Synthesis and Solid-State Structure of Substituted Arylphosphine Oxides

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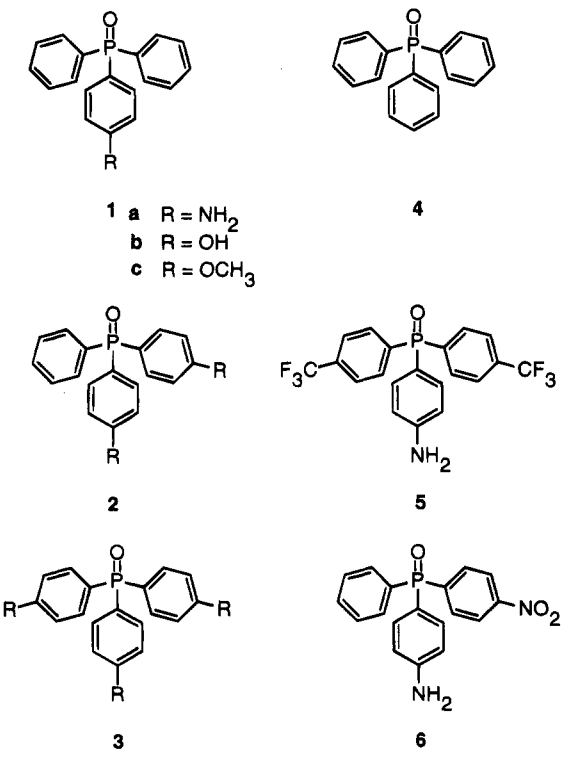
We describe the preparation and characterization of several new arylphosphine oxides, which are of interest as second-order nonlinear optical materials. (4-Aminophenyl)diphenylphosphine oxide (**1a**), bis(4-aminophenyl)phenylphosphine oxide (**2a**), and (4-aminophenyl)bis[4′-(trifluoromethyl)-phenyl]phosphine oxide (**5**) were prepared by addition of aryl Grignard and organolithium reagents containing protected amines to phosphorus oxyhalides. Alternatively, **1a** was prepared by treatment of (4-bromophenyl)diphenylphosphine oxide with azidomethyl phenyl sulfide, followed by hydrolysis. (4-Aminophenyl)(4′-nitrophenyl)phenylphosphine oxide (**6**) was prepared by nucleophilic aromatic substitution of bis(4-fluorophenyl)phenylphosphine oxide to give the corresponding dinitro compound, followed by selective mono-reduction. The X-ray crystal structure of (4-aminophenyl)-diphenylphosphine oxide (**1a**), along with those of mono-, di-, and trihydroxy triphenylphosphine oxides **1b**, **2b**, and **3b**, exhibit extensive intermolecular hydrogen bonding. The hydrogen bonding in **1a** and **1b** produces chains of arylphosphine oxide molecules with a head-to-tail alignment; the chains pack in an antiparallel manner to produce solid-state structures that display only slight deviations from centrosymmetry.

Introduction

Our efforts concerning the design and synthesis of novel nonlinear optical materials led us to investigate donor- and acceptor-substituted arylphosphine oxides as second-order nonlinear optical materials.[1,2] Our particular interest in the arylphosphine oxide functionality originated from two distinct considerations: one microscopic (molecular) and one macroscopic (bulk). From the molecular point of view, we felt that donor-substituted arylphosphine oxides might exhibit optical nonlinearities comparable to those of other small donor/acceptor-substituted aromatic compounds without interference from undesirable electronic absorptions in the visible region. From the bulk point of view, we felt that the combination of hydrogen bond donor (NH_2 or OH) and hydrogen bond acceptor (P=O) could influence the propensity of the material to form an acentric crystal,[3] an important consideration in second-order nonlinear optical materials.

The standard methods for the synthesis of arylphosphine oxides are not readily applicable to the synthesis of many of the desired compounds **1**–**6** (*vide infra*). In this report, we describe methods for the synthesis of *p*-amino triphenylphosphine oxides **1a**, **2a**, **3a**, **5**, and **6** (Scheme 1). In addition, we comment on the role of hydrogen bonding in determining centric or acentric solid-state structures for arylphosphine oxides.

Scheme 1



Background

Practical preparative methods for the syntheses of substituted arylphosphine oxides typically involve treatment of phosphorus oxyhalides with organolithium or Grignard reagents.[4] This general methodology is not readily applicable to the synthesis of phosphine oxides containing primary amino substituents. The organolithium and Grignard reagents typically used to prepare dialkylamino-substituted arylphosphine oxides[5–7] are

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(1) For general references concerning organic nonlinear optical materials, see: (a) Prasad, P. N.; Williams, D. J. *Introduction to Nonlinear Optical Effects in Molecules and Polymers*; Wiley: New York, 1992. (b) *Materials for Nonlinear Optics*; Marder, S. R., Sohn, J. E., Stucky G. D., Eds.; ACS Symposium Series 455; American Chemical Society: Washington, DC, 1991. (c) *Nonlinear Optical Properties of Organic Molecules and Crystals*, Chemla, D. S., Zyss, J., Eds.; Academic: New York, 1987.

(2) Kott, K. L.; Whitaker, C. M.; McMahon, R. J. *Chem. Mater.* **1995**, *7*, 426–439.

(3) (a) Etter, M. C.; Baures, P. W. *J. Am. Chem. Soc.* **1988**, *110*, 639–640. (b) Etter, M. C.; Huang, K.-S. *Chem. Mater.* **1992**, *4*, 824–827. (c) Etter, M. C. *J. Phys. Chem.* **1991**, *95*, 4601–4610. (d) Etter, M. C.; Frankenbach, G. M.; Adsmond, D. A. *Mol. Cryst. Liq. Cryst.* **1990**, *187*, 25–39. (e) Etter, M. C.; Frankenbach, G. M. *Chem. Mater.* **1989**, *1*, 10–12. (f) Panunto, T. W.; Urbanczyk-Lipowska, Z.; Johnson, R.; Etter, M. C. *J. Am. Chem. Soc.* **1987**, *109*, 7786–7797.

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incompatible with primary amines. Arylphosphine oxides bearing primary amino substituents in the *meta* position are readily obtained by electrophilic nitration of triphenylphosphine oxide followed by reduction.[8-11] The *o*- and *p*-amino arylphosphine oxides, however, cannot be straightforwardly prepared from the unsubstituted arylphosphine oxide by electrophilic aromatic substitution. (Electrophilic aromatic substitution of the corresponding arylphosphine is thwarted by the ease of oxidation of the phosphine moiety itself.) Consequently, the literature contains few reports concerning the synthesis of triarylphosphine oxides substituted with primary amines in the *ortho*[12] or *para*[13,14] positions.

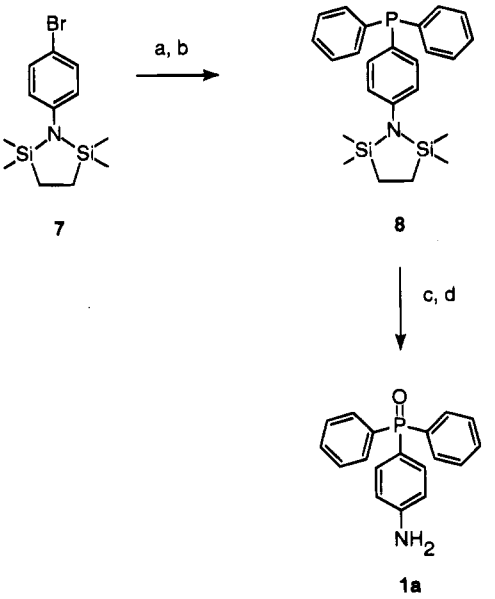
Horner et al. synthesized (4-aminophenyl)diphenylphosphine oxide (**1a**), the first primary *p*-amino triphenylphosphine oxide, by reduction of a (4-nitrophenyl)triphenylphosphonium salt followed by cleavage of an unsubstituted phenyl ring.[13] Schiemenz and Röhlk prepared **1a** from the same phosphonium salt, but reversed the sequence of reactions: they first cleaved the salt to (4-nitrophenyl)diphenylphosphine oxide, and then reduced the nitro group to yield **1a**.[14] Neither procedure allows for the systematic incorporation of multiple *p*-amino substituents in triphenylphosphine oxide or the incorporation of primary arylamines in phosphines containing other functionalized aryl groups.

In this manuscript, we describe several methods for the synthesis of triarylphosphine oxides with primary *p*-amino substituents. We introduce primary amine substituents into arylphosphine oxides using three different strategies: (1) addition of STABASE-protected aryl amino Grignard and organolithium reagents to phosphorus oxyhalides, (2) conversion of Grignard reagents derived from arylphosphine oxides to amines using azidomethyl phenyl sulfide, or (3) conversion of fluoro-substituted arylphosphine oxides to nitro compounds (via nucleophilic aromatic substitution with nitrite) followed by reduction to the amines. Utilization of these synthetic methods provides simple routes to multiply-substituted phosphine oxides possessing primary amines.

