low-field $-SO_2H$ absorptions; (c) charge distribution (and vicinal coupling) patterns very similar to those observed for pyrenium ions of protonation; and (d) preferential desulfinylation upon quenching of the Wheland intermediates.

Experimental Section

Syntheses and purification of pyrenes **1–7** are already described.[1] FSO_3H (Allied), CF_3SO_3H, and SbF_5 (both Aldrich) were distilled twice under dry nitrogen in an all-glass distillation unit prior to use. Anhydrous SO_2 (Linde) and doubly distilled SO_2ClF (Aldrich) were used as received.

Protonation Procedure. To a slurry of the pyrene (20–30 mg) in 0.5 mL of cold SO_2 or SO_2ClF inside a 10-mm NMR tube, was added a clear solution of ca. 1 mL of the superacid (FSO_3H, CF_3SO_3H or $FSO_3H.SbF_5$ (1:1)) diluted with 1 mL of SO_2 or SO_2ClF with efficient vortex mixing at dry ice–acetone temperature. A cold aliquot of the ion solution was transferred via a precooled pipet (liquid SO_2) into a cold 5-mm NMR tube, and 5 drops of cold CD_2Cl_2 was added as internal standard and lock (vortex mixing).

Ion Quenching. The cold NMR tube containing the ion solution was carefully poured into ice–bicarbonate. The organic layer was extracted (CH_2Cl_2), dried ($MgSO_4$), and evaporated to dryness. The residue was taken up in $CDCl_3$ and analyzed by ^1H NMR spectroscopy.

NMR spectra were recorded on a GN-300 wide-bore instrument. The probe was precooled to −70 °C while shimming on an acetone-d_6 sample; the cold ion solution was quickly introduced into the cold probe at −70 °C and spun for 5 min prior to data collection.

MMX force field energy calculations on **4**-H_1^+ and **5**-H_6^+ (see refs 34, 36) were carried out using the PCMODEL program (Serene Software). All pyrene carbons were assigned π atoms (SCF-π calculations were unavailable). The π system in the minimized structures was planar. The sp^3 carbon was specified C^+.

Acknowledgment. We thank Kent State University for research support, the Ohio Academic Challenge Program for the funds for a high-field NMR spectrometer, and Professor Arne Berg (Aarhus University) for his past contributions to pyrene chemistry and his interest in our work. We are grateful to one of the reviewers for important remarks and constructive suggestions and to Professor George Olah for his encouragement and keen interest.

Registry No. **1**, 78751-46-9; **1**-H_6^+, 136827-78-6; **1**-H_8^+, 136827-79-7; **1**-H_3^+, 136827-80-0; **1**-(6-SO_2H)$^+$, 136827-81-1; **1**-(8-SO_2H)$^+$, 136827-82-2; **2**, 78751-61-8; **2**-H_1^+, 136827-83-3; **2**-(1-SO_2H)$^+$, 136827-84-4; **2**-(8-SO_2H)$^+$, 136827-85-5; **3**, 74869-51-5; **3**-H_6^+, 136827-86-6; **3**-H_8^+, 136827-87-7; **3**-(8-SO_2H)$^+$, 136827-88-8; **3**-(1-SO_2H)$^+$, 136827-89-9; **4**, 24300-95-6; **4**-H_1^+, 136827-90-2; **4**-(1,8-SO_2H)$^{2+}$, 136827-99-1; **4a**-H_5^+, 136827-91-3; **5**, 78751-94-7; **5**-H_6^+, 136827-92-4; **5**-(6-SO_2H)$^+$, 136827-93-5; **5**-H_1^+, 136827-94-6; **6**, 24300-91-2; **6**-H_1^+, 136827-95-7; **7**, 78751-88-9; **7**-H_6^+, 136827-96-8; **8**, 78751-92-5; **8**-H_1^+, 136827-97-9; **8**-H_3^+, 136827-98-0; FSO_3H, 7789-21-1; SO_2ClF, 13637-84-8; Magic acid, 23854-38-8.

Supplementary Material Available: Selected NMR spectra of pyrenium ions of protonation and sulfinylation and tables of ^1H $\Delta\delta$'s (27 pages). Ordering information is given on any current masthead page.

(43) The most deshielded CH(sp^3) reported so far for an arenium ion of protonation (9-methyl-1,8-dichloroanthracenium ion) is at 5.69 ppm (see ref 20).

Selective Ortho Lithiation of (2,5-Dimethoxyphenyl)diphenylphosphine Oxide and Trapping of the Resulting Aryllithium with Electrophiles

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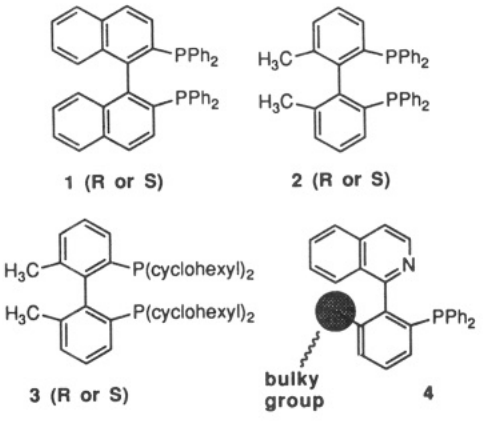
Received April 2, 1991

The title compound undergoes predominant 6-lithiation, ortho to the methoxy and phosphinoyl groups, on reaction with t-BuLi in THF under conditions of thermodynamic control at low temperature. The organolithium compound is stable at least to 0 °C and can be trapped by a range of electrophiles to give the corresponding tetrasubstituted (diphenylphosphinoyl)arenes in moderate to good yield. The iodide formed by this sequence undergoes Ullman coupling to the diphenyl, which exhibits a novel restricted rotation phenomenon, in good yield under mild conditions. (2,5-Dimethoxyphenyl)diphenylphosphine sulfide lithiates exclusively at the 4-position under the same conditions, whilst the corresponding phosphine is unreactive.

Introduction

Much recent catalytic asymmetric synthesis has utilized atropisomeric diphosphine ligands, among which BINAP **1** is preeminent.[1] Others of interest in this context include ligands **2**[2] and **3**,[3] and a number of related compounds have been reported recently.[4] Diphosphines are the ligands of choice for asymmetric hydrogenation with rhodium or ruthenium catalysts and also likely to be so for catalytic asymmetric hydroboration, olefin isomerization, and allylic alkylation. In many other applications in asymmetric

Chart I. Atropisomeric Ligands



(1) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. Noyori, R. *Chem. Soc. Rev.* **1989**, *18*, 187. Cf. Sawamura, M.; Yamauchi, A.; Takegawa, T.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 874.

