3H), 7.37−7.51 (m, 5H), 7.58−7.70 (m, 3H), 7.87−7.89 (m, 1H), 8.03−8.12 (m, 2H), 8.28−8.32 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 124.7 (d, J_{C-P} = 13.6 Hz), 126.2; 126,7 (d, J_{C-P} = 5.5 Hz), 126.8; 128.9 (d, J_{C-P} = 10.9 Hz), 128.6 (d, J_{C-P} = 60.0 Hz), 128.9; 130.6 (d, J_{C-P} = 11.8 Hz), 131.3 (d, J_{C-P} = 2.7 Hz), 132.4 (d, J_{C-P} = 6.4 Hz), 133.2 (d, J_{C-P} = 2.7 Hz), 133.7 (d, J_{C-P} = 15.4 Hz), 133.8 (d, J_{C-P} = 66.3 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 96.31 (m). Anal. Calcd for $C_{12}H_{12}BF_2OP$: C, 57.19; H, 4.80. Found: C, 57.01; H, 4.50.

*Di-p-fluorophenylphosphine−Borane (**15d**).*[36] According to the general procedure, **10d** (0.148 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **15d** (0.0201 g, 17%) as an oil; R_f = 0.71 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65−1.69 (m, 3H), 6.32 (dq, J_{P-H} = 387.77 Hz, 1H), 7.15−7.19 (m, 4H), 7.63−7.68 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 116.7 (dd, J_{C-P} = 21.8 Hz, J_{C-F} = 11.8 Hz), 126.5 (dd, J_{C-P} = 59.0 Hz, J_{C-F} = 3.6 Hz), 134.8 (dd, J_{C-P} = 8.2 Hz, J_{C-F} = 10.9 Hz), 165.3 (d, J_{C-F} = 254.3 Hz, J_{C-P} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ −1.09 (m). Anal. Calcd for $C_{12}H_{12}BF_2P$: C, 61.07; H, 5.13. Found: C, 60.70; H, 5.43.

*(1-Hydroxy-1-methylethyl)(methyl)phenylphosphine−Borane (**12j**).* According to the general procedure, **10j** (0.099 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 2 h. The reaction afforded product **12j** (0.0853 g, 87%) as an oil; R_f = 0.47 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.38−1.01 (bm, 3H), 1.32 (d, J_{H-P} = 12.30 Hz, 2H), 1.41 (d, J_{H-P} = 12.93 Hz, 2H), 1.65 (d, J_{H-P} = 10.09 Hz, 2H), 1.87 (bs, 1H), 7.46−7.50 (m, 2H), 7.51−7.55 (m, 1H), 7.75−7.80 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.1 (d, J_{P-C} = 39.1 Hz), 25.2 (d, J_{P-C} = 5.5 Hz), 25.3 (d, J_{P-C} = 2.7 Hz), 69.7 (d, J_{P-C} = 39.1 Hz), 126.1 (d, J_{P-C} = 50.0 Hz), 128.6 (d, J_{P-C} = 9.1 Hz), 131.6 (d, J_{P-C} = 2.7 Hz), 132.8 (d, J_{P-C} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 25.34 (m). Anal. Calcd for $C_{10}H_{18}BOP$: C, 61.27; H, 9.25. Found: C, 61.47; H, 9.35.

*p-Anisyl(1-hydroxy-1-methylethyl)phenylphosphine−Borane (**12n**).* According to the general procedure, **10n** (0.145 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **12n** (0.0125 g, 87%) as a solid; mp = 85.8−86.6 °C; R_f = 0.49 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.62−1.31 (bm, 3H), 1.41 (d, J_{P-H} = 13.56 Hz, 3H), 1.65 (d, J_{P-H} = 14.19 Hz, 3H), 3.70 (s, 3H), 6.99−7.03 (m, 1H), 7.13−7.16 (m, 1H), 7.35−7.43 (m, 3H), 7.54−7.58 (m, 1H), 7.74−7.79 (m, 2H), 8.12−8.16 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2 (d, J_{C-P} = 10.9 Hz), 28.2 (d, J_{C-P} = 10.9 Hz), 55.9, 72.2 (d, J_{C-P} = 32.7 Hz), 111.9 (d, J_{C-P} = 4.5 Hz), 116.0 (d, J_{C-P} = 46.3 Hz), 122.2 (d, J_{C-P} = 11.8 Hz), 128.1 (d, J_{C-P} = 10.0 Hz), 128.3 (d, J_{C-P} = 61.8 Hz), 130.4 (d, J_{C-P} = 2.7 Hz), 132.5 (d, J_{C-P} = 9.1 Hz), 133.9, 137.9 (d, J_{C-P} = 12.7 Hz), 159.8 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 35.77 (m). Anal. Calcd for $C_{16}H_{22}BO_2P$: C, 66.7; H, 7.7. Found: C, 66.41; H, 7.59.

*Di-p-tolyl(1-hydroxy-1-methylethyl)phosphine−Borane (**12o**).* According to the general procedure, **10o** (0.144 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at room temperature for 3 h. The reaction afforded product **12o** (0.103 g, 72%) as a solid; mp = 104.4−105.4 °C; R_f = 0.53 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.57−1.33 (bm, 3H), 1.47 (d, J_{P-H} = 13.24 Hz, 6H), 1.19 (bs, 1H), 2.39 (s, 3H), 7.25−7.28 (m, 4H), 7.83−7.88 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.5, 26.5 (d, J_{C-P} = 10.0 Hz), 72.4 (d, J_{C-P} = 38.2 Hz), 123.2 (d, J_{C-P} = 53.6 Hz), 129.4 (d, J_{C-P} = 10.0 Hz), 133.9 (d, J_{C-P} = 9.1 Hz), 141.8 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 29.40 (m). Anal. Calcd for $C_{17}H_{24}BOP$: C, 71.35; H, 8.45. Found: C, 71.34; H, 8.29.