Results and Discussion

Synthesis. The amino-substituted compound **1a** was synthesized as shown in Scheme 2 (method A). Deprotonation of 4-bromoaniline with *n*-butyllithium at −78 °C followed by reaction with 1,2-bis(chlorodimethylsilyl)ethane (STABASE) successfully protects the amine.[15] Transmetalation of the protected aryl bromide **7** with *n*-butyllithium at 0 °C followed by reaction with chlorodiphenylphosphine yields the protected monoamino phosphine **8**. Deprotection by acid hydrolysis followed by oxidation with hydrogen peroxide yields the desired monoamino phosphine oxide **1a**. Alternatively, cleavage of the STABASE protecting group can be accomplished by subjecting the material to silica gel chromatography. Similarly, the diamino phosphine oxide **2a** can be synthesized using dichlorophenylphosphine, albeit in lower yield due to difficulties with the hydrolysis of the protecting group and difficulties in isolating the product after the hydrolysis step. The triamino phosphine oxide **3a** could not be synthesized by method A due to these same difficulties. Although the protected triamino phosphine intermediate analogous to **8** could be synthesized and identified, the product from the deprotection step (acid hydrolysis, silica gel chromatography, or reaction with tetrabutylammonium fluoride) could not be isolated.

Scheme 2[a]



[a] (a) *n*-BuLi, Et_2O, 0 °C; (b) $ClPPh_2$, Et_2O, 25 °C; (c) HCl; (d) H_2O_2.

Alternatively, the monoamino compound **1a** can be synthesized more efficiently using the procedure outlined in Scheme 3 (method B). Formation of the Grignard reagent of 1,4-dibromobenzene (**9**) followed by reaction with chlorodiphenylphosphine yields the monobromo phosphine **10**. Conversion of the aryl bromide to the arylamine is accomplished by formation of the Grignard reagent of **10** followed by reaction with azidomethyl phenyl sulfide.[16] Hydrolysis of the resulting triazene to the amine followed by oxidation of the phosphine with hydrogen peroxide yields the desired monoamino phosphine oxide **1a**.

(4) For general references see: (a) Hartley, F. R. *The Chemistry of Organophosphorus Compounds*; Wiley & Sons: England, 1992; Volume 2. (b) Hays, H. R.; Peterson, D. J. *Organic Phosphorus Compounds*; Wiley-Interscience: New York, 1972, Volume 3, Chapter 6, p 341. (c) Berlin, K. D.; Butler, G. B. *Chem. Rev.* **1960**, *60*, 243–260. (d) Johnson, A. W. *Ylides and Imines of Phosphorus*; Wiley & Sons, 1993; Chapter 11, p 359. (e) Crofts, P. C. *Quart. Rev.* **1958**, *12*, 341–366.

(5) (a) Michaelis, A.; Schenk, A. *Liebigs Ann. Chem.* **1890**, *260*, 1–39. (b) Schenk, A.; Michaelis, A. *Chem. Ber.* **1888**, *21*, 1497–1504. (c) Hanimann, J. *Chem. Ber.* **1876**, *9*, 844–848.

(6) Robins, R. K.; Christensen, B. E. *J. Org. Chem.* **1951**, *16*, 324–327.

(7) Schiemenz, G. P. *Chem. Ber.* **1965**, *98*, 65–66.

(8) Michaelis and Soden reported that nitration of triphenylphosphine oxide produced the tris(*p*-nitro) isomer.[9] Challenger and Wilkinson later established the structure as the tris(*m*-nitro) isomer; they also prepared the tris(*m*-amino) derivative by reduction of the nitro compound.[10]

(9) Michaelis, A.; Soden, H. *Liebigs Ann. Chem.* **1885**, *229*, 295–333.

(10) Challenger, F.; Wilkinson, J. F. *J. Chem. Soc.* **1924**, *125*, 2675–2676.

(11) (a) Schiemenz, G. P.; Röhlk, K. *Chem. Ber.* **1971**, *104*, 1219–1233. (b) Schiemenz, G. P.; Röhlk, K. *Phosphorus* **1972**, *1*, 187–190.

(12) Cadogan, J. I. G.; Sears, D. J.; Smith, D. M. *J. Chem. Soc. (C)* **1969**, 1314–1318.

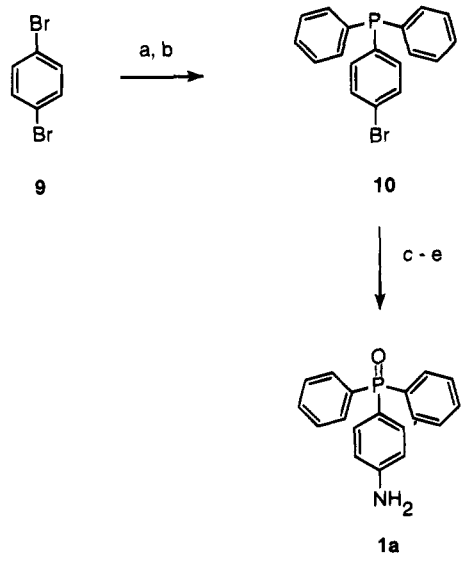
(13) Horner, L.; Hoffmann, H.; Wippel, H. G.; Hassel, G. *Chem. Ber.* **1958**, *91*, 52–57.

(14) Schiemenz, G. P.; Röhlk, K. *Chem. Ber.* **1971**, *104*, 1722–1727.

(15) (a) Djuric, S.; Venit, J.; Magnus, P. *Tetrahedron Lett.* **1981**, *22*, 1787–1790. (b) Weisenfeld, R. B.; Miller, M. D. *Synth. Commun.* **1986**, *16*, 809–817.

(16) (a) Trost, B. M.; Pearson, W. H. *J. Am. Chem. Soc.* **1981**, *103*, 2483–2485. (b) Trost, B. M.; Kunz, R. A. *J. Org. Chem.* **1974**, *39*, 2648–2649.

Scheme 3[a]



[a] (a) Mg, THF, reflux; (b) $ClPPh_2$, THF, 25 °C; (c) Mg, THF, reflux; (d) $PhSCH_2N_3$, THF, −78 °C, warm to 25 °C; (e) H_2O_2.

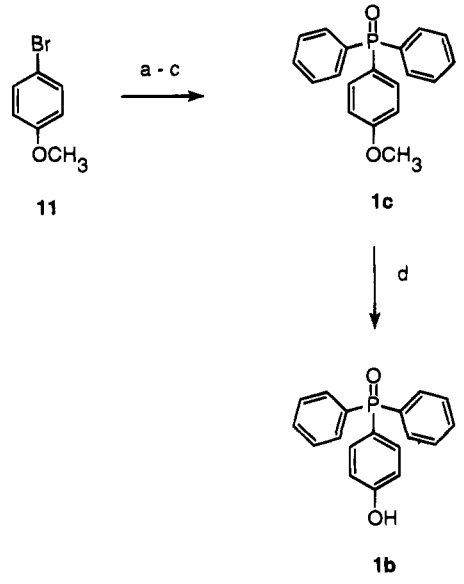
Although bis(4-bromophenyl)phenylphosphine and tris(4-bromophenyl)phosphine can be readily synthesized, the corresponding di- and tri-Grignard reagents cannot; transmetalation occurs at only one *para* site, even in the presence of excess magnesium. Thus, method B is specific for the synthesis of the monoamino compound **1a**. The mono-, di-, and triamino triphenylphosphine oxides **1a**−**3a** may also be conveniently synthesized by reduction of the corresponding nitro triphenylphosphine oxides.[17]

The synthesis of the hydroxy-substituted phosphine oxides **1b**, **2b**, and **3b** proceeds in a straightforward manner as shown in Scheme 4 for **1b**.[18,19] Formation of the Grignard reagent of 4-bromoanisole (**11**) followed by reaction with chlorodiphenylphosphine and subsequent oxidation with potassium permanganate affords the monomethoxy phosphine oxide **1c**. Reaction of **1c** with boron tribromide[20] in dichloromethane yields the desired monohydroxy phosphine oxide **1b**. Synthesis of bis(4-methoxyphenyl)phenylphosphine oxide (**2c**) and tris(4-methoxyphenyl)phosphine oxide (**3c**) proceeds in the same manner using dichlorophenylphosphine and trichlorophosphine, respectively. Reaction of **2c** and **3c** with BBr_3 affords compounds **2b** and **3b**, respectively.

Nonlinear optical measurements of (4-aminophenyl)diphenylphosphine oxide (**1a**) and bis(4-aminophenyl)phenylphosphine oxide (**2a**) indicated that these molecules possess a small molecular hyperpolarizability in the direction of the dipole moment.[2] We therefore sought to introduce electronegative CF_3 (**5**) or NO_2 (**6**) substituents, reasoning that the substituents would tip the dipole moment vector in the direction of maximum hyperpolarizability. Subsequent nonlinear optical measurements of **5** and **6** demonstrated the success of this strategy.[2]

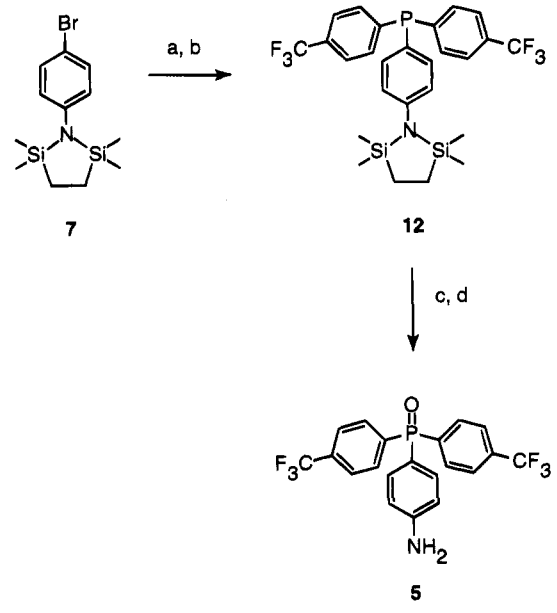
(17) Schiemenz, G. P.; Nielsen, P. *Phosphorus Sulfur* **1985**, *21*, 259–266.
(18) Senear, A. E.; Valient, W.; Wirth, J. *J. Org. Chem.* **1960**, *25*, 2001–2006.
(19) Friedrichsen, B. P.; Powell, D. R.; Whitlock, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 8931–8941.
(20) Williard, P.; Fryhle, C. B. *Tetrahedron Lett.* **1980**, *21*, 3731–3734.