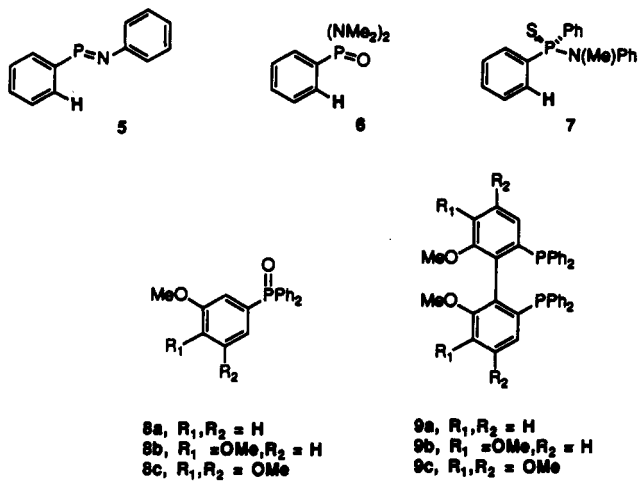
(2) Schmid, R.; Cereghetti, M.; Heiser, B.; Schonholzer, P.; Hansen, H.-J. *Helv. Chim. Acta* **1988**, *71*, 897. Frejd, T.; Klingstedt, T. *Acta. Chem. Scand.* **1989**, *43*, 670.

(3) Miyashita, A.; Karino, H.; Shimamura, J.; Chiba, T.; Nagano, K.; Nohira, H.; Takaya, H. *Chem. Lett.* **1989**, 1849.

(4) Takaya, H.; Ohta, T.; Mashima, K. *Homogeneous Catalysis*; Seventh International Symposium, Lyon, France, Sept 1990; Abstract I12, p 51.

0022-3263/91/1956-6803$02.50/0

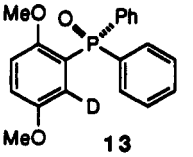
Chart II. Precedents for Directed Metalation of Phosphine Oxides

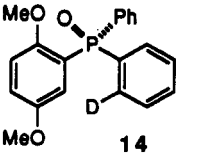


catalysis it is advantageous to bring one or more ligating nitrogens into the coordination sphere. Cross-coupling is a particular case in point, and here the best enantiomer excesses are obtained with Pd or Ni complexes of P–N ligands based on an amino acid derived[5] or 1,2-disubstituted ferrocene chelate backbone.[6] In earlier work we had studied the solution structure of intermediates in asymmetric cross-coupling.[7] The species generated in these experiments are much more labile than are similar intermediates in a related sequence involving a diphosphine–palladium complex.[8] For this reason an alternative P–N chelate ligand was sought which might provide more tractable intermediates, and an atropisomerically chiral compound of type 4 is an attractive target, since the isoquinolyl nitrogen should provide a softer coordination site and hence more stable palladium complexes in the catalytic cycle of cross-coupling. Ligands of this type have not previously been investigated in catalytic asymmetric synthesis.

Reaction of a carbon nucleophile α- to a triarylphosphine or some simple derivative with the appropriate 1-substituted isoquinoline would in principle provide a route for formation of the critical C–C bond linking the aromatic and heterocyclic entities. Very few anionic species of this kind are known. The obvious route to the anion is directed ortho lithiation[9] of the appropriate triarylphosphine oxide. This may be achieved for the parent compound Ph_3PO, but only when PhLi is used as the base[10] because there is a tendency for competing nucleophilic attack at phosphorus with exchange of a phenyl residue for the base fragment R, avoided in the cited case by their degeneracy. Attempted ortho lithiation of 2-(diphenylphosphinoyl)-naphthalene by t-BuLi leads to addition rather than deprotonation.[11] The related phenyliminophosphorane 5 can be lithiated specifically at an *ortho*-site[12] but this reaction has been demonstrated only for the parent PPh_3-derived compound. Other P(V)-directed lithiations are rare, but substrates include phosphonic diamide 6[13] and thiophosphoryl amide 7[14] which give moderately successful results. The introduction of a second directing group at the *meta*-position of the arene ring ought to facilitate the deprotonation *ortho* to a phosphine oxide; many precedents exist for the augmentation of a directing effect in metallation by this means.[9] In an approach which parallels our own, Schmid and co-workers[15] have synthesized the effective asymmetric ligands 9a–c, employing the methoxyl-augmented directed metalation of 8a–c (Chart II) in the key step.

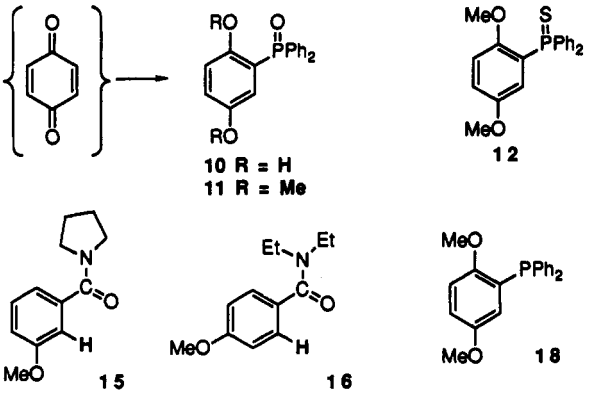
Table I. Lithiation of Compound 11 in THF at −100 °C Followed by Equilibration at −78 °C





reaction time	% D at position-6	% D at Ph-ortho positions
2 min	25	75
30 min	30	70
3 h	80	20
4 h	90	10

Scheme I. Reactants for Lithiation



Results and Discussion

Lithiation Experiments. The starting point for our work was the easy preparation of 2-(diphenylphosphinoyl)quinhydrol 10[16] by Michael addition of $Ph_2P(H)O$ to benzoquinone. The product can be methylated to form dimethyl ether 11 (75% overall). The corresponding phosphine sulfide 12 can be prepared similarly in 75% yield. Initial experiments involved the attempted lithiation with t-BuLi of compound 11 in THF with D_2O quench and assay by NMR. It was found that addition of the organolithium reagent was best carried out at −100 °C, since there was significant darkening at higher temperatures (>−78 °C), empirically associated with inefficient metalation experiments; at the lower temperature the solution was initially a dark yellow-brown eventually fading to a pale yellow, with a white precipitate. The reaction mixture was warmed to −78 °C and maintained there for a defined length of time before adding an excess of D_2O. The reaction was worked up and the NMR spectrum taken at 500 MHz for comparison with the