*Diphenyl(1-hydroxycyclohexanyl)phosphine−Borane (**13m**).*[34] According to the general procedure, **11m** (0.15 g, 0.5 mmol) was treated with BH_3·SMe_2 (142 μL, 1.5 mmol) and stirred at 60 °C for 24 h. The reaction afforded product **13m** (0.11 g, 74%) as a solid; mp = 113.8−114.0 °C; R_f = 0.51 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.66−1.36 (bm, 3H), 1.15−1.26 (m, 1H), 1.51−1.59 (m, 10H), 7.44−7.53 (m, 6H), 7.97−8.01 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 20.4, 25.0, 32.4, 32.5, 74.3 (d, J_{P-C} = 38.2 Hz), 126.2 (d, J_{P-C} = 51.8 Hz), 128.5 (d, J_{P-C} = 9.1 Hz), 131.3 (d, J_{P-C} = 2.7 Hz), 134.3 (d, J_{P-C} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$): δ 29.42 (m). Anal. Calcd for $C_{18}H_{24}BOP$: C, 72.51; H, 8.11. Found: C, 72.54; H, 8.15

General Procedure for the Reaction of β-Hydroxyphosphine Oxides with BH_3·SMe_2. In a two-necked round-bottom flask (25 mL) equipped with magnetic stirrer and argon inlet was placed β-hydroxyphosphine (0.5 mmol) in anhydrous toluene (5 mL). Then BH_3·SMe_2 (237 μL, 1.5 mmol) was added via syringe over a period of 1 min to avoid uncontrolled bubbling. After addition of BH_3 complex, the reaction mixture was stirred for an indicated time at 80 °C. Then the reaction mixture was cooled to room temperature and evaporated to dryness, and the residue was purified by column chromatography using hexane/ethyl acetate (2:1) as eluent.

*o-Anisyl-(2-hydroxyethyl)phenylphosphine−Borane (**18a**).*[37] The reaction was performed analogously to that described above using **16a** (0.138 g, 0.5 mmol), BH_3·SMe_2 (474 μL, 5.0 mmol) and stirred for 24 h. The reaction afforded **18a** (0.085 g, 62%) as a thick oil; R_f = 0.25 (hexane/ethyl acetate = 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67−1.37 (m, 3H), 1.97 (bs, 1H), 2.62−2.70 (m, 1H), 2.81−2.89 (m, 1H), 3.71 (s, 3H), 3.84−3.92 (m, 2H), 6.88−6.90 (m, 1H), 7.06−7.10 (m, 1H), 7.37−7.47 (m, 3H), 7.49−7.53 (m, 1H), 7.62−7.68 (m, 2H), 7.89−7.93 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7 (d, J_{C-P} = 38.2 Hz), 55.4, 57.9 (d, J_{C-P} = 1.8 Hz), 111.2 (d, J_{C-P} = 3.6 Hz), 115.8 (d, J_{C-P} = 54.5 Hz), 121.3 (d, J_{C-P} = 11.8 Hz), 128.4 (d, J_{C-P} = 10.9 Hz), 129.8 (d, J_{C-P} = 59.9 Hz), 130.6 (d, J_{C-P} = 2.7 Hz), 131.4 (d, J_{C-P} = 10.0 Hz), 134.0 (d, J_{C-P} = 1.8 Hz), 136.3 (d, J_{C-P} = 14.5 Hz), 161.21 (d, J_{C-P} = 1.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 11.01 (m). Anal. Calcd for $C_{15}H_{20}BO_2P$: C, 65.73; H, 7.35. Found: C, 65.41; H, 7.22.

*(2-Hydroxyethyl)(1-naphthyl)phenylphosphine−Borane (**18b**).* The reaction was performed analogously to that described above using **16b** (0.148 g, 0.5 mmol), BH_3·SMe_2 (474 μL, 5.0 mmol) and stirred for 24 h. The reaction afforded **18b** (0.094 g, 64%) as a thick oil; R_f = 0.26 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.46−1.70 (bm, 3H), 2.17 (bs, 1H), 2.54−2.58 (m, 2H), 3.88−3.96 (m, 2H), 7.43−7.47 (m, 4H), 7.48−7.53 (m, 2H), 7.67−7.73 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.2 (d, J_{C-P} = 36.3 Hz), 57.5 (d, J_{C-P} = 2.7 Hz), 124.1 (d, J_{C-P} = 52.7 Hz), 125.0 (d, J_{C-P} = 12.7 Hz), 126.2 (d, J_{C-P} = 5.5 Hz), 126.3, 126.9, 129.0 (d, J_{C-P} = 10.0 Hz), 129.5, 130.2 (d, J_{C-P} = 56.3 Hz), 131.0 (d, J_{C-P} = 2.7 Hz), 131.4 (d, J_{C-P} = 10.0 Hz), 132.8 (d, J_{C-P} = 5.5 Hz), 133.2 (d, J_{C-P} = 1.8 Hz), 134.0 (d, J_{C-P} = 7.3 Hz), 134.6 (d, J_{C-P} = 11.8 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 12.56 (m). Anal. Calcd for $C_{18}H_{20}BOP$: C, 73.50; H, 6.85. Found: C, 73.32; H, 6.50.

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

*(2-Hydroxyethyl)diphenylphosphine–Borane (**18m**).* According to the general procedure, **16m** (0.123 g, 0.5 mmol) was treated with BH_3·SMe_2 (237 μL, 1.5 mmol) and stirred 12 h. The reaction afforded product **18m** (0.102 g, 84%) as a solid; mp = 68.1–68.2 °C; R_f = 0.29 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.70–1.42 (bm, 3H), 2.17 (bs, 1H), 2.54–2.58 (m, 2H), 3.88–3.93 (m, 2H), 7.43–7.53 (m, 6H), 7.67–7.71 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ δ 29.2 (d, J_{C-P} = 36.3 Hz), 57.5 (d, J_{C-P} = 2.7 Hz), 128.89 (d, J_{C-P} = 56.3 Hz), 128.9 (d, J_{C-P} = 10.0 Hz), 131.4 (d, J_{C-P} = 2.7 Hz), 132.0 (d, J_{C-P} = 9.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 11.53 (m). Anal. Calcd for $C_{14}H_{18}BOP$: C, 68.89; H, 7.43; found: C, 68.88; H, 7.21.