Scheme 4[a]



[a] (a) Mg, THF, reflux; (b) $ClPPh_2$, THF, reflux; (c) $KMnO_4$, H_2O, 25 °C; (d) BBr_3, CH_2Cl_2, −78 °C, warm to 25 °C.

Scheme 5[a]



[a] (a) *n*-BuLi, Et_2O, 0 °C; (b) $ClP(C_6H_4CF_3)_2$, Et_2O, 25 °C; (c) HCl; (d) H_2O_2.

The novel (4-aminophenyl)bis[4′-(trifluoromethyl)phenyl]phosphine oxide (**5**) was synthesized using the techniques described in method A. Transmetalation of the STABASE-protected aryl bromide **7** with *n*-butyllithium at 0 °C, followed by reaction with bis[4-(trifluoromethyl)-phenyl]phosphorus chloride,[21] yields the protected (4-aminophenyl)bis[4′-(trifluoromethyl)phenyl]phosphine (**12**) (Scheme 5). Deprotection by acid hydrolysis, followed by oxidation with hydrogen peroxide, affords the desired amino phosphine oxide **5**.

The synthesis of (4-aminophenyl)(4′-nitrophenyl)phenylphosphine oxide (**6**) utilized double nucleophilic aromatic substitution on bis(4-fluorophenyl)phenylphosphine oxide (**14**) to generate bis(4-nitrophenyl)phenyl-

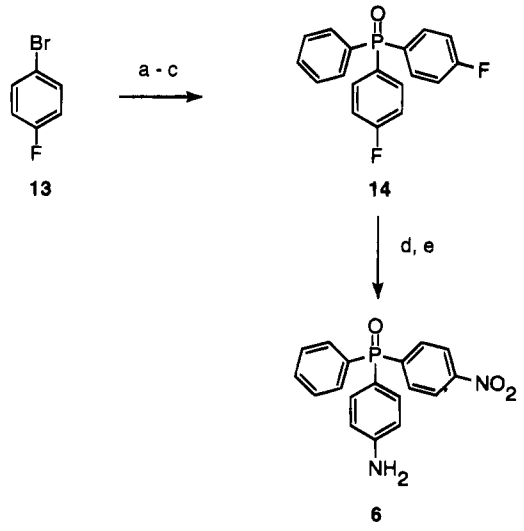
(21) Unruh, J. D.; Christenson, J. R. *J. Mol. Cat.* **1982**, *14*, 19–34.

Table 1. Crystal Structure Data for 1a, 1b, 2b, and 3b (radiation Mo Kα (λ = 0.71073 Å))[a]

compound	1a	1b	2b	3b
empirical formula	$C_{18}H_{16}NOP$	$C_{18}H_{15}O_2P$	$C_{22}H_{23}O_5P$[b]	$C_{18}H_{15}O_4P$[c]
crystal system	monoclinic	orthorhombic	monoclinic	monoclinic
space group	*Cc*	*Pca*2$_1$	*P*2$_1$/*c*	*P*2$_1$/*c*
cell constants				
a	17.462(3) Å	18.092(9) Å	8.940(6) Å	9.225(3) Å
b	17.557(4) Å	10.325(5) Å	15.101(3) Å	15.033(4) Å
c	21.301(4) Å	16.292(8) Å	15.954(3) Å	15.874(5) Å
β	98.40(3)°		101.14(2)°	102.59(3)°
V	6460(2) Å^3	3043(3) Å^3	2113(4) Å^3	2148(5)Å^3
Z	16	8	4	4
formula weight	293.3	294.3	398.4	405.0
density (calcd)	1.206 g/cm^3	1.284 g/cm^3	1.254 g/cm^3	1.252 g/cm^3
F(000)	2464	1232	840	852
2*θ* range	3.5–45.0°	3.5–50.0°	4.0–50.0°	3.0–50.0°
no. reflections	5162	3729	4128	4188
no. reflections used in refinement	3767	2148	2663	2736
no. parameters	761	380	255	240
GOF	1.37	1.12	1.60	2.20

[a] The atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ UK. [b] Compound **2b** crystallized with inclusion of ethyl acetate (1:1): $C_{18}H_{15}O_3P$ + 1.0 ($C_4H_8O_2$). [c] Compound **3b** crystallized with inclusion of ethyl acetate: $C_{18}H_{15}O_4P$ + 0.866 ($C_4H_8O_2$) + 0.134 (H_2O).

Scheme 6[a]



[a] (a) Mg, THF, reflux; (b) Cl_2PPh, THF, reflux; (c) H_2O_2; (d) $LiNO_2$, HMPA, 150 °C, 16 h; (e) NaSH, methanol, 25 °C.

phosphine oxide. Selective mono-reduction using NaSH in methanol[22] afforded (4-aminophenyl)(4′-nitrophenyl)-phenylphosphine oxide (**6**) (Scheme 6).

Solid State Structure. X-ray crystal structures of phosphine oxides **1a**, **1b**, **2b**, and **3b** (Table 1) confirm extensive intermolecular hydrogen bonding in the solid state. Both monoamino phosphine oxide **1a** and monohydroxy phosphine oxide **1b** crystallize in noncentrosymmetric space groups (*Cc* and *Pca*2$_1$, respectively). The crystal structure of (4-aminophenyl)diphenylphosphine oxide (**1a**) is comprised of four layers of phosphine oxide molecules. Within each layer, intermolecular hydrogen bonding produces chains with head-to-tail alignment (Figure 1). Although the "zig-zag" pattern of chain propagation aligns the phosphoryl moieties in one direction, the orientation of the aminoaryl groups alternates along the chain (Figure 1). By virtue of the molecular orientation, each layer possesses a polar face consisting of exposed NH_2 and P=O functionalities, and a nonpolar face consisting of exposed aromatic rings. A second layer, adjacent to the polar face of the first layer, consists of chains that propagate in a direction antiparallel to those of the first layer (Figure 2). The two layers are bridged by intermolecular hydrogen bonds. This pair of hydrogen-bonded layers forms a dimeric unit in which both exposed faces consist of nonpolar aromatic rings (Figure 2). The bulk structure is composed of stacks of these dimeric units. Interestingly, the chains comprising an individual dimeric unit (which are antiparallel to one another) are orthogonal to the chains in the adjacent dimeric unit. This orientation facilitates edge-to-face *π*-stacking of aromatic rings between the nonpolar faces of the adjacent dimeric units (Figure 2). From the perspective of nonlinear optics, the desired head-to-tail alignment induced by intermolecular hydrogen bonding in (4-aminophenyl)-diphenylphosphine oxide (**1a**) is effectively negated by the fact the crystal structure is virtually centrosymmetric. This nearly-centrosymmetric structure accounts for small bulk nonlinear optical response of the material (powder second-harmonic generation signal = 0.1 × urea).[2]

The crystal structure of (4-hydroxyphenyl)diphenylphosphine oxide (**1b**) consists of an intricate array of molecules interacting by both intermolecular hydrogen bonding and edge-to-face *π*-stacking of aromatic rings (Figure 3). Again, intermolecular hydrogen bonds induce head-to-tail alignment of the phosphine oxides with concomitant chain growth. The aryl groups of phosphine oxide **1b** are involved in significant aryl–aryl interactions with adjacent chains. The layers of intermolecular hydrogen bonded (4-hydroxy)diphenylphosphine oxides (**1b**) appear to propagate in one general direction, but without any large net alignment of the molecular hyperpolarizability vector. Although the distortions from a centrosymmetric structure are more pronounced in (4-hydroxyphenyl)-diphenylphosphine oxide (**1b**), only a slightly larger bulk nonlinear optical response (powder second-harmonic generation signal = 1 × urea) is observed.[2]

The influence of hydrogen bonding is also reflected in the high melting points for hydroxy- and amino-phosphine oxides **1**, **2**, and **3**. The hydroxy-phosphine oxides (**1b**, **2b**, **3b**) exhibit extensive intermolecular hydrogen bonding and melt at temperatures roughly 130 °C higher than the corresponding methoxy derivatives (**1c**, **2c**, **3c**),

(22) Idoux, J. P. *J. Chem. Soc. (C)* **1970**, 435–437.