(5) Hayashi, T.; Konishi, M.; Fukushima, M.; Kanehira, A.; Hioki, T.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2195.
(6) Hayashi, T.; Yamamoto, A.; Hojo, M.; Ito, Y. J. *Chem. Soc., Chem. Commun.* **1989**, 495.
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(8) Brown, J. M.; Cooley, N. A. *Organometallics* **1990**, *9*, 353.
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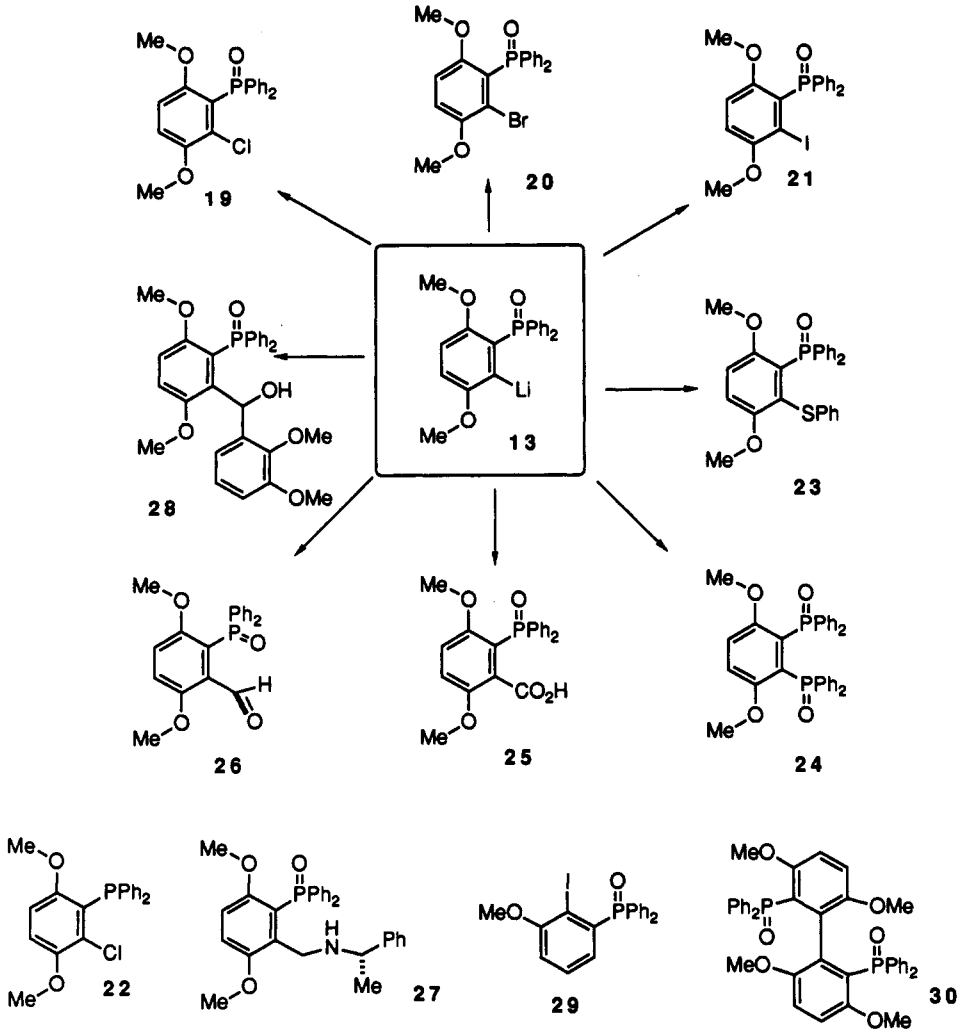
(16) Magdeev, I. M.; Levin, Yu. A.; Ivanov, B. E. *Zh. Obshch. Khim.* **1972**, *42*, 2415. Osipova, M. P.; Stepanova, A. G.; Znakomova, V. L. *Fosfororg. Soedin. Prolim.* **1978**, *4*, 21; *Chem. Abstr.* **1980**, *92*, 76608.

Scheme II. Trapping of the Lithiated Species 13 with Electrophiles



starting material. As indicated in Table I, the composition of the product is a function of time. Each of the reaction products contains a single deuterium, but in the early stages it is statistically distributed between the five sites ortho to the phosphine oxide, giving a mixture of 13 and 14 in which the latter predominates. As time progresses, the thermodynamically preferred 6-lithio compound 13 accumulates and after several hours this is essentially the sole species present. The additional stabilization of a C–Li bond provided by an *o*-OMe group[17] thus drives the equilibrium, but does not exert kinetic control (Scheme I). There are parallels for dual substituent involvement in the metalation of tertiary benzamides. For the 3-OMe-substituted compound 15, lithiation by s-BuLi occurs only at the 2-position,[18] whereas lithiation occurs with complete regiospecificity ortho to the amide rather than adjacent to the OMe group[19] for the 4-OMe-substituted compound 16.

The related phosphine sulfide 12 is metalated rather more slowly under these conditions and gives recovered starting material with 82% deuterium incorporation at C4 after D_2O quench. This implies that the metalation is controlled by an *o*-OMe group and P=S participation is lacking. Deprotonation at C4 can occur through the conformation 17 shown in Chart III; the alternatives involve either a hindered site (C6) or unfavorable steric repulsions in the conformer where the OMe lone pair is syn to C–H (C3).