*o-Anisyl-(2-hydroxypropyl)phenylphosphine–Borane (**19a**).* According to the general procedure, **17a** (0.145 g, 0.5 mmol) was treated with BH_3·SMe_2 (237 μL, 1.5 mmol) and stirred 12 h. The reaction afforded product **19a** (0.13 g, 93%) as two diastereomers isolated as a mixture (dr = 53:47). R_f = 0.25 (hexane/ethyl acetate = 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.70–1.35 (bm, 6H), 1.24 and 1.30 (dd, J_{H-H} = 1.58 and 6.31 Hz, 3H), 2.44–2.50 (m, 1H), 2.60 (bs, 2H), 2.81–2.88 (m, 1H), 3.68 and 3.72 (s, 3H), 4.07–4.10 (m, 1H), 4.22–4.28 (m, 1H), 6.87–6.93 (m, 2H), 7.04–7.13 (m, 2H), 7.22–7.36 (m, 3H), 7.35–7.47 (m, 6H), 7.48–7.54 (m, 2H), 7.60–7.67 (m, 4H), 7.83–7.88 (m, 1H), 7.96–8.01 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.8 and 24.9 (d, J_{C-P} = 12.7 Hz), 34.0 and 34.1 (d, J_{C-P} = 37.2), 55.3 and 55.4, 63.8 and 63.9, 111.2, and 111.3 (d, J_{C-P} = 4.5 Hz), 115.5 (d, J_{C-P} = 53.6 Hz) and 116.6 (d, J_{C-P} = 55.4 Hz), 121.2 and 121.3 (d, J_{C-P} = 10.0 Hz), 128.3 (d, J_{C-P} = 10.9 Hz) and 128.4 (d, J_{C-P} = 10.0 Hz), 129.8 (d, J_{C-P} = 55.4 Hz) and 130.2 (d, J_{C-P} = 55.6 Hz), 130.5 and 130.6 (d, J_{C-P} = 2.7 Hz), 131.2 (d, J_{C-P} = 10.0 Hz) and 131.3 (d, J_{C-P} = 9.1 Hz), 133.9 (d, J_{C-P} = 1.8 Hz) and 134.1 (d, J_{C-P} = 2.0 Hz), 135.6 (d, J_{C-P} = 13.6 Hz) and 136.7 (d, J_{C-P} = 14.5 Hz), 161.1 (d, J_{C-P} = 1.8 Hz) and 161.2 (d, J_{C-P} = 1.4 Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 10.21 (m) and 11.12 (m); GC t_R = 16.84 min; GC–MS (EI, 70 eV) *m*/*z* = 274 (M − BH_3) (16), 228 (13), 215 (16), 196 (10), 183 (16), 165 (13), 152 (11), 141 (17), 138 (22), 137 (26), 136 (10), 121 (15), 109 (20), 108 (19), 107 (22), 91 (100). Anal. Calcd for $C_{16}H_{22}BO_2P$: C, 66.70; H, 7.70. Found: C, 66.91; H, 7.80.

*(2-Hydroxypropyl)(1-naphthyl)phenylphosphine–Borane (**19b**).* According to the general procedure, **17b** (0.155 g, 0.5 mmol) was treated with BH_3·SMe_2 (237 μL, 1.5 mmol) and stirred 12 h. The reaction afforded product **19b** (0.131 g, 85%) as two diastereomers isolated as a mixture (dr = 53:47). R_f = 0.50 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84–1.62 (bm, 6H), 1.22 and 1.30 (dd, J_{H-H} = 1.58 and 6.31 Hz, 3H), 2.67–2.72 and 2.73–2.78 (m, 2H), 2.77 (bs, 2H), 4.17–4.24 and 4.26–4.43 (m, 1H), 7.34–7.50 (m, 9H), 7.54–7.63 (m, 6H), 7.75–7.76 (m, 1H), 7.89–7.97 (m, 3H), 8.02–8.09 (m, 3H), 8.25–8.29 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.8 (d, J_{C-P} = 12.7 Hz) and 25.0 (d, J_{C-P} = 11.8 Hz), 35.8 (d, J_{C-P} = 35.4 Hz) and 36.1 (d, J_{C-P} = 35.4 Hz), 63.8 and 63.9, 124.0 (d, J_{C-P} = 52.7 Hz) and 125.0 (d, J_{C-P} = 53.6 Hz), 124.97 (d, J_{C-P} = 12.72 Hz) and 125.11 (d, J_{C-P} = 14.53 Hz), 126.1 (d, J_{C-P} = 5.5 Hz), 126.3 (d, J_{C-P} = 3.6 Hz), 126.4 (d, J_{C-P} = 6.4 Hz), 126.9 and 127.0, 129.0 (d, J_{C-P} = 10.9 Hz) and 129.1 (d, J_{C-P} = 10.0 Hz), 129.4 and 129.7, 130.3 (d, J_{C-P} = 57.2 Hz) and 130.8 (d, J_{C-P} = 57.2 Hz), 130.9 (d, J_{C-P} = 2.7 Hz) and 131.22 (d, J_{C-P} = 2.7 Hz), 131.18 (d, J_{C-P} = 10.0 Hz) and 131.7 (d, J_{C-P} = 9.1 Hz), 132.7 (d, J_{C-P} = 3.6 Hz) and 132.9 (d, J_{C-P} = 6.4 Hz), 133.1 (d, J_{C-P} = 10.9 Hz) and 134.12 (d, J_{C-P} = 10.9 Hz), 135.7 (d, J_{C-P} = 14.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 11.83 (m) and 12.59 (m). Anal. Calcd for $C_{19}H_{22}BOP$: C, 74.05; H, 7.20. Found: C, 74.34; H, 7.36.