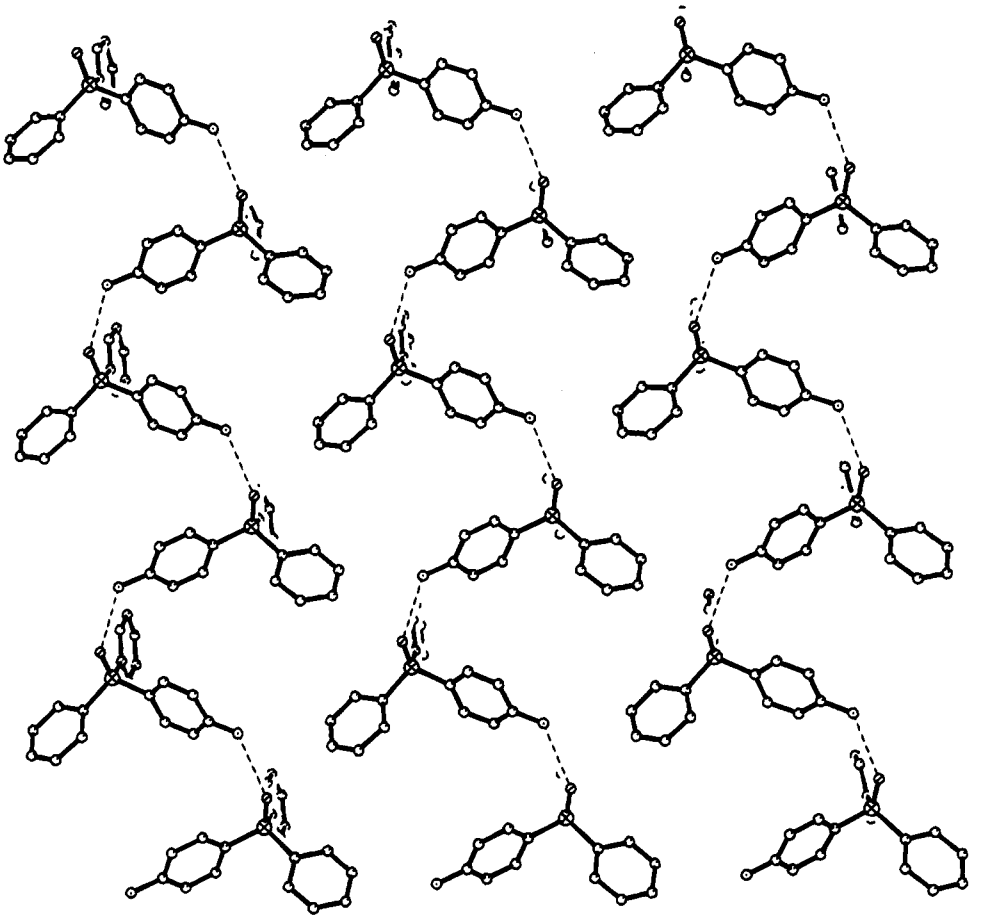


Figure 1. Crystal structure of (4-aminophenyl)diphenylphosphine oxide (**1a**) showing single layer of oriented chains.

Table 2. Melting Points of Triphenylphosphine Oxide Derivatives (°C)

cmpd	$-NH_2$ (**a**)	$-N(CH_3)_2$	$-OH$ (**b**)	$-OCH_3$ (**c**)
1	245.5–246.5	186–189[a]	241.5–242.5	115.5–116.5
2	264.0–265.0	203.5–204.5[a]	231.5–232.5	94.5–95.0
3		305–306[b]	275.0–276.0	143.0–144.0

[a] Reference 14. [b] Reference 6.

which lack the ability for intermolecular hydrogen bonding (Table 2). X-ray crystal structures of **2b** and **3b** reveal both O—H···O=P and O—H···O—H hydrogen bonds. Similarly, amino-phosphine oxides **1a** and **2a** melt at temperatures roughly 60 °C higher than the corresponding dimethylamino derivatives (Table 2). From the perspective of nonlinear optics, the crystalline hydroxy- and amino-phosphine oxides exhibit excellent thermal and mechanical stability.

Summary

We describe the synthesis of several new substituted arylphosphine oxides, which are of interest as second-order nonlinear optical materials. Our syntheses represent general methods for the preparation of arylphosphine oxides containing primary amine substituents. The solid-state structures of the arylphosphine oxides reflect extensive intermolecular hydrogen bonding. The hydrogen bonding in (4-aminophenyl)diphenylphosphine oxide (**1a**) and (4-hydroxyphenyl)diphenylphosphine oxide (**1b**) produces chains of oriented aryl-phosphine oxide molecules with head-to-tail alignment; the chains stack in an antiparallel manner to produce solid-state structures that display only slight deviations from centrosymmetry.

Experimental Section

General Methods. NMR spectra were obtained with a Bruker WP-200 spectrometer (^1H spectra: 200 MHz) or a Bruker WP-270 spectrometer (^{13}C spectra: 68 MHz). Chemical shifts (δ) are reported as ppm downfield from internal tetramethylsilane. High resolution mass spectra were recorded on a Kratos MS-80RFA (DS55/DS90 detector). Infrared (IR) spectra were recorded on a Nicolet Model 740 FT-IR spectrometer (MCT detector). Ultraviolet/visible (UV/vis) spectra were recorded on a Hitachi Model U-3210 spectrophotometer. Melting points were measured using a Thomas Hoover capillary melting point apparatus and are uncorrected.

All glassware was flame-dried and purged with nitrogen prior to use. All reactions were run under a nitrogen atmosphere. Solvents were purified and dried immediately before use: CH_2Cl_2 and CH_3CN were dried over and distilled from CaH_2; THF was dried over KOH, predistilled from CaH_2, and distilled from Na/benzophenone; *p*-dioxane was refluxed with HCl, dried over KOH, and distilled from Na. Magnesium turnings were prepared for use in Grignard reactions by stirring with dilute HCl for 10 min, thoroughly rinsing with H_2O, and drying in an oven at 150 °C for 48 h. Chlorodiphenylphosphine, dichlorophenylphosphine, phosphorus trichloride, boron tribromide, and 4-bromoanisole (**11**) were purchased from Aldrich. Triphenylphosphine oxide (**4**) was prepared from triphenylphosphine (Aldrich) using the oxidation procedure described for **1a** (see below).

4-Bromoaniline-STABASE Adduct (7).[15] A solution of 6.41 g (37 mmol) of 4-bromoaniline (Aldrich) in 100 mL of dry ether was cooled to −78 °C in a dry ice/acetone bath. Dropwise addition of 50 mL (86 mmol) of *n*-BuLi/hexane was accomplished over a period of 1 h. When addition was complete, the resulting mixture was stirred for 20 min at −78 °C and then for 1 h at −40 °C (CH_3CN/N_2 slush bath). A solution of 8.00 g (37 mmol) of 1,2-bis(chlorodimethylsilyl)ethane (Petrarch Systems, Inc.) in 30 mL dry ether was cautiously added.

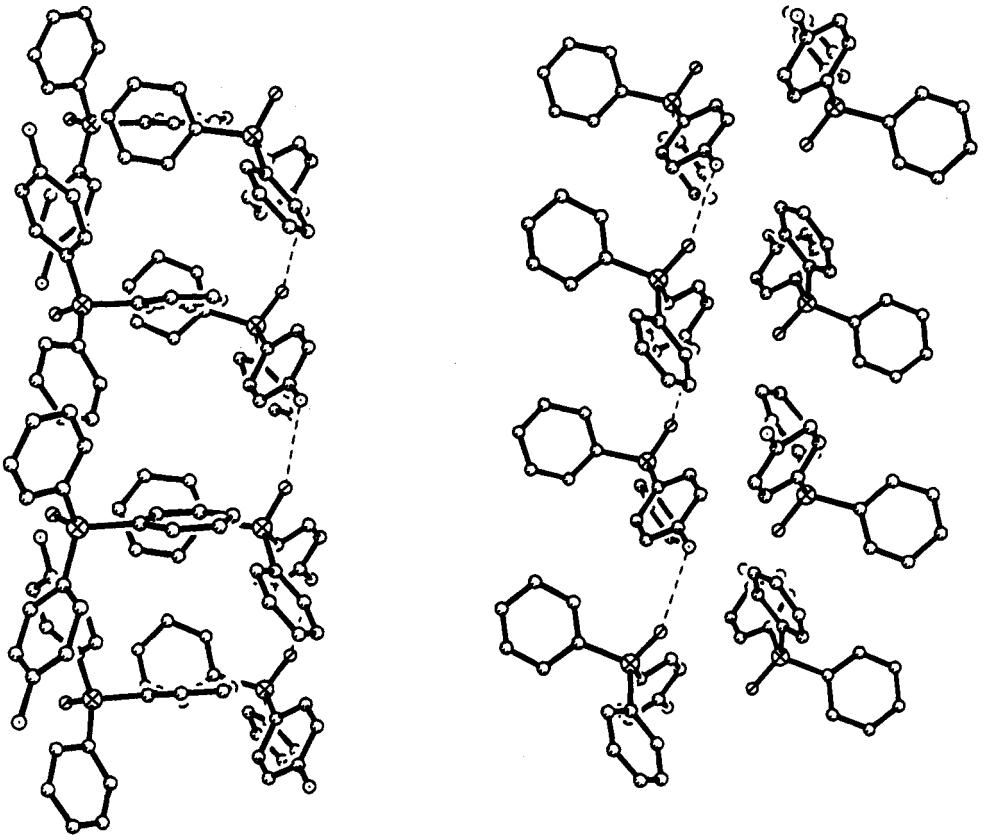


Figure 2. Right: Crystal structure of (4-aminophenyl)diphenylphosphine oxide (**1a**) showing adjacent layers with antiparallel orientation of chains. Left: Crystal structure of **1a** showing adjacent layers with orthogonal orientation of chains and edge-to-face π-stacking of aryl rings.

Stirring was continued for 3 h at −40 °C and then for 15 h at room temperature. The reaction was quenched by addition of 150 mL of H_2O. After diluting the organic layer with 100 mL ether, the layers were separated, and the aqueous layer was extracted with three 100 mL portions of ether. The combined ether layers were dried over Na_2SO_4. The ether was removed by evaporation under reduced pressure to yield 11.50 g (99%) of an orange oil. Purification of the crude product by vacuum distillation gave 6.79 g (58%) of the protected aryl bromide **7** as a viscous, yellow oil: boiling range 80−87 °C at 0.2−0.3 torr; ^{1}H NMR ($CDCl_3$) δ 7.28 and 6.78 (2 d, 4 H), 0.86 (s, 4 H), 0.19 (s, 12 H); IR (CH_2Cl_2, cm^{-1}) 1487, 1269, 1260; mass spectrum, calcd for $C_{12}H_{20}BrNSi_2$ 315.0298, 313.0318, found 315.0294, 313.0300; *m*/*z* (relative intensity) 315, 313 (M^+, 16, 15), 300, 298 (62, 64), 235 (27), 220 (100).