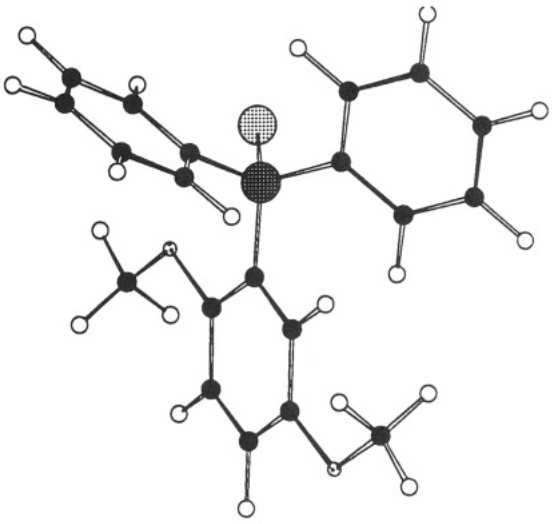
Finally, metalation of the parent phosphine 18, prepared by $HSiCl_3$ reduction of the oxide 11, was attempted. Lithiation was carried out under the previously described conditions and the reaction mixture quenched with D_2O. No deuterium incorporation was apparent. Even when the lithiation reaction mixture was ultimately allowed to warm to 25 °C, it proved impossible to detect deuterium in the product.

Trapping of the Lithiation Product from 11. The conditions described above permit the small-scale preparation of the organolithium reagent 13 and its chemistry was systematically investigated, as shown in Scheme II. In all cases it was possible to isolate the product with the reactive electrophile bonded to the C6 site flanked by $Ph_2P{=}O$ and OMe groups. This regiochemistry was ascertained readily from the NMR of the product in the aromatic region, since the C3- and C4-protons in the substituted ring are high field of the remainder and readily distinguished through the ^4J P–H coupling to H3 of around 6 Hz. In addition the starting material possesses a readily observable ^4J coupling of 3 Hz between H6 and H4, which is absent in any product where a substituent has been introduced at C6 (making this C2 for a heavy-atom substitution).

All three 2-halo derivatives 19–21 were readily prepared in around 60% yield employing *N*-chloro- or *N*-bromo-

(17) Fraser, R. R.; Bresse, M.; Mansour, T. S. *J. Chem. Soc., Chem. Commun.* **1983**, 620.
(18) Snieckus, V. *Bull. Soc. Chim. Fr.* **1988**(2), 67.
(19) Mills, R. J.; Snieckus, V. *J. Org. Chem.* **1989**, *54*, 4386.

Chart III. Conformation 17 Leading to 4-Lithiation of the Substituted Ring. Torsion Angles Are Taken from MM2 Calculations on the Corresponding P-Oxide

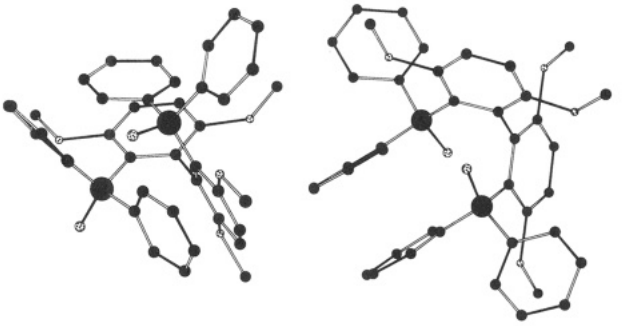


succinimide and I_2, respectively. The first compound **19** could be reduced by $HSiCl_3$ to the corresponding phosphine **22** (46%) but in the other cases reduction of the carbon–halogen bond occurred competitively. Incorporation of a C–S or C–P bond was carried out conventionally with PhS–SPh, giving **23** (38%), and $Ph_2P(O)Cl$, giving **24** (36%), respectively. Carbonation of the anion led to the corresponding benzoic acid **25** in 45% yield. Attempts to formylate the anionic species **13** with tertiary formamides gave disappointingly low yields of product, but direct reaction with $Fe(CO)_5$ as the acylating agent was more successful, and the aldehyde **26** was formed in 42% yield. The formyl proton resonates at 10.68 ppm, implying a conformation in which it is strongly deshielded by the adjacent phosphine oxide, perhaps through alignment of the positive dipole of the C=O group and the negative dipole of the P=O group. Reductive amination of the aldehyde with (*S*)-phenylethylamine gave the expected phosphinamine **27** as a white crystalline solid (45%). The highest yielding experiment in this series involved trapping the organolithium compound **13** with 2,3-dimethoxybenzaldehyde, giving 90% of the substituted benzhydrol **28**. The availability of this series of compounds permits the synthesis of a range of chiral cis-chelating P–N ligands, and further experiments are in progress.

Ullman Condensation of the Iodide 21. As has been noted for the iodide **29** and related compounds, Ullman reaction of **21** in the presence of copper powder occurs very readily, and a high yield (85%) of the high-melting and rather insoluble biphenyl **30** was formed after 8 h of reflux at 155 °C in DMF. Preliminary attempts to form the corresponding diphosphine by $HSiCl_3$ reduction have given <20% yield of the desired product.

The NMR spectra of the bisphosphine oxide **30** reveal an interesting conformational isomerism. Whilst the ^1H NMR spectrum at 500 MHz of a fresh solution revealed only one set of resonances, the corresponding ^{13}C NMR spectrum was more complicated and indicated the presence of two constitutionally similar species in ca. 2:1 ratio. This is most evident in the OMe region where there are four resonances— the major pair at 53.9 and 56.2 ppm and the minor pair at 51.6 and 58.4 ppm. Similar splitting of all the resonances of the tetrasubstituted ring was observed, and the phenyl region was more complex than would be expected (≫12 resonances). The ^{31}P NMR spectrum exhibits only a single line at −26.2 ppm ($CDCl_3$), and the ^1H NMR spectrum at 500 MHz of material recovered from the ^{13}C spectral analysis suggests a single pure species, although cooling the sample to −70 °C causes one of the –OMe resonances to shift and broaden more than the other. Taken together, these observations suggest a slow equilibrium on the NMR time scale between species which have dissimilar ^{13}C NMR spectra, for the biphenyl moiety at least, but very similar ^1H NMR spectra. A tentative explanation, supported by examination of molecular models, is that C_2-symmetrical diastereomeric rotamers about the Ph_2P–aryl bond are separated by a moderate energy barrier.[20] We speculate that the observed equilibrium takes place between conformers **30a** and **30b** (Chart IV) but supportive evidence is required before this can be advanced with any confidence.

Chart IV. Conformational Isomerism through Restricted Rotation about the Substituted P-Aryl group. The Structures Show Conformations with O–P- -C–C(OMe) Torsion Angles of 60° and 180°, Respectively



Experimental Section

Reactions were carried out under argon, where appropriate, using solvents dried and distilled under anaerobic conditions immediately before use.

The compounds diphenylphosphine oxide[21] and 2-diphenylthiophosphinoylhydroquinone[22] were prepared by literature procedures.