*tert-Butyl-(2-hydroxypropyl)phenylphosphine–Borane (**19f**).* According to the general procedure, **17f** (0.12 g, 0.5 mmol) was treated with BH_3·SMe_2 (237 μL, 1.5 mmol) and stirred 12 h. The reaction afforded product **19f** (0.035 g, 29%) as two diastereomers isolated as a mixture (dr = 50:50). R_f = 0.48 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.45–1.12 (bm, 6H), 1.08 and 1.11 (d, J_{H-P} = 4.41 and 4.73 Hz, 9H), 1.25 (dd, J_{H-H} = 0.95 and 6.31 Hz, 3H) and 1.32 (dd, J_{H-H} = 1.58 and 6.31 Hz, 3H), 2.04–2.14 (m, 2H), 2.34–2.44 (m, 2H), 2.53 (bs, 1H), 3.92–3.95 and 4.34–4.39 (m, 1H), 7.43–7.56 (m, 6H), 7.68–7.77 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.9 (d, J_{C-P} = 10.9 Hz) and 25.0 (d, J_{C-P} = 10.0 Hz), 25.25 and 25.32 (d, J_{C-P} = 2.7 Hz), 28.6 (d, J_{C-P} = 31.8 Hz) and 29.0 (d, J_{C-P} = 32.7 Hz), 29.1 (d, J_{C-P} = 35.4 Hz) and 29.2 (d, J_{C-P} = 33.6 Hz), 63.3, 64.4, 125.6 (d, J_{C-P} = 58.1 Hz) and 126.9 (d, J_{C-P} = 50.0 Hz), 128.2 (d, J_{C-P} = 10.0 Hz) and 128.5 (d, J_{C-P} = 9.1 Hz), 131.2 and 131.4 (d, J_{C-P} = 2.7 Hz), 133.2 (d, J_{C-P} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 25.26 (m) and 26.35 (m); GC t_R = 16.84 min; GC–MS (EI, 70 eV) *m*/*z* = 224 (M − BH_3) (11), 168 (14), 166 (11), 150 (63), 135 (43), 125 (17), 124 (15), 123 (11), 121 (11), 110 (14), 109 (24), 108 (81), 107 (15), 79 (18), 78 (16), 77 (13), 57 (100). Anal. Calcd for $C_{13}H_{24}BOP$: C, 65.57; H, 10.16. Found: C, 65.32; H, 10.00.

*Diphenyl(o-hydroxyphenyl)phosphine–Borane (**21**).*[38] The reaction was performed analogously to that described above using diphenyl(*o*-hydroxyphenyl)phosphine oxide (**20**) (0.1 g, 0.34 mmol), BH_3·SMe_2 (0.16 mL, 1.7 mmol) and stirred at 80 °C for 48 h. The reaction mixture was quenched with 10% HCl (5 mL). The reaction afforded product **21** (0.0622 g, 67%) and **20** (0.028 g, 28%). **21:** Solid; mp = 153.2–153.4 °C; R_f = 0.6 (hexane/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09–1.85 (bm, 3H), 6.88–6.97 (m, 2H), 6.98–7.02 (m, 1H), 7.41–7.48 (m, 5H), 7.52–7.57 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 111.6 (d, J_{C-P} = 58.1 Hz), 118.4 (d, J_{C-P} = 6.3 Hz), 120.6 (d, J_{C-P} = 8.2 Hz), 127.9 (d, J_{C-P} = 61.8 Hz), 128.9 (d, J_{C-P} = 10.9 Hz), 131.5 (d, J_{C-P} = 2.7 Hz), 132.9 (d, J_{C-P} = 10.0 Hz), 134.0 (d, J_{C-P} = 1.9 Hz), 134.4 (d, J_{C-P} = 3.6 Hz), 160.5 (d, J_{C-P} = 9.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 12.65 (m); GC t_R = 17.93 min; GC–MS (EI, 70 eV) *m*/*z* = 279 (21), 278 (M − BH_3, 100) 277 (63), 200 (17), 199 (98), 184 (9), 183 (66), 170 (12), 167 (12), 153 (8), 152 (34), 149 (47), 108 (20), 107 (27), 95 (10). Anal. Calcd for $C_{18}H_{18}BOP$: C, 74.01; H, 6.21. Found: C, 74.32; H, 6.17.

*Attempted Reduction of tert-Butylmethylphenylphosphine Oxide **23**.* This reaction was performed analogously to that described above using **23** (0.064 g, 0.23 mmol), BH_3·SMe_2 (220 μL, 2.3 mmol) and heated at 80 °C for 4 days. The analysis by NMR showed presence only of the starting material.

*Synthesis of Optically Active tert-Butyl(hydroxymethyl)-phenylphosphine Oxide (**1f**).*[9] This compound was synthesized according to the general procedure for the synthesis of phosphine oxides **4**–**6** using (*R*)-*tert*-butylphenylphosphine oxide (0.67 g, 3.68 mmol), DBU (55 μL, 0.368 mmol) and paraformaldehyde (0.332 g, 11.04 mmol). Yield: (*R*)-(**1f**) (0.69 g, 88%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (d, J_{H-P} = 14.19 Hz, 9H), 4.23–4.46 (m, 2H), 5.37 (bs, 1H), 7.39–7.50 (m, 3H), 7.66–7.69 (m, 2H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 46.54 (s). Anal. Calcd for $C_{11}H_{17}O_2P$: C, 62.25; H, 8.07. Found: C, 62.30; H, 8.10; $[\alpha]_D$ +4.8 (*c* 1, MeOH); $[\alpha]_D$ −13.0 (*c* 1, $CHCl_3$) (100% ee); HPLC: t_R = 9.409 min, 90:10 hexane/2-propanol, flow: 1 mL/min.