Azidomethyl Phenyl Sulfide.[16a] A solution of 40.0 g (0.62 mol) of NaN_3 (Aldrich) in 400 mL CH_3CN was added to a solution of 94.6 g (0.60 mol) of chloromethyl phenyl sulfide in 100 mL of CH_3CN, and the resulting mixture was refluxed for 16 h. The cloudy white reaction mixture was cooled to room temperature and 500 mL of H_2O added. The mixture was extracted twice with 500 mL of ether. The combined ether layers were washed once with 200 mL of 5% Na_2SO_3 and three times with 500 mL portions of saturated aqueous NaCl. After drying over Na_2SO_4, the ether was removed by evaporation under reduced pressure to yield 92.3 g (97%) of the crude product as a yellow oil. Purification of the crude product by vacuum distillation gave 79.5 g (84%) of the pure product as a clear, colorless oil: boiling range 65−70 °C at 0.4−0.5 torr; ^{1}H NMR ($CDCl_3$) δ 7.29−7.52 (m, 5 H), 4.54 (s, 2 H); IR (CH_2Cl_2, cm^{-1}) 2104, 740, 690; mass spectrum, calcd for $C_7H_7N_3S$ 165.0361, found 165.0360; *m*/*z* (relative intensity) 165 (9), 137 (2), 123 (2), 110 (64), 109 (69), 77 (13), 69 (100).

(4-Bromophenyl)diphenylphosphine (10). The synthesis of **10** followed a literature procedure.[23] Purification by vacuum distillation (boiling range 182−184 °C at 0.2−0.3 torr) and recrystallization from MeOH gave 32.72 g (51%) of pure **10** as a white, crystalline solid: mp 77−78 °C (lit.[23] mp 79−80 °C); ^{1}H NMR (CD_2Cl_2) δ 7.48 (dd, 2H ($^3J_{HH}$ = 8.4 Hz, $^4J_{PC}$ = 1.2 Hz)), 7.27−7.38 (m, 10 H), 7.17 (dd, 2H ($^3J_{HH}$ = 8.4, $^3J_{PH}$ = 6.9 Hz)); IR (CH_2Cl_2, cm^{-1}) 1478, 1069; mass spectrum, calcd for $C_{18}H_{14}BrP$ 341.9997, 339.9995, found 341.9979, 340.0017; *m*/*z* (relative intensity) 342, 340 (M^+, 50, 68), 183 (100).

(4-Aminophenyl)diphenylphosphine Oxide (1a). Method A. A solution of 1.00 g (3.18 mmol) of the 4-bromoaniline-STABASE adduct **7** in 10 mL of dry ether was cooled to 0 °C. The dropwise addition of 2.42 mL (4.14 mmol) of *n*-BuLi/hexane was accomplished over a period of 20 min. After stirring the resulting mixture for 1.5 h at 0 °C, the dropwise addition of a solution of 0.70 g (3.18 mmol) of chlorodiphenylphosphine in 10 mL of dry ether occurred over a period of 30 min at 0 °C, and the reaction was stirred for 15 h at room temperature. The reaction was quenched by the addition of 60 mL of H_2O, and the organic layer was diluted with 100 mL of ether. The aqueous layer was extracted twice with 50 mL of ether, and the combined ether layers were dried over Na_2SO_4. The ether was concentrated to 40 mL, and 3 drops of concentrated HCl were added to hydrolyze the STABASE protecting group. After stirring for 30 min at room temperature, an additional 30 mL of 10% HCl was added to dilute the aqueous layer. The layers were separated. The organic layer was discarded, and the yellowish aqueous layer was neutralized with 5% NaOH. The aqueous layer was then extracted three times with 30 mL portions of ether, and the combined ether layers were dried over Na_2SO_4. The solvent was then removed by evaporation under reduced pressure to yield an orange oil. The oil was redissolved in 25 mL of ether, and 0.36 mL of 30% H_2O_2 was added with stirring. In seconds,

(23) Schiemenz, G. P. *Organic Syntheses;* Wiley: New York, 1973; Coll. Vol. V, pp 496−499.

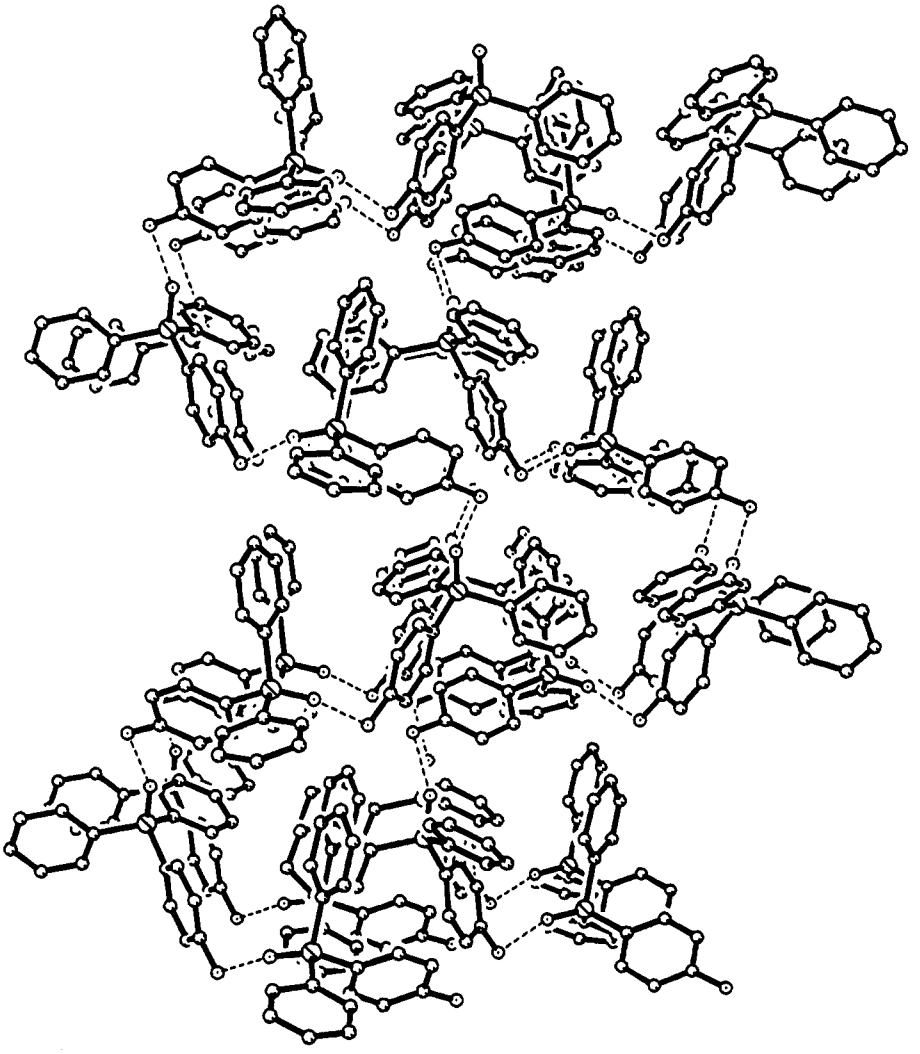


Figure 3. Crystal structure of (4-hydroxyphenyl)diphenylphosphine oxide (**1b**) showing oriented chains and edge-to-face π-stacking of aryl rings.

a white solid precipitated from solution. The solid was collected by filtration and rinsed several times with ether. The solid was then redissolved in CH_2Cl_2, and this solution was extracted with 5% NaOH to remove residual H_2O_2. After drying over Na_2SO_4, the solvent was reduced in volume. Upon cooling, white crystals precipitated which were collected by filtration. Recrystallization from CH_3CN gave 0.24 g (26%) of pure (4-aminophenyl)diphenylphosphine oxide (**1a**) as a white, crystalline solid: mp 245.5–246.5 °C (lit. 235 °C,[13] 238–239 °C);[14] ^{1}H NMR (CD_2Cl_2) δ 7.62–7.72 (m, 4 H), 7.36–7.52 (m, 8 H), 6.70 (dd, 2 H ($^3J_{HH}$ = 8.7, $^4J_{PH}$ = 2.3 Hz), 4.05 (s (br), 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 149.95 (s, 1 C), 133.77 (d, 2 C, J_{PC} = 11.0 Hz), 133.39 (d, 2 C, $^1J_{PC}$ = 103.9 Hz), 132.04 (d, 4 C, J_{PC} = 9.8 Hz), 131.56 (s, 2 C), 128.30 (d, 4 C, J_{PC} = 11.6 Hz), 119.77 (d, 1 C, $^1J_{PC}$ = 113.3 Hz), 114.24 (d, 2 C, J_{PC} = 13.1 Hz); IR (CH_2Cl_2, cm^{-1}) 3493, 3402, 1623, 1600, 1180, 1120; UV/vis (*p*-dioxane), λ_{max} = 264 nm; ϵ = 18,600 M^{-1} cm^{-1}; mass spectrum, calcd for $C_{18}H_{16}NOP$ 293.0969, found 293.0968; *m*/*z* (relative intensity) 293 (M$^+$, 78), 292 (100), 216 (33), 200 (21).