Proton NMR spectra were recorded at 500 MHz on a Bruker AM-500. ^{31}P, ^{13}C, and ^2H NMR spectra were recorded on a Bruker AM-250 operating at 101.3, 62.9, and 38.4 MHz respectively. Infrared spectra were recorded on a Perkin-Elmer 1750 Fourier-transform instrument. Mass spectra were obtianed on Varian CH7, ZAB 1F, and VG Micromass instruments using chemical ionization with NH_3.

(2,5-Dihydroxyphenyl)diphenylphosphine Oxide (10). A solution of $Ph_2P(O)H$ (22.70 g, 0.11 mol) in toluene (250 cm^3) was added to a solution of *p*-benzoquinone (**TOXIC**!) (12.15 g, 0.11 mol) in toluene (250 cm^3) over a 10-min period. After being stirred (10 min), the mixture became warm and an oil precipitated. Upon further stirring (1.5 h) the oil solidified and copious quantities of a white solid precipitated which was collected by filtration, washed with toluene (3 × 100 cm^3) and light petroleum (3 × 100 cm^3), and dried under vacuum to yield (34.10 g, 100%) of **10** as a white solid: mp 214–215 °C ($MeOH–Et_2O$); IR (KBr) ν 3234 br (OH), 1134 s (P=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.05 (1 H, s, OH), 6.43 (1 H, dd, $J_{3,5}$ = 3.0 Hz, J_{PH} = 13.9 Hz, 3-H), 6.85 (1 H dd, $J_{5,6}$ = 8.9 Hz, J_{PH} = 5.3 Hz, 6-H), 6.91 (1 H, ddd, $J_{5,6}$ = 8.9 Hz, $J_{3,5}$ = 3.0 Hz, J_{PH} = 0.6 Hz, 5-H), 7.44–7.50 (4, H, m, Ph-*m*), 7.55–7.60 (2 H, m, Ph-*p*), 7.63–7.69 (4 H, m, Ph-*o*), 10.51 (1 H, s, OH); ^{13}C NMR (62.9 MHz, MeOH, external D_2O lock)

(20) For an example of conformational locking in crowded polysubstituted arenes see: Nicolau, K. C.; Ebata, T.; Stylianides, N. A.; Groneberg, R. D.; Carrol, P. J. Angew, *Chem. Int. Ed. Engl.* **1988**, *27*, 1097.

(21) Hunt, B. B.; Saunders, B. C. *J. Chem. Soc.* **1957**, 2413.

(22) Goda, K.; Gomi, H.; Yoshifuji, M.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2453.

δ 116.4 (d, J_{PC} = 106 Hz, 1-C), 118.7 (d, J_{PC} = 9 Hz, 3-C), 119.8 (d, J_{PC} = 8 Hz, 6-C), 123.1 (5-C), 129.4 (d, J_{PC} = 13 Hz, Ph-*o*), 132.8 (d, J_{PC} = 10 Hz, Ph-*m*), 133.1 (d, J_{PC} = 108 Hz, Ph-*i*), 133.2 (Ph-*p*), 151.3 (d, J_{PC} = 15 Hz, 1-C), 157.7 (4-C); δ_P (101.3 MHz, MeOH, external D_2O lock) 30.1 (P=O); MS 311 $(M + 1)^+$. Anal. Calcd for $C_{18}H_{15}O_3P$: C, 69.7; H, 4.9. Found: C, 69.7; H, 4.9.

(2,5-Dimethoxyphenyl)diphenylphosphine Oxide (11). Finely ground KOH (12.32 g, 0.22 mol) was added to a solution of **10** (34.10 g, 0.11 mol) in DMF (500 cm³) causing the solution to become bright yellow. Methyl iodide (14.0 cm³, 31.92 g, 0.22 mol) was added promptly and the reaction stirred (2 h) during which time it became pale yellow and the KOH dissolved. The mixture was poured onto ice and then extracted with CH_2Cl_2 (3 × 250 cm³). The organic layer was washed with dilute HCl (4 × 250 cm³) and water (2 × 250 cm³) and dried (Na_2SO_4). The solvent was removed to give a pink oil which crystallized upon addition of CH_2Cl_2–Et_2O and cooling to yield pure **11** (27.75 g, 75%) as a white powder (three crops, CH_2Cl_2–Et_2O): mp 142–143 °C; IR (KBr) δ 1226 s (C=C), 1183 s (P=O) cm⁻¹; ^1H NMR (500 MHz, C_6D_6) δ 2.87 (3 H, s, OMe), 3.34 (3 H, s, OMe), 6.32 (1 H, dd, $J_{3,4}$ = 8.9 Hz, J_{PH} = 6.0 Hz, 3-H), 6.90 (1 H, dd, $J_{3,4}$ = 8.9 Hz, $J_{4,6}$ = 3.2 Hz, 4-H), 7.02–7.11 (6 H, m, Ph-*m* + *p*), 7.89–7.97 (4 H, m, Ph-*o*), 8.10 (1 H, dd, $J_{4,6}$ = 3.2 Hz, J_{PH} = 13.9 Hz, 6-H); δ_C (62.9 MHz, $CDCl_3$) 55.7 (OMe), 55.8 (OMe), 113.1 (d, J_{PC} = 8 Hz, 3-C), 118.9 (d, J_{PC} = 7 Hz, 6-C), 120.2 (4-C), 121.3 (d, J_{PC} = 103 Hz, 1-C), 128.0 (d, J_{PC} = 13 Hz, Ph-*o*), 131.3 (Ph-*p*), 131.6 (d, J_{PC} = 10 Hz, Ph-*m*), 133.2 (d, J_{PC} = 108 Hz, Ph-*i*), 153.8 (d, J_{PC} = 14 Hz, 2-C), 154.7 (5-C); δ_P (101.3 MHz, $CDCl_3$) 23.9 (P=O); MS 339 $(M + 1)^+$. Anal. Calcd for $C_{20}H_{19}O_3P$: C, 71.0; H, 5.7. Found: C, 70.9; H, 5.8.