*Synthesis of Optically Active tert-Butyl(methoxymethyl)-phenylphosphine Oxide (**24f**).* To a solution of phosphine oxide (*R*)-(**1f**) (0.07 g, 0.33 mmol) in THF (5 mL) was added sodium hydride (16 mg, 60% dispersion in mineral oil, 0.4 mmol) at 0 °C, and the mixture was stirred for 15 min. Then methyl iodide (51 μL, 0.83 mmol) was added, and the reaction mixture was allowed to warm to room temperature and stirred for 24 h. The reaction was then quenched by saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The crude reaction mixture was analyzed by NMR and then purified by column chromatography using chloroform/ethyl acetate/methanol (v/v/v = 30:5:1) as eluent. The reaction afforded product (*R*)-(**24f**) (0.062 g, 83%) as an oil; R_f = 0.29 (chloroform/ethyl acetate/methanol = 30:5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (d, J_{H-P} = 14.82 Hz, 9H), 3.47 (s, 3H), 4.09 (dd, J_{P-H} = 13.42 Hz, J_{H-H} = 6.62 Hz, 1H), 4.14 (dd, J_{P-H} = 12.93 Hz, J_{H-H} = 5.99 Hz, 1H), 7.43–7.48 (m, 2H), 7.50–7.55 (m, 1H), 7.81–7.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4, 32.9 (d, J_{P-C} = 67.2 Hz), 61.8 (d, J_{P-C} = 11.8 Hz), 69.2 (d, J_{P-C} = 78.1 Hz), 128.1 (d, J_{P-C} = 10.9 Hz), 129.5 (d, J_{P-C} = 87.2 Hz), 131.6 (d, J_{P-C} = 8.2 Hz), 131.7 (d, J_{P-C} = 2.7 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 42.55 (s); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{12}H_{20}O_2P$ 227.1195; found 227.1143. Anal. Calcd for $C_{12}H_{19}O_2P$: C, 63.70; H, 8.46. Found: C, 63.50; H, 8.62. $[\alpha]_D$ +7.4 (*c*

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672–1688

1, MeOH), $[\alpha]_D$ +13.4 (*c* 1, $CHCl_3$) (100% ee). HPLC: t_R = 15.387 min, 90:10 hexane/2-propanol, flow: 1 mL/min.

*Reduction of Optically Active tert-Butyl(hydroxymethyl)-phenylphosphine Oxide (**1f**)[9] to tert-Butyl(hydroxymethyl)-phenylphosphine−Borane (**2f**)[4e] and Its Chemical Corelation to tert-Butyl(methoxymethyl)phenylphosphine Oxide (**24f**).* The reduction of optically active **1f** was performed starting from (*R*)-**1f** (0.2 g, 0.943 mmol) using $BH_3{\cdot}SMe_2$ (447 μL, 4.72 mmol) at 0 °C for 4 h. The reaction yielded *tert*-butyl(hydroxymethyl)phenylphosphine−borane (*R*)-(**2f**) (0.196 g, 99%) as a solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.34−1.01 (bm, 3H), 1.18 (d, J_{P-H} = 13.56 Hz, 9H), 1.92 (bs, 1H), 4.34−4.47 (m, 2H), 7.45−7.55 (m, 3H), 7.70−7.73 (m, 2H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 31.45 (m). Anal. Calcd for $C_{11}H_{20}BOP$: C, 62.90; H, 9.60. Found: C, 62.80; H, 9.55. $[\alpha]_D$ +8.1 (*c* 1, $CHCl_3$), $[\alpha]_D$ −4.0 (*c* 1, MeOH) (100% ee). HPLC t_R = 14.140 min, 90:10 hexane/2-propanol; flow: 1 mL/min.

To a solution of phosphine−borane (*R*)-(**2f**) (0.144 g, 0.69 mmol) in THF (5 mL) was added sodium hydride (41 mg, 60% dispersion in mineral oil, 1.03 mmol) at 0 °C, and the mixture was stirred for 15 min. Then methyl iodide (107 μL, 1.71 mmol) was added, and the reaction mixture was stirred at 0 °C for 2.5 h. The reaction was then quenched by saturated NH_4Cl solution (5 mL) and extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The crude reaction mixture was analyzed by NMR and then purified by column chromatography (hexane/ethyl acetate = 40:1). The reaction yielded *tert*-butyl(methoxymethyl)phenylphosphine−borane (*R*)-(**25f**) (0.089 g, 81%) and *tert*-butyl(methyl)phenylphosphine−borane (**26f**)[39] (6.6 mg, 5%). (*R*)-(**25f**) was isolated as a waxy solid. R_f = 0.51 (hexane/ethyl acetate = 6:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.25−0.97 (m, 3H), 1.19 (d, J_{H-P} = 13.87 Hz, 9H), 3.48 (s, 3H), 4.13 (dd, J_{P-H} = 12.93 Hz, J_{H-H} = 3.15 Hz, 1H), 4.23 (dd, J_{P-H} = 12.93 Hz, J_{H-H} = 1.89 Hz, 1H), 7.42−7.47 (m, 2H), 7.49−7.53 (m, 1H), 7.89−7.93 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2 (d, J_{P-C} = 1.8 Hz), 29.8 (d, J_{P-C} = 31.8 Hz), 61.7 (d, J_{P-C} = 9.1 Hz), 68.7 (d, J_{P-C} = 41.8 Hz), 126.5 (d, J_{P-C} = 50.0 Hz), 128.2 (d, J_{P-C} = 9.1 Hz), 131.3 (d, J_{P-C} = 1.8 Hz), 134.0 (d, J_{P-C} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 28.90 (m). Anal. Calcd for $C_{12}H_{22}BOP$: C, 64.32; H, 9.90. Found: C, 64.20; H, 9.98. $[\alpha]_D$ −5.1 (*c* 1, MeOH), $[\alpha]_D$ −12.0 (*c* 1, $CHCl_3$) (100%). HPLC t_R = 19.228 min, 90:10 hexane/2-propanol; flow: 0.5 mL/min.