Method B. A solution of 2.00 g (5.86 mmol) of (4-bromophenyl)diphenylphosphine (**10**) in 10 mL of dry THF was gradually added to a mixture of 0.14 g (5.86 mmol) of magnesium turnings and 5 mL of dry THF, resulting in a deep red solution. The reaction was refluxed for 4 h before cooling to −78 °C. A solution of 0.99 g (6.00 mmol) of azidomethyl phenyl sulfide in 12 mL THF was added to the reaction and the resulting mixture stirred for 72 h at room temperature. The reaction was then cooled to 0 °C and quenched by addition of 30 mL of saturated aqueous NH_4Cl. To dissolve the orange precipitate, 25 mL of CH_2Cl_2 was added, and the mixture was transferred to a separatory funnel. The aqueous layer was extracted twice with 50 mL portions of CH_2Cl_2. The combined organic layers were then extracted with 50 mL of saturated aqueous NaCl and dried over Na_2SO_4. The solvent was then removed by evaporation under reduced pressure to yield the crude triazene as an orange-red solid. The crude triazene was dissolved in 6 mL of THF and 6 mL of MeOH (reagent grade), giving a deep red solution. A volume of 6 mL of 50% aqueous KOH was added and the resulting mixture stirred for 24 h at room temperature. The reaction was then diluted with 10 mL of H_2O and extracted five times with 50 mL portions of CH_2Cl_2. The combined CH_2Cl_2 layers were washed with 100 mL of saturated aqueous NaCl and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave 1.45 g (89%) of the crude monoamino phosphine as a yellow/orange gummy solid. The crude phosphine was purified by column chromatography (silica gel/hexane:EtOH (3:1)) to yield 0.82 g (50%) of the phosphine as an off-white, crystalline solid. However, both ^{1}H NMR and mass spectrum analyses reveal the presence of the phosphine oxide in addition to the phosphine. The material was dissolved in 30 mL of CH_3CN, and 1.67 mL of 30% H_2O_2 was added. After stirring for 16 h at room temperature, 10 mL of 10% aqueous NaOH was added. The reaction mixture was then transferred to a separatory funnel and diluted with 75 mL of H_2O. Extraction of the aqueous layer five times with 50 mL portions of CH_2Cl_2, followed by extraction of the combined organic layers with 100 mL of saturated aqueous NaCl and removal of the solvent by evaporation under reduced pressure gave 0.79 g (46%) of the desired monoamino phosphine oxide **1a**. The product could

be further purified by column chromatography (silica gel/EtOAc:EtOH (20:1)) and recrystallization from EtOAc.

Bis(4-aminophenyl)phenylphosphine Oxide (2a). Bis(4-aminophenyl)phenyl phosphine was synthesized from 1.00 g (3.18 mmol) of the 4-bromoaniline-STABASE adduct **7**, 1.34 mL (3.35 mmol) of *n*-BuLi/hexane, and 0.22 mL (1.62 mmol) of dichlorophenylphosphine using method A described above for the monoamino phosphine. However, cleavage of the STABASE protecting group was effected by column chromatography (silica gel/EtOAc), and 0.056 g (12%) of pure bis(4-aminophenyl)phenylphosphine was isolated as a clear, colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 5 H), 7.12 (dd, 4 H), 6.63 (dd, 4 H), 3.73 (s(br), 4 H).

Subsequent oxidation was accomplished by dissolving the phosphine in 2 mL of acetone (reagent grade) and refluxing with 0.20 mL of 30% H_2O_2 for 4 h. The acetone was removed by evaporation under reduced pressure. After redissolving the residue in benzene, 3.0 mL of 10% aqueous NaOH was added and the resulting mixture stirred for 20 min. The layers were then diluted by addition of 10 mL of benzene and 10 mL of H_2O, and the organic layer was extracted with 10 mL of saturated aqueous NaCl solution. The aqueous layer was extracted twice with 15 mL of acetonitrile, and the combined organic layers were dried over Na_2SO_4. Removal of the solvent by evaporation under reduced pressure gave 0.055 g (96%) of the crude phosphine oxide. Purification by column chromatography (silica gel/EtOAc:EtOH (10:1)) followed by recrystallization from EtOAc gave 0.043 g (76%) of pure bis(4-aminophenyl)phenylphosphine oxide (**2a**) as an off-white, crystalline solid: mp 264.0–265.0 °C; ^{1}H NMR ($CDCl_3$) δ 7.65 (m, 2 H), 7.41 (m, 7 H), 6.67 (dd, 4 H ($^3J_{HH}$ = 8.6, $^4J_{PH}$ = 2.4 Hz)), 3.96 (s (br), 4 H); mass spectrum, calcd for $C_{18}H_{17}N_2OP$ 308.1078, found 308.1077; *m/z* (relative intensity) 308 (M^+, 98), 307 (100), 231 (18), 214 (17), 200 (25).

(4-Methoxyphenyl)diphenylphosphine Oxide (1c). (4-Methoxyphenyl)diphenylphosphine was synthesized by reaction of the Grignard reagent of 4-bromoanisole (**11**, 25.25 mL, 0.20 mol) with chlorodiphenylphosphine (35.19 mL, 0.20 mol), using a procedure described for the preparation of tris(4-methoxyphenyl)phosphine.[19] The crude product was purified by column chromatography (silica gel/EtOAc) to yield 48.17 g (84%) of the pure phosphine as a clear, colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 12 H), 6.89 (dd, 2 H ($^3J_{HH}$ = 8.8, $^4J_{PH}$ = 0.8 Hz), 3.80 (s, 3 H); mass spectrum, calcd for $C_{19}H_{17}OP$ 292.1017, found 292.1025; *m/z* (relative intensity) 292 (M^+, 100), 277 (5), 215 (18), 183 (27), 108 (20).

Subsequent oxidation of (4-methoxyphenyl)diphenylphosphine (48.17 g, 0.165 mol) to (4-methoxyphenyl)diphenylphosphine oxide (**1c**) was accomplished using aqueous $KMnO_4$ (27.66 g, 0.175 mol in 1.5 L H_2O).[19] Purification by recrystallization from cyclohexane gave pure **1c** (46.42 g, 91%) as a white, crystalline solid: mp 115.5–116.5 °C (lit.[18] 117–118 °C); ^{1}H NMR ($CDCl_3$) δ 7.71–7.44 (m, 12 H), 6.97 (dd, 2 H ($^3J_{HH}$ = 8.9, $^4J_{PH}$ = 2.2 Hz)), 3.85 (s, 3 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 162.46 (s, 1 C), 133.94 (d, 2 C, J_{PC} = 11.1 Hz), 132.02 (d, 4 C, J_{PC} = 9.5 Hz), 131.75 (s, 2 C), 128.40 (d, 4 C, J_{PC} = 12.3 Hz), 123.61 (d, 1 C, $^1J_{PC}$ = 109.8 Hz), 114.05 (d, 2 C, J_{PC} = 13.2 Hz), 55.30 (s, 1 C) [quaternary carbons of phenyl rings (expected d, 2 C) not observed, presumably due to overlap with other resonances in the range of 125–135 ppm]; IR (CH_2Cl_2, cm^{-1}) 1599, 1179, 1120; mass spectrum, calcd for $C_{19}H_{17}O_2P$ 308.0966, found 308.0954; *m/z* (relative intensity) 308 (M^+, 58), 307 (100), 231 (23), 215 (19).

(4-Hydroxyphenyl)diphenylphosphine Oxide (1b). A solution of 25.00 g (0.081 mol) of (4-methoxyphenyl)diphenylphosphine oxide (**1c**) in 500 mL of dry CH_2Cl_2 was cooled to −78 °C, and 14.72 mL (0.155 mol) of BBr_3 was added over a period of 10 min.[19,20] The resulting mixture was stirred at room temperature for 24 h and quenched by cautiously pouring into 800 mL of ice/H_2O. The mixture was heated until the organic solvent completely evaporated. After cooling to room temperature, the aqueous layer was extracted four times with 800 mL portions of EtOAc. The combined EtOAc layers were dried over Na_2SO_4, and then the solvent was concentrated to induce precipitation of the product. Recrystallization from EtOAc gave 21.63 g (91%) of pure (4-hydroxyphenyl)diphenylphosphine oxide (**1b**) as a white, crystalline solid: mp 241.5–242.5 °C (lit.[18] 243–244 °C); ^{1}H NMR ($CDCl_3$) δ 9.19 (s (br), 1 H), 7.74–7.46 (m, 12 H), 6.98 (dd, 2 H ($^3J_{HH}$ = 8.7, $^4J_{PH}$ = 2.3 Hz)); ^{13}C{^{1}H} NMR (Me_2CO-d_6) δ 160.70 (s, 1 C), 133.51 (d, 2 C, J_{PC} = 10.9 Hz), 133.48 (d, 2 C, $^1J_{PC}$ = 101.7 Hz), 131.71 (s, 2 C), 131.39 (d, 4 C, J_{PC} = 9.5 Hz), 128.59 (d, 4 C, J_{PC} = 11.3 Hz), 121.57 (d, 1 C, $^1J_{PC}$ = 110.9 Hz), 115.65 (d, 2 C, J_{PC} = 12.9 Hz); UV/vis (*p*-dioxane), λ_{max} nm (ϵ, M^{-1} cm^{-1}) 281 (1,000), 272 (2,500), 265 (2,900), 237 (19,000), 274 (20,700); mass spectrum, calcd for $C_{18}H_{15}O_2P$ 294.0810, found 294.0794; *m/z* (relative intensity) 294 (M^+, 46), 293 (100), 217 (20), 201 (21).