(2,5-Dimethoxyphenyl)diphenylphosphine Sulfide (12). In a similar method to the synthesis of **11** reaction of 2-diphenylthiophosphinoylquinhydrol (9.33 g, 28.62 mmol) with KOH (3.21 g, 57.32 mmol) and MeI (3.6 cm³, 8.13 g, 57.25 mmol) in DMF (250 cm³) gave white crystalline **12** (7.60 g, 75%): mp 159–160 °C ex. CH_2Cl_2–hexane; IR (KBr) ν 643 s (P=S) cm⁻¹; ^1H NMR (500 MHz, $CDCl_3$) δ 3.39 (3 H, s, OMe), 3.79 (3 H, s, OMe), 6.85 (1 H, dd, $J_{3,4}$ = 8.9 Hz, J_{PH} = 6.2 Hz, 3-H), 7.06 (1 H, dd, $J_{3,4}$ = 8.9 Hz, $J_{4,6}$ = 3.0 Hz, 4-H), 7.37–7.42 (4 H, m, Ph-*m*), 7.43–7.48 (2 H, m, Ph-*p*), 7.62 (1 H, dd, $J_{4,6}$ = 3.0 Hz, J_{PH} = 17.1 Hz, 6-H), 7.72–7.79 (4 H, m, Ph-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.8 (2-OMe), 113.5 (d, J_{PC} = 7 Hz, 3-C), 120.1 (4-C), 120.2 (d, J_{PC} = 12 Hz, 6-C), 120.6 (d, J_{PC} = 113 Hz, 1-C), 128.0 (d, J_{PC} = 13 Hz, Ph-*o*), 130.9 (Ph-*p*), 131.8 (d, J_{PC} = 11 Hz, Ph-*m*), 133.6 (d, J_{PC} = 89 Hz, Ph-*i*), 153.7 (d, J_{PC} = 15 Hz, 2-C), 154.5 (5-C); δ_P (101.3 MHz, $CDCl_3$) 38.8 (P=O); MS 355 $(M + 1)^+$. Anal. Calcd for $C_{20}H_{19}O_2PS$: C, 67.8; H, 5.4. Found: C, 67.5; H, 5.4.

Lithiation of Compound 11 and D_2O Quench. A solution of Bu^tLi (0.18 cm³, 1.7 M in pentane, 0.31 mmol) was added to the oxide **11** (100 mg, 0.30 mmol) in THF (5 cm³) at −100 °C. The dark yellow solution was allowed to warm to −70 °C (30 min) and then stirred (3.5 h) at this temperature during which time the color lightened and the white lithio species **13** precipitated. When excess D_2O (0.4 cm³, 0.40 g, 22 mmol) was added at −70 °C the solution became homogeneous. The reaction was warmed to room temperature, the solvent removed, and the residue extracted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and evaporated to a colorless oil which crystallized from CH_2Cl_2–Et_2O to yield **[6-$^2H_1$](2,5-dimethoxyphenyl)diphenylphosphine oxide** (98 mg, 98%): MS 340 (M + 1); ^2H NMR (38.4 MHz, C_6H_6) δ 8.03 (1 D, s, 6-D); other spectroscopic properties (excepting deuterium coupling effects) identical with **11**. In a set of related experiments Bu^tLi was reacted with **11** at −70 °C for various times and then quenched with D_2O. One deuteron per mole of **11** was always incorporated; however, the site of deuteration was a function of time (Table I).

Lithiation of 12 and D_2O Quench. In a manner similar to the synthesis of **13** reaction of Bu^tLi (0.16 cm³, 1.7 M in pentane, 0.28 mmol) with the sulfide **12** (100 mg, 0.28 mmol) in THF (5 cm³) afforded the anion. Quenching with D_2O (0.4 cm³, 0.40 g, 22.22 mmol) yielded white crystalline **[4-$^2H_1$](2,5-dimethoxyphenyl)diphenylphosphine sulfide** (82 mg, 82%) from CH_2Cl_2–hexane: MS 356 $(M + 1)^+$; ^2H NMR δ (38.4 MHz, $CHCl_3$) 7.09 (1 D, s, 4-D); other spectroscopic properties akin to **12**. Shorter reaction times resulted in less deuterium incorporation; no deuterium incorporation at any other site was apparent.

Attempted Lithiation of (2,5-Dimethoxyphenyl)diphenylphosphine (18). A small sample of **18** (0.16 g, 0.49 mmol) was prepared by reduction of **11** (0.30 g, 0.89 mmol) with $HSiCl_3$ (1.00 g, 0.75 cm³, 7.29 mmol) and NEt_3 (0.74 g, 1.0 cm³, 7.29 mmol) in toluene for 1 h and characterized by ^1H NMR [(500 MHz, $CDCl_3$) δ 3.61 (3 H, s, OMe), 3.71 (3 H, s, OMe), 6.27 (1 H, m, 3-H), 6.86 (2 H, m, 4-H + 6-H); 7.20–7.41 (10 H, m, Ph)]. Reaction with Bu^tLi under various conditions [(−90 °C, 10 min), (−75 °C, 2 h), or (−70 °C, 4 h then 25 °C, 30 min)] followed by D_2O quench resulted in no deuteron incorporation. Due to these negative results further reactions were not pursued and **18** was not further characterized.

(2-Chloro-3,6-dimethoxyphenyl)diphenylphosphine Oxide (19). Solid *N*-chlorosuccinimide (40 mg, 0.30 mmol) was added against a counter flow of argon to the anion **13** (0.30 mmol) in THF (5 cm³) at −70 °C. The mixture was allowed to come to 0 °C and was quenched with water. The solvent was removed and the residue extracted with CH_2Cl_2, washed with water, and dried (Na_2SO_4). The CH_2Cl_2 was evaporated to give an oil which crystallized from CH_2Cl_2–Et_2O to give white **19** (66 mg, 60%): mp 196–197 °C (CH_2Cl_2–Et_2O); IR (KBr) δ 1268 s (C=C), 1183 s (P=O) cm⁻¹; ^1H NMR (500 MHz, $CDCl_3$) δ 3.13 (3 H, s, OMe), 3.85 (3 H, s, OMe), 6.75 (1 H, dd, $J_{4,5}$ = 9.1 Hz, J_{PH} = 5.2 Hz, 5-H), 7.07 (1 H, d, $J_{4,5}$ = 9.1 Hz, 4-H), 7.38–7.43 (4 H, m, Ph-*m*), 7.44–7.49 (2 H, m, Ph-*p*), 7.66–7.77 (4 H, m, Ph-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.9 (OMe), 57.2 (OMe), 111.3 (d, J_{PC} = 7 Hz, 5-C), 117.4 (4-C), 121.2 (d, J_{PC} = 100 Hz, 1-C), 128.0 (d, J_{PC} = 13 Hz, Ph-*o*), 131.0 (m, J_{PC} 10 Hz, Ph-*m* + overlapping Ph-*p*), 135.4 (d, J_{PC} = 110 Hz, Ph-*i*), 150.8 (d, J_{PC} = 10 Hz, 6-C), 156.0 (3-C), 2-C not apparent; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 22.6 (P=O); MS 373 $(M + 1)^+$. Anal. Calcd for $C_{20}H_{18}ClO_3P$: C, 64.4; H, 4.9. Found: C, 64.5; H, 5.2. Reaction of **13** with C_2Cl_6 affords similar yields of **19** but purification is more tedious.