*tert-Butyl(methyl)phenylphosphine−Borane (**26f**).*[39] Solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.36−1.04 (bm, 3H), 1.10 (d, J_{P-H} = 13.87 Hz, 9H), 1.58 (d, J_{P-H} = 9.77 Hz, 3H), 7.43−7.53 (m, 3H), 7.69−7.73 (m, 2H); ^{13}C NMR (125 MHz) δ 5.2 (d, J_{P-C} = 38.2 Hz), 25.1 (d, J_{P-C} = 2.7 Hz), 28.5 (d, J_{P-C} = 36.6 Hz), 127.6 (d, J_{P-C} = 50.9 Hz), 128.2 (d, J_{P-C} = 10.0 Hz), 131.0 (d, J_{P-C} = 2.7 Hz), 132.8 (d, J_{P-C} = 8.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 24.93 (m). Anal. Calcd for $C_{11}H_{20}BP$: C, 68.08; H, 10.39. Found: C, 68.20; H, 10.50.

In a Schlenk tube (20 mL), *tert*-butyl(mesyloxymethyl)-phenylphosphine−borane (**25f**) (0.089 g, 0.39 mmol) in anhydrous toluene (2 mL) was dissolved. Then DABCO (0.076 g, 0.67 mmol) was added, and the mixture was stirred at 40 °C for 6 h. After cooling, solvent was removed under reduced pressure and 2 mL of DCM was added. Then 1 mL of H_2O_2 was added, and the mixture was stirred at room temperature for 1.5 h. The mixture was extracted with DCM (3 × 30 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The residue was purified by column chromatography (chloroform/ethyl acetate/methanol = 30:5:1) yielding *tert*-butyl(methoxymethyl)phenylphosphine oxide (*S*)-(**24f**) (0.055 g, 62%) as a waxy solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (d, J_{H-P} = 14.50 Hz, 9H), 3.48 (s, 3H), 4.08−4.17 (m, 2H), 7.45−7.55 (m, 3H), 7.83−7.86 (m, 2H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 42.33 (s). Anal. Calcd for $C_{12}H_{19}O_2P$: C, 63.70; H, 8.46. Found: C, 63.75; H, 8.50. $[\alpha]_D$ −8.8 (*c* 1, MeOH), $[\alpha]_D$ −14.7 (*c* 1, $CHCl_3$) (100% ee.). HPLC t_R = 10.604 min, 90:10 hexane/2-propanol; flow: 1 mL/min.

*Reduction of Optically Active o-Anisyl(2-hydroxyethyl)-phenylphosphine Oxide (R)-(**16a**)[23] to o-Anisyl(2-hydroxyethyl)-phenylphosphine−Borane (**18a**)[37] and Its Chemical Corelation to o-Anisyl(2-hydroxyethyl)phenylphosphine Oxide (R)-(**16a**).* (*R*)-**16a**: a solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.68−2.72 (m, 2H), 3.75 (s, 3H), 3.69−3.96 (m, 1H), 3.97−4.00 (m, 1H), 6.88−6.91 (m, 1H), 6.96−7.03 (m, 1H), 7.10−7.13 (m, 1H), 7.40−7.43 (m, 2H), 7.46−7.53 (m, 2H), 7.74−7.78 (m, 2H), 7.96−8.00 (m, 1H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 34.01 (s). Anal. Calcd for $C_{15}H_{17}O_3P$: C, 65.21; H, 6.20. Found: C, 64.99; H, 6.30. $[\alpha]_D$ +13.2 (*c* 1, MeOH) (53% ee). HPLC t_R = 39.127 min (minor diastereoisomer), t_R = 42.410 min (major diastereoisomer); 90:5:5 hexane/2-propanol/ethanol; flow: 0.5 mL/min.

The reduction of optically active **16a** was performed analogously to the general procedure using **16a** (0.392 g, 1.42 mmol) and $BH_3{\cdot}SMe_2$ (1.35 mL, 14.2 mmol) in anhydrous toluene (5 mL) at 60 °C for 48 h. The reaction yielded *o*-anisyl(hydroxyethyl)phenylphosphine−borane (*R*)-(**18a**) (0.35 g, 90%) as an oil. (*R*)-(**18a**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67−1.37 (m, 3H), 1.97 (bs, 1H), 2.62−2.70 (m, 1H), 2.81−2.89 (m, 1H), 3.71 (s, 3H), 3.84−3.92 (m, 2H), 6.88−6.90 (m, 1H), 7.06−7.10 (m, 1H), 7.37−7.47 (m, 3H), 7.49−7.53 (m, 1H), 7.62−7.68 (m, 2H), 7.89−7.93 (m, 1H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 11.02 (m). Anal. Calcd for $C_{15}H_{20}BO_2P$: C, 65.73; H, 7.35. Found: C, 65.40; H, 7.20. $[\alpha]_D$ −3.65 (*c* 1, MeOH) (53% ee). HPLC t_R = 37.246 min (minor diastereoisomer), t_R = 40.390 min (major diastereoisomer); 90:5:5 hexane/2-propanol/ethanol; flow: 0.5 mL/min.