Bis(4-methoxyphenyl)phenylphosphine oxide (2c). Bis(4-methoxyphenyl)phenylphosphine was synthesized by reaction of the Grignard reagent of 4-bromoanisole (**11**, 25.25 mL, 0.20 mol) with dichlorophenylphosphine (13.30 mL, 0.098 mol), using a procedure described for the preparation of tris(4-methoxyphenyl)phosphine.[19] Pure bis(4-methoxyphenyl)phenylphosphine (26.90 g, 82%) was isolated a clear, colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 9 H), 6.88 (dd, 4 H ($^3J_{HH}$ = 8.0 Hz)), 3.80 (s, 6 H).

Subsequent oxidation of bis(4-methoxyphenyl)phenylphosphine (26.00 g, 0.078 mol) to bis(4-methoxyphenyl)phosphine oxide (**2c**) was accomplished using aqueous $KMnO_4$ (13.00 g, 0.082 mol, 800 mL of H_2O).[19] Purification by recrystallization from cyclohexane gave pure **2c** (26.40 g, 97%) as a white, crystalline solid: mp 94.5–95.0 °C (lit.[18] 96–97 °C); ^{1}H NMR ($CDCl_3$) δ 7.65–7.48 (m, 9 H), 7.03 (dd, 4 H ($^3J_{HH}$ = 8.9, $^4J_{PH}$ = 2.2 Hz), 3.83 (6 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 162.18 (s, 2 C), 133.69 (d, 4 C, J_{PC} = 10.9 Hz), 132.52 (one resonance of expected doublet, 1 C; other portion of doublet presumably obscured by overlapping resonances), 131.77 (d, 2 C, J_{PC} = 9.3 Hz), 131.44 (s, 1 C), 128.18 (d, 2 C, J_{PC} = 12.3 Hz), 123.92 (d, 2 C, $^1J_{PC}$ = 110.8 Hz), 113.82 (d, 4 C, J_{PC} = 13.0 Hz), 55.11 (s, 2 C); IR (CH_2Cl_2, cm^{-1}) 1598, 1503, 1178, 1120; mass spectrum, calcd for $C_{20}H_{19}O_3P$ 338.1072, found 338.1082; *m/z* (relative intensity) 338 (M^+, 69), 337 (100), 261 (19), 245 (13), 215 (19).

Bis(4-hydroxyphenyl)phenylphosphine Oxide (2b). Compound **2b** was synthesized by reaction of 10.00 g (29.6 mmol) of bis(4-methoxyphenyl)phenylphosphine oxide (**2c**) and 11.20 mL of BBr_3 in 200 mL dry CH_2Cl_2 as described for **1b**. Purification by recrystallization from EtOAc/hexane gave 8.76 g (96%) of pure bis(4-hydroxyphenyl)phenylphosphine oxide (**2b**) as a white, crystalline solid: mp 231.5–232.5 °C (lit.[18] 233–234 °C); ^{1}H NMR ($CDCl_3$) δ 9.63 (s (br), 2 H), 7.73–7.43 (m, 5 H), 7.49 (dd, 4 H ($^3J_{HH}$ = 8.7, $^4J_{PH}$ = 11.5 Hz), 6.98 (dd, 4 H ($^3J_{HH}$ = 8.7, $^4J_{PH}$ = 2.3 Hz); ^{13}C{^{1}H} NMR (Me_2CO-d_6) δ 160.47 (s, 2 C), 133.42 (d, 4 C, J_{PC} = 11.1 Hz), 131–132 (m, 3 C), 128.46 (d, 2 C, J_{PC} = 11.2 Hz), 122.42 (d, 2 C, $^1J_{PC}$ = 110.0 Hz), 115.50 (d, 4 C, J_{PC} = 12.8 Hz) [quaternary carbon of phenyl ring (expected d, 1 C) not observed, presumably due to overlap with other resonances in the range of 125–135 ppm]; UV/vis (*p*-dioxane), λ_{max} nm (ϵ, M^{-1} cm^{-1}) 280 (2,300), 271 (3,500), 240 (29,100); mass spectrum, calcd for $C_{18}H_{15}O_3P$ 310.0759, found 310.0745; *m/z* (relative intensity) 310 (M^+, 58), 309 (100), 233 (19), 217 (22), 201 (22).

Drying under high vacuum at 165 °C for 72 h was necessary to completely remove all traces of the EtOAc solvent.

Tris(4-methoxyphenyl)phosphine Oxide (3c). Tris(4-methoxyphenyl)phosphine was synthesized by reaction of the Grignard reagent of 4-bromoanisole (**11**, 8.42 mL, 67 mmol) with phosphorus trichloride (1.89 mL, 22 mmol).[19] Tris(4-methoxyphenyl)phosphine (6.79 g, 89%) was isolated as a white, crystalline solid: mp 130.0–131.0 °C (lit.[18] 130–131 °C); ^{1}H NMR ($CDCl_3$) δ 7.22 (dd, 6 H ($^3J_{HH}$ = 8.8, $^3J_{PH}$ = 7.3 Hz)), 6.87 (dd, 6 H ($^3J_{HH}$ = 8.8, $^4J_{PH}$ = 0.8 Hz)), 3.79 (s, 9 H); IR (CH_2Cl_2, cm^{-1}) 1597, 1499, 1178, 1120; mass spectrum, calcd for $C_{21}H_{21}O_3P$ 352.1228, found 352.1236; *m/z* (relative intensity) 352 (M^+, 100), 337 (8), 245 (17), 138 (50).

Subsequent oxidation of tris(4-methoxyphenyl)phosphine (6.00 g, 17 mmol) to tris(4-methoxyphenyl)phosphine oxide (**3c**) was accomplished using aqueous $KMnO_4$ (2.84 g, 18 mmol, 200 mL of H_2O).[19] Purification by recrystallization from cyclohexane gave pure **3c** (6.25 g, 99%) as a white, crystalline solid: mp 143.0–144.0 °C (lit.[18] 143–144 °C); ^{1}H NMR ($CDCl_3$) δ 7.57 (dd, 6 H ($^3J_{HH}$ = 8.5, $^3J_{PH}$ = 11.3 Hz)), 6.95 (dd, 6 H ($^3J_{HH}$ = 8.5, $^4J_{PH}$ = 1.9 Hz)), 3.84 (s, 9 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 162.22

(s, 3 C), 133.80 (c, 6 C, J_{PC} = 11.2 Hz), 124.55 (d, 3 C, $^1J_{PC}$ = 110.9 Hz), 113.88 (d, 6 C, J_{PC} = 13.0 Hz), 55.24 (s, 3 C); IR (CH_2Cl_2, cm^{-1}) 1598, 1504, 1179, 1120; mass spectrum, calcd for $C_{21}H_{21}O_4P$ 368.1177, found 368.1181; *m/z* (relative intensity) 368 (M^+, 65), 367 (100), 353 (10), 261 (24), 245 (53).

Tris(4-hydroxyphenyl)phosphine Oxide (3b). Compound **3b** was synthesized by reaction of 2.00 g (5.43 mmol) of tris(4-methoxyphenyl)phosphine oxide (**3c**) with 2.95 mL (31.20 mmol) of BBr_3 in 40 mL of dry CH_2Cl_2, as described for **1b**. Purification by recrystallization from EtOAc gave 1.65 g (93%) of pure tris(4-hydroxyphenyl)phosphine (**3b**) as a white, crystalline solid: mp 275.0–276.0 °C (lit.[18] 273–275 °C); ^1H NMR ($CDCl_3$) δ 9.55 (s (br), 3 H), 7.48 (dd, 6 H ($^3J_{HH}$ = 8.7, $^3J_{PH}$ = 11.5 Hz)), 6.97 (dd, 6 H ($^3J_{HH}$ = 8.7, $^4J_{PH}$ = 2.3 Hz)); $^{13}C\{^1H\}$ NMR (Me_2CO-d_6) δ 160.24 (s, 3 C), 133.33 (d, 6 C, J_{PC} = 10.8 Hz), 123.23 (d, 3 C, $^1J_{PC}$ = 110.6 Hz), 115.35 (d, 6 C, J_{PC} = 12.8 Hz); UV/vis (*p*-dioxane), λ_{max} nm (ϵ, M^{-1} cm^{-1}) 282 (3,600), 273 (4,800), 242 (43,800); mass spectrum, calcd for $C_{18}H_{15}O_4P$ 326.0708, found 326.0693; *m/z* (relative intensity) 326 (56), 325 (100), 233 (27), 217 (47).

Drying under high vacuum at 170 °C for 72 h was necessary to completely remove all traces of the EtOAc solvent.

(Diethylamino)phosphinous Dichloride.[21] A solution of 20 g (0.27 mol) diethylamine in 100 mL of dry ether was cooled in an ethylene glycol/N_2 slush bath (−10 °C). Phosphorus trichloride (22 g, 0.16 mol) was added dropwise over a period of 1 h. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. A precipitate was removed by vacuum filtration and washed with water. The filtrate was isolated and the solvent evaporated under reduced pressure to give the crude dichloride. The product was purified by vacuum distillation (boiling range 32–35 °C at 0.5 torr) to yield 11.6 g (0.07 mol, 42% yield) of Et_2NPCl_2 as a clear, colorless liquid: ^1H NMR ($CDCl_3$) δ 3.35 (dq, 4 H), 1.17 (t, 6 H).