(2-Bromo-3,6-dimethoxyphenyl)diphenylphosphine Oxide (20). Using the method for the synthesis of **19** *N*-bromosuccinimide (160 mg, 0.90 mmol) and the lithio species **13** (0.88 mmol) in THF (10 cm³) gave white crystalline **20** (204 mg, 56%) in two crops of crystals: mp 199–200 °C (CH_2Cl_2–Et_2O); IR (KBr) ν 1266 s (C=C), 1192 s (P=O) cm⁻¹; δ_H (500 MHz, $CDCl_3$) 3.09 (3 H, s, OMe), 3.85 (3 H, s, OMe), 6.80 (1 H, dd, $J_{4,5}$ = 9.0 Hz, J_{PH} = 5.3 Hz, 5-H), 7.05 (1 H, d, $J_{4,5}$ = 9.0 Hz, 4-H); 7.38–7.43 (4 H, m, Ph-*m*), 7.44–7.49 (2 H, m, Ph-*p*), 7.65–7.71 (4 H, m, Ph-*o*); δ_C (62.9 MHz, $CDCl_3$) 55.8 (OMe), 57.3 (OMe), 112.1 (d, J_{PC} = 6 Hz, 5-C), 117.1 (4-C), 118.9 (2-C), 122.7 (d, J_{PC} = 102 Hz, 1-C), 128.0 (d, J_{PC} = 13 Hz, Ph-*O*), 130.9 (Ph-*p*), 131.0 (d, J_{PC} = 11 Hz, Ph-*m*), 135.3 (d, J_{PC} = 110 Hz, Ph-*i*), 151.6 (d, J_{PC} 11 Hz, 6-C), 156.2 (3-C); δ_P (101.3 MHz, $CDCl_3$) 24.3 (P=O). Anal. Calcd for $C_{20}H_{18}BrO_3P$: C, 57.6; H, 4.3. Found: C, 57.4; H, 4.6.

(3,6-Dimethoxy-2-iodophenyl)diphenylphosphine Oxide (21). In a manner similar to the synthesis of **19**, I_2 (115 mg, 0.45 mmol) and a suspension of **13** (0.44 mmol) in THF (5 cm³) afforded two crops of white crystalline **21** (137 mg, 69%): mp 212–213 °C (CH_2Cl_2–Et_2O); IR (KBr) δ 1262 s (C=C), 1194 s (P=O) cm⁻¹; ^1H NMR (500 MHz, $CDCl_3$) δ 3.05 (3 H, s, OMe), 3.84 (3 H, s, OMe), 6.83 (1 H, dd, $J_{4,5}$ = 9.0 Hz, J_{PH} = 5.3 Hz, 5-H), 6.98 (1 H, *d*, $J_{4,5}$ = 9.0 Hz, 4-H); 7.38–7.43 (4 H, m, Ph-*m*), 7.44–7.49 (2 H, m, Ph-*p*), 7.65–7.71 (4 H, m, Ph-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.6 (OMe), 57.6 (OMe), 113.1 (d, J_{PC} = 7 Hz, 5-C), 115.8 (4-C), 125.0 (d, J_{PC} = 103 Hz, 1-C), 128.0 (d, J_{PC} = 13 Hz, Ph-*o*), 131.0 (Ph-*p*), 131.3 (d, J_{PC} = 10 Hz, Ph-*m*), 134.8 (d, J_{PC} = 110 Hz, Ph-*i*), 154.0 (d, J_{PC} = 13 Hz, 6-C), 156.2 (3-C); 2-C not apparent; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 26.0 (P=O); MS 465 $(M + 1)^+$. Anal. Calcd for $C_{20}H_{18}IO_3P$: C, 51.75; H, 3.9. Found: C, 52.0; H, 3.9.

(2-Chloro-3,6-dimethoxyphenyl)diphenylphosphine (22). A solution of $HSiCl_3$ (0.2 cm³, 0.29 g, 2.15 mmol) in toluene (5 cm³) was added to the chloride **19** (100 mg, 0.28 mmol) in toluene (5 cm³) containing NEt_3 (0.3 cm³, 0.22 g, 2.18 mmol). The mixture was stirred at room temperature (2 h) and cooled to 0 °C and excess silane reagent destroyed with 20% NaOH solution (10 cm³). The toluene layer was separated and the aqueous layer washed with CH_2Cl_2 (2 × 20 cm³). The toluene layer was separated and the aqueous layer washed with CH_2Cl_2 (2 × 20 cm³). The organics were combined, dried (Na_2SO_4), and evaporated to a white solid. Purification by preparative TLC (20 × 20 cm, SiO_2, CH_2Cl_2) afforded white **22** (46 mg, 46%) (R_f 0.90): mp 194–195 °C

(CH_2Cl_2–hexane); IR (KBr) 1268 s (C=C) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.20 (3 H, s, OMe), 3.87 (3 H, s, OMe), 6.71 (1 H, d, $J_{4,5}$ = 9.0 Hz, 5-H), 6.97 (1 H, d, $J_{4,5}$ = 9.0 Hz, 4-H), 7.25–7.30 (6 H, m, Ph-*m* + *p*), 7.35–7.40 (4 H, m, Ph-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.7 (OMe), 56.9 (OMe), 110.9 (5-C), 114.9 (4-C), 127.9 (m, Ph-*m* + *p*), 132.6 (d, J_{PC} = 11 Hz, Ph-*o*), 136.5 (d, J_{PC} = 12 Hz, Ph-*i*), 149.9 (6-C), 156.7 (3-C), 1-C and 2-C not apparent; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ −14.8 (P=O); MS 373 $(M + 1)^+$. Anal. Calcd for $C_{20}H_{18}ClO_2P$: C, 67.3; H, 5.1. Found: C, 67.5; H, 5.2. A second band (R_f 0.15) yielded recovered **19** (11 mg, 11%). Related reductions of the bromide **20** and iodide **22** lead only to **11** and small amounts of impure **(2,5-dimethoxyphenyl)diphenylphosphine (18)**: ^1H NMR (500 MHz, $CDCl_3$), δ 3.61 (3 H, s, OMe), 3.71 (3 H, s, OMe), 6.27 (1 H, m, 3-H), 6.86 (2 H, m, 4-H + 6-H); 7.20–7.41 (10 H, m, Ph).