In a Schlenk tube (50 mL), (*R*)-(**18a**) (0.28 g, 1.02 mmol) in anhydrous DCM (10 mL) was dissolved and cooled to 0 °C. Then tetrafluoroboric acid (0.69 mL, 5.21 mmol) was added, and the mixture was stirred at 0 °C for 10 min. The ice−water bath was removed, and the mixture was stirred for 1.5 h at room temperature. Then saturated $NaHCO_3$ solution (2 mL) was added, and the mixture was extracted with DCM (3 × 20 mL). To the combined organic phases was added H_2O_2 (5 mL), and the mixture was vigorously stirred for 2 h at room temperature. Then the mixture was extracted with DCM (3 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The residue was purified by column chromatography yielding *o*-anisyl(2-hydroxyethyl)phenylphosphine oxide (*S*)-(**16a**) (0.195 g, 69%) as a solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.68−2.72 (m, 2H), 3.75 (s, 3H), 3.69−3.96 (m, 1H), 3.95−4.00 (m, 1H), 6.88−6.91 (m, 1H), 6.96−7.03 (m, 1H), 7.10−7.13 (m, 1H), 7.40−7.43 (m, 2H), 7.46−7.53 (m, 2H), 7.74−7.78 (m, 2H), 7.96−8.00 (m, 1H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 33.77 (s). Anal. Calcd for $C_{15}H_{17}O_3P$: C, 65.21; H, 6.20. Found: C, 65.06; H, 6.17; $[\alpha]_D$ −10.7 (*c* 1, MeOH) (45% ee). HPLC t_R = 38.396 min (major diastereoisomer), t_R = 41.411 min (minor diastereoisomer); 90:5:5 hexane/2-propanol/ethanol; flow: 0.5 mL/min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The crystal structure of **1f** and NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org. The experimental details and final atomic parameters have been deposited with the Cambridge Crystallographic Data Centre (no. CCDC 967625) and are presented as Supporting Information.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: kazimierz.pietrusiewicz@poczta.umcs.lublin.pl. Phone: (+48) 81 524-22-51 (ext. 134). Fax: (+48) 81 524-22-51 (ext. 135).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the Polish Ministry of Science and Higher Education through a grant (N N204 111 035).

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688

REFERENCES

(1) For some recent examples, see: (a) Märkl, G.; Reisinger, J.; Kreitmeier, P.; Langer, J.; Nöth, H. *Helv. Chim. Acta* **2002**, *85*, 1714. (b) Toffano, M.; Dobrota, C.; Fiaud, J.-C. *Eur. J. Org. Chem.* **2006**, 650. (c) Hiney, R. M.; Higham, L. J.; Müller-Bunz, H.; Gilheany, D. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7248. (d) Byrne, P. A.; Rajendran, K. V.; Muldoon, J.; Gilheany, D. G. *Org. Biomol. Chem.* **2012**, *10*, 3531. (e) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, Sh.; Varsolona, R.; Wei, X.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277. (f) Busacca, C. A.; Raju, R.; Grinberg, N.; Haddad, N.; James-Jones, P.; Lee, H.; Lorenz, J. C.; Saha, A.; Senanayake, C. H. *J. Org. Chem.* **2008**, *73*, 1524. (g) Ghosh, A. K.; Nicponski, D. R.; Kass, J. *Tetrahedron Lett.* **2012**, *53*, 3699.

(2) (a) Huang, Z.; Lim, L. H.; Chen, Z.; Li, Y.; Zhou, F.; Su, H.; Zhou, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 4906. (b) Ebner, C.; Müller, C. A.; Markert, C.; Pfaltz, A. *J. Am. Chem. Soc.* **2011**, *133*, 4710. (c) Vinokurov, N.; Pietrusiewicz, K. M.; Frynas, S.; Wiebcke, M.; Butenschön, H. *Chem. Commun.* **2008**, 5408. (d) Berthod, M.; Favre-Réguillon, A.; Mohamad, J.; Mignani, G.; Docherty, G.; Lemaire, M. *Synlett* **2007**, *10*, 1545. (e) Li, Y.; Das, S.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2012**, *134*, 9727. (f) Li, Y.; Lu, L.-Q.; Das, S.; Pisiewicz, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2012**, *134*, 18325.

(3) (a) Stankevič, M.; Wójcik, K.; Jaklińska, M.; Pietrusiewicz, K. M. *Eur. J. Org. Chem.* **2012**, *13*, 2521. (b) Vandyck, K.; Matthys, B.; Willen, M.; Robeyns, K.; van Meervelt, L.; van der Eycken, J. *Org. Lett.* **2006**, *8*, 363. (c) Barbaro, P.; Bianchini, C.; Giambastani, G.; Togni, A. *Chem. Commun.* **2002**, 2672.

(4) For a related direct conversion of phosphine oxides to phosphine−boranes by $(COCl)_2/NaBH_4$ or $(Et_3O)BF_4/NaBH_4$, see: (a) Köster, R.; Morita, Y. *Angew. Chem.* **1965**, *77*, 589; *Angew. Chem., Int. Ed.* **1965**, *4*, 593. (b) Köster, R.; Schüßler, W.; Synoradzki, L. *Chem. Ber.* **1987**, *120*, 1105. (c) Keglevich, G.; Fekete, M.; Chuluunbaatar, T.; Dobó, A.; Harmat, V.; Tőke, L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4451. (d) Keglevich, G.; Chuluunbaatar, T.; Ludányi, K.; Tőke, L. *Tetrahedron* **2000**, *56*, 1. (e) Kiełbasiński, P.; Albrycht, M.; Żurawinski, R.; Mikołajczyk, M. *J. Mol. Catal. B: Enzym.* **2006**, *39*, 45.

(5) (a) Rajendran, K. V.; Gilheany, D. G. *Chem. Commun.* **2012**, *48*, 817. (b) Kenny, N. P.; Rajendran, K. V.; Jennings, E. V.; Gilheany, D. G. *Chem.—Eur. J.* **2013**, *19*, 14210.

(6) Stankevič, M.; Pietrusiewicz, K. M. *Synlett* **2003**, 1012.

(7) Stankevič, M.; Andrijewski, G.; Pietrusiewicz, K. M. *Synlett* **2004**, 311.

(8) Kwiatkowska, M.; Krasiński, G.; Cypryk, M.; Cierpiał, T.; Kiełbasiński, P. *Tetrahedron: Asymmetry* **2011**, *22*, 1581.