Bis[4-(trifluoromethyl)phenyl]phosphinous Chloride.[21] A solution of 3.3 g (0.14 mol) magnesium and 30 g (0.13 mol) 1-bromo-4-(trifluoromethyl)benzene (Pierce) in 100 mL of anhydrous ether was stirred. After the exothermic reaction had ceased, the mixture was refluxed for 2 h. The dark brown mixture was transferred via cannula to an addition funnel, and slowly added to a solution of 11 g (0.06 mol) of Et_2NPCl_2 and 23 g (0.29 mol) of pyridine cooled in an ice/water bath. The mixture was allowed to warm and was stirred overnight at room temperature. HCl was bubbled through the dark mixture for 30 min, and then the reaction mixture was vacuum filtered under nitrogen atmosphere. The filtrate was isolated and the solvent removed by evaporation under reduced pressure to yield an orange-brown oil. Purification by vacuum distillation (boiling range 90–110 °C at 0.3–0.5 torr) gave 8.7 g (0.03 mol, 49% yield) of a clear, colorless liquid: ^1H NMR ($CDCl_3$) δ 7.68 (s, 8 H).

(4-Aminophenyl)bis[4′-(trifluoromethyl)phenyl]phosphine Oxide (5). A solution of 2.1 g (6.7 mmol) of the 4-bromoaniline-STABASE adduct **7** in 20 mL of dry ether was cooled to 0 °C. The dropwise addition of 3.0 mL (7.5 mmol) of *n*-BuLi/hexane was accomplished over a period of 10 min. After stirring the mixture for 2 h at 0 °C, the dropwise addition of a solution of 2.0 g (6.3 mmol) bis[4-(trifluoromethyl)phenyl]-phosphinous chloride in 15 mL dry ether occurred over a period of 10 min at 0 °C. The mixture was stirred overnight at room temperature. The reaction was quenched by addition of water and the aqueous layer was extracted three times with 50 mL portions of ether. The combined ether layers were dried over $MgSO_4$ and the ether was concentrated to 20 mL. Five drops of concentrated HCl was added to hydrolyze the STABASE protecting group. The aqueous layer was diluted with 50 mL of 20% HCl, and the layers were separated. The organic layer was discarded and the aqueous layer neutralized with 5% NaOH and 10% $NaHCO_3$. The aqueous layer was extracted three times with 50 mL portions of ether, and the combined ether layers were dried over $MgSO_4$. The solvent was removed by evaporation under reduced pressure to yield an orange oil. The oil was redissolved in 25 mL of ether, and 0.75 mL of 30% H_2O_2 was added with stirring. The reaction mixture was quenched by addition of 10% NaOH, and then the aqueous layer was extracted three times with 50 mL portions of benzene. The organic layers were combined and dried over $MgSO_4$. The solvent was removed by evaporation under reduced pressure to yield a brown oil. The crude product was purified by column chromatography (silica gel/EtOAc) to yield 0.35 g (0.08 mmol, 13% yield) of the phosphine oxide **5** as a light yellow powder: mp 80–82 °C; ^1H NMR ($CDCl_3$) δ 7.79 (m, 8 H), 7.37 (dd, 2 H ($^3J_{HH}$ = 9 Hz, $^3J_{PH}$ = 12 Hz)), 6.71 (dd, 2 H ($^3J_{HH}$ = 9 Hz, $^4J_{PH}$ = 3 Hz)), 4.22 (s (br), 2 H); IR (KBr pellet, cm^{-1}) 3413, 3228, 1598, 1325, 1171, 1125, 1065, 833, 706; UV/vis (*p*-dioxane), λ_{max} nm (ϵ, M^{-1} cm^{-1}) 266 (14,900), 298 (5,600); mass spectrum, calcd for $C_{20}H_{14}F_6NPO$ 429.0714, found 429.0717; *m/z* (relative intensity) 429 (M^+, 100), 284 (33), 268 (22), 108 (9), 51 (10).

Sodium Hydrogen Sulfide.[24] A solution of 20 g (0.08 mol) sodium sulfide (Aldrich) in 50 mL water was added to 7.3 g (0.08 mol) sodium bicarbonate in a cold water bath. After stirring in the cold bath for 10 min, 50 mL of methanol was added and the reaction mixture was allowed to stir for 30 min at room temperature. A precipitate was removed via vacuum filtration and washed with 25 mL of methanol. The filtrate isolated contained NaSH (0.06 mol/100 mL) as a clear, colorless liquid.

Bis(4-fluorophenyl)phenylphosphine.[25] A solution of 5.0 g (0.03 mol) of 1-bromo-4-fluorobenzene (**13**, Aldrich) in 15 mL of dry ether was added to 0.8 g (0.03 mol) of magnesium. After the exothermic reaction had ceased, the mixture was refluxed for 2 h. The reaction mixture was then cooled to 0 °C, and a solution of 1.8 g (9.9 mmol) of dichlorophenylphosphine in 25 mL of dry ether was added very slowly over a period of 30 min. The resulting mixture was then stirred for 4 h at room temperature. The reaction was quenched by addition of 100 mL saturated aqueous NH_4Cl. The aqueous layer was extracted three times with 50 mL portions of ether. The organic layers were combined, dried over $MgSO_4$, and the solvent removed by evaporation under reduced pressure. The crude product was purified by column chromatography (silica gel/CH_2Cl_2) to yield 1.9 g (6.3 mmol, 21% yield) of bis(4-fluorophenyl)phenylphosphine as a yellow liquid: ^1H NMR ($CDCl_3$) δ 7.28 (m, 9 H), 7.04 (td, 4 H).

Bis(4-fluorophenyl)phenylphosphine Oxide (14).[26] A solution of 1.9 g (6.3 mmol) bis(4-fluorophenyl)phenylphosphine in 20 mL of dry ether was stirred, and 1.8 mL (0.02 mol) of 30% hydrogen peroxide was added dropwise. After the addition was complete the solution was refluxed for 2 h. The solvent was removed under reduced pressure, and the residue was dissolved in a minimal amount of benzene. A volume of 5 mL of a 0.3 M NaOH solution was added. The layers were separated, and the benzene solution was dried over $MgSO_4$. The solvent was removed by evaporation under reduced pressure to yield the crude phosphine oxide. The product was purified by column chromatography (silica gel/$CHCl_3$:EtOAc (10:1)) to yield 0.8 g (2.7 mmol, 43% yield) of **14** as a white solid: mp 123–125 °C (lit.[26] 124 °C); ^1H NMR ($CDCl_3$) δ 7.76 (m, 6 H), 7.53 (m, 2 H), 7.18 (td, 4 H).

Lithium Nitrite.[27] A solution of 4.6 g (0.04 mol) of lithium sulfate and 3.0 g (0.04 mol) of potassium nitrite in 50 mL of water was stirred at room temperature. The water was evaporated to 10 mL and the mixture filtered. The filtrate was further evaporated to 5 mL, vacuum filtered, and dried in vacuo. The residue was extracted with 25 mL of absolute ethanol and the solvent evaporated under reduced pressure to yield 1.1 g (0.02 mol, 41% yield) of the hydrated product as a white solid.

Bis(4-nitrophenyl)phenylphosphine Oxide. The synthesis of bis(4-nitrophenyl)phenylphosphine oxide followed a literature procedure.[17] A solution of 3.4 g (0.01 mol) of bis(4-fluorophenyl)phenylphosphine oxide (**14**) and 3.4 g (0.06 mol) of lithium nitrite in 12 mL of HMPA was heated to 150 °C for

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16 h. The reaction was quenched with water and the aqueous layer was extracted three times with 50 mL portions of chloroform. The combined organic layers were added to a solution of benzene/water. The organic layer was separated and dried over $MgSO_4$ and the solvent removed under reduced pressure. The phosphine oxide was purified by column chromatography (silica gel/$CHCl_3$:EtOAc (9:1)) to yield 1.7 g (4.6 mmol, 46% yield) of a red-orange oil: ^{1}H NMR ($CDCl_3$) δ 8.35 (dd, 4 H ($^3J_{HH}$ = 8 Hz, $^4J_{PH}$ = 3 Hz)), 7.5–8.2 (m, 9 H); IR (KBr pellet, cm^{-1}) 1526, 1350, 1204.

(4-Aminophenyl)(4'-nitrophenyl)phenylphosphine Oxide (6). A solution of 1.4 g (3.9 mmol) of bis(4-nitrophenyl)-phenylphosphine oxide in 25 mL of methanol was added to 7 mL (4.2 mmol) of a freshly prepared solution of NaSH at room temperature. After the reaction mixture had stirred for 3 h, the solution was vacuum filtered to remove a white impurity. The filtrate was poured into an excess of water and the aqueous layer extracted three times with 50 mL portions of CH_2Cl_2. The organic layers were combined and dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel/EtOAc) to yield 0.7 g (1.9 mmol, 50% yield) of the phosphine oxide **6** as a yellow solid: mp 125–127 °C; ^{1}H NMR ($CDCl_3$) δ 8.27 (dd, 2 H ($^3J_{HH}$ = 9Hz, $^4J_{PH}$ = 3 Hz)), 7.88 (dd, 2 H ($^3J_{HH}$ = 9Hz, $^3J_{PH}$ = 12 Hz)), 7.51 (m, 7 H), 6.70 (dd, 2 H ($^3J_{HH}$ = 9Hz, $^4J_{PH}$ = 3 Hz)), 4.08 (s (br), 2 H); IR (KBr pellet, cm^{-1}) 3458, 3317, 1598, 1479, 1352, 1169, 1120, 739; UV/vis (p-dioxane) λ_{max} nm (ϵ, M^{-1} cm^{-1}) 266 (37,600), 340 (1,400); mass spectrum, calcd for $C_{18}H_{15}N_2O_3P$ 338.0817, found 338.0805; m/z (relative intensity) 338 (M$^+$,100), 337 (76), 291 (27), 216 (36), 108 (22).

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Supplementary Material Available: ORTEP plots and packing diagrams for the crystal structures of phosphine oxides **1a**, **1b**, **2b**, **3b**, and **3c** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS. Ordering information is given on any current masthead page.

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