[3,6-Dimethoxy-2-(phenylthio)phenyl]diphenylphosphine Oxide (23). Using the method for the preparation of **19**, reaction of Ph_2S_2 (100 mg, 0.46 mmol) with the species **13** (0.44 mmol) in THF (10 cm^3) led to **23** to a white powder (75 mg, 38%): mp 148–149 °C (CH_2Cl_2–Et_2O); IR (KBr) ν 1268 s (C=C), 1186 s (P=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.13 (3 H, s, OMe), 3.56 (3 H, s, OMe), 6.87 (1 H, dd, $J_{4,5}$ = 9.1 Hz, J_{PH} = 5.6 Hz, 5-H), 6.90 (2 H, m, SPh-*o*); 6.97–7.05 (4 H, m, SPh-*m* + *p* overlapping 4-H) 7.29–7.40 (6 H, m, PPh-*m* + *p*), 7.69–7.70 (4 H, m, PPh-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.9 (OMe), 56.7 (OMe), 114.1 (d, J_{PC} = 8 Hz, 5-C), 117.4 (4-C), 125.2 (SPh-*p*), 127.8–130.8 (Ph), 135.8 (d, J_{PC} = 110 Hz, PPh-*i*), 155.2 (d, J_{PC} = 11 Hz, 6-C), 155.8 (3-C); 1-C and 2-C not apparent; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 22.0 (P=O); MS 447 $(M + 1)^+$. Anal. Calcd for $C_{26}H_{23}O_3PS$: C, 69.9; H, 5.2. Found: C, 69.6; H, 5.0.

1,4-Dimethoxyphenylene-2,3-bis(diphenylphosphine oxide) (24). In a manner similar to the synthesis of **21**, addition of $Ph_2P(O)Cl$ (128 mg, 0.54 mmol) to the anion **13** (0.54 mmol) in THF (10 cm^3) yielded white needles of **24** (104 mg, 36%): mp >250 °C (CH_2Cl_2–Et_2O) IR (KBr) ν 1261 s (C=C), 1189 s (P=O) cm^{-1}; δ_H ^1H NMR (500 MHz, $CDCl_3$) δ 3.06 [6 H, s, 2(OMe)], 5.28 [2 H, dd, $J_{P1,H}$ = 3.3 Hz, $J_{P2,H}$ = 2.6 Hz, 2(5-H)], 7.26–7.30 (8 H, m, Ph-*m*), 7.30–7.37 (4 H, m, Ph-*p*), 7.55–7.61 (8 H, m, Ph-*o*); δ_C ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.7 [2(OMe)], 117.7 [2(5-C)], 127.5 (m, Ph-*o*), 130.3 (Ph-*p*), 131.3 (m, Ph-*m*), 136.3 (d, J_{PC} = 110 Hz, PPh-*i*), 156.2 (m, 1-C), 2-C not detected at signal-to-noise ratio in spectrum; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 26.6 (P=O); MS 447 $(M + 1)^+$. Anal. Calcd for $C_{32}H_{28}O_4P_2$: C, 71.4; H, 5.2. Found: C, 71.1; H, 5.2.

[3,6-Dimethoxy-2-(diphenylphosphinoyl)]benzoic Acid (25). Dry CO_2 gas was bubbled through a suspension of the anion **13** (1.48 mmol) in THF (20 cm^3) as the reaction temperature allowed to warm slowly from −25 to 0 °C (40 min). The reaction was quenched with NH_4Cl solution, and volatiles were removed at reduced pressure. Water and CH_2Cl_2 were added and the pH of the aqueous layer adjusted to 14 with NaOH. The aqueous layer was retained and the CH_2Cl_2 layer washed with water (2 × 50 cm^3). The washings and aqueous layer were combined and the pH readjusted to 5 with HCl. The copious white precipitate was collected by filtration, washed with water and Et_2O, and dried to give white virtually insoluble **25** (293 mg, 52%): mp >250 °C (CH_2Cl_2–Et_2O) IR (KBr) ν 2941 br (OH), 1729 s (C=O), 1253 s (C=C), 1158 m (P=O) cm^{-1}; ^1H NMR (500 MHz, D_2O–NaOD) δ 3.18 (3 H, s, OMe), 3.66 (3 H, s, OMe), 6.85 (1 H, dd, $J_{4,5}$ = 9.1 Hz, J_{PH} = 5.9 Hz, 4-H), 7.20 (1 H, d, $J_{4,5}$ = 9.1 Hz, 5-H), 7.36–7.41 (4 H, m, Ph-*o*), 7.47–7.55 (6 H, m, Ph-*m* + *p*); ^{13}C NMR (62.9 MHz, D_2O–NaOD) δ 55.7 (OMe), 57.2 (OMe), 112.1 (d, J_{PC} = 7 Hz, 4-C), 113.2 (d, J_{PC} = 7 Hz, 4-C), 113.2 (d, J_{PC} = 107 Hz, 2-C), 119.3 (5-C), 128.0 (d, J_{PC} = 13 Hz, Ph-*o*), 131.5 (d, J_{PC} = 11 Hz, Ph-*m*), 131.7 (d, J_{PC} = 110 Hz, Ph-*i*), 132.1 (Ph-*p*), 137.0 (1-C), 149.4 (d, J_{PC} = 11 Hz, 3-C), 156.2 (6-C), 172.2 (CO_2H); ^{31}P NMR (101.3 MHz, D_2O–NaOD) δ 30.3 (P=O); MS 383 $(M + 1)^+$. Anal. Calcd for $C_{21}H_{19}O_5P$: C, 66.0; H, 5.3. Found: C, 65.9; H, 5.1.

[3,6-Dimethoxy-2-(diphenylphosphinoyl)]benzaldehyde (26). Dry $Fe(CO)_5$ **(