(9) Shioji, K.; Kurauchi, Y.; Okuma, K. *Bull. Chem. Soc. Jpn.* **2003**, *76* (4), 833.

(10) (a) Imamoto, T.; Kusumoto, T.; Suzuki, N.; Sato, K. *J. Am. Chem. Soc.* **1985**, *107*, 5301. (b) Brisset, H.; Gourdel, Y.; Pellon, P.; Le Corre, M. *Tetrahedron Lett.* **1993**, *34*, 4523.

(11) Horner, L. *Pure Appl. Chem.* **1964**, *9*, 225.

(12) Wife, R. L.; van Oort, A. B.; van Doorn, J. A.; van Leeuwen, P. W. N. M. *Synthesis* **1983**, 71.

(13) Xu, Q.; Zhao, C.-Q.; Han, L.-B. *J. Am. Chem. Soc.* **2008**, *130* (38), 12648.

(14) Janjah, M.; Alame, M.; Pellet-Rostaing, S.; Lemaire, M. *Tetrahedron: Asymmetry* **2007**, *18*, 2305.

(15) Jin, M.; Nakamura, M. *Chem. Lett.* **2013**, *42*, 1035.

(16) Holt, J.; Maj, A. M.; Schudde, E. P.; Pietrusiewicz, K. M.; Sieroń, L.; Wieczorek, W.; Jerphagnon, T.; Arends, I. W. C. E.; Hanefeld, U.; Minnaard, A. J. *Synthesis* **2009**, *12*, 2061.

(17) Emmick, T. L.; Letsinger, R. L. *J. Am. Chem. Soc.* **1968**, *90*, 3459.

(18) Bigeault, J.; Giordano, L.; Buono, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4753.

(19) Achard, T.; Giordano, L.; Tenaglia, A.; Buono, G.; Gimbert, Y. *Organometallics* **2010**, *29*, 3936.

(20) Arad-Yellin, R.; Zangen, M.; Gottlieb, H.; Warshawsky, A. *J. Chem. Soc., Dalton Trans.* **1990**, 2081.

(21) (a) Pietrusiewicz, K. M.; Wiśniewski, W.; Zabłocka, M. *Tetrahedron* **1989**, *45*, 337. (b) Stankevič, M.; Włodarczyk, A. *Tetrahedron* **2013**, *69*, 73. (c) Hoffmann, H.; Schellenbeck, P. *Chem. Ber.* **1966**, *99*, 1134.

(22) (a) Haynes, R. K.; Au-Yeung, T.-L.; Chan, W.-K.; Lam, W.-L.; Li, Z.-Y.; Yeung, L.-L.; Chan, A. S. C.; Li, P.; Koen, M.; Mitchell, C. R.; Vonwiller, S. C. *Eur. J. Org. Chem.* **2000**, 3205. (b) Chan, T. H. *Chem. Commun.* **1968**, 895.

(23) Pietrusiewicz, K. M.; Dziuba, K. Manuscript in preparation.

(24) Patsanovskii, I. I.; Ishmaeva, E. A.; Sundukova, E. N.; Yarkevich, A. N.; Tsvetkov, E. N. *J. Gen. Chem. USSR (Engl. Transl.)* **1986**, *56* (567), 501.

(25) Shioji, K.; Kurauchi, Y.; Terada, K.; Kodera, Y.; Okuma, K. *Synth. Commun.* **2007**, *37*, 2163.

(26) Shioji, K.; Ueno, Y.; Kurauchi, Y.; Okuma, K. *Tetrahedron Lett.* **2001**, *42*, 6569.

(27) Matrosov, E. I.; Kabachnik, M. I. *Spectrochim. Acta Mol. A: Biomol. Spectrosc.* **1972**, *28*, 313.

(28) Cherkasov, R. A.; Garifzyanov, A. R.; Talan, A. S.; Davletshin, R. R.; Kurnosova, N. V. *Russ. J. Gen. Chem.* **2009**, *79*, 1835.

(29) Haynes, R. K.; Lam, W.-L.; Yeung, L.-L. *Tetrahedron Lett.* **1996**, *37*, 4729.

(30) Keglevich, G.; Toth, V. R.; Drahos, L. *Heteroatom Chem.* **2011**, *22*, 15.

(31) Nurtdinov, S. Kh.; Kashirskaya, I. M.; Ismagilova, N. M.; Gubaidullina, R. Sh.; Zykova, T. V.; Salakhutdinov, R. A.; Tsivunin, V. S. *J. Gen. Chem. USSR (Engl. Transl.)* **1980**, *50* (1297), 1049.

(32) Gonzalez-Nogal, A. M.; Cuadrado, P.; Sarmentero, M. A. *Eur. J. Org. Chem.* **2009**, *6*, 850.

(33) Hatano, M.; Ishihara, K.; Miyamo, T. *J. Org. Chem.* **2006**, *71*, 6474.

(34) Barozzino, C. G.; Harrison-Marchand, A.; Maddaluno, J.; Oulyadi, H.; Mordini, A.; Queval, P.; Lohier, J.-F.; Delacroix, O.; Gaumont, A.-C.; Gerard, H. *J. Am. Chem. Soc.* **2011**, *133*, 6472.

(35) Moraleda, D.; Gatineau, D.; Martin, D.; Giordano, L.; Buono, G. *Chem. Commun.* **2008**, *26*, 3031.

(36) Takeda Chemicals Industries Ltd. Patent EP1452537 A1, 2004.

(37) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244.

(38) Mamat, C.; Pretze, M.; Wuest, F.; Koeckerling, M.; Peppel, T. *Tetrahedron Lett.* **2010**, *51*, 6410.

(39) Wolfe, B.; Livinghouse, T. *J. Am. Chem. Soc.* **1998**, *120*, 5116.

DOI: 10.1021/jo502623g
J. Org. Chem. 2015, 80, 1672−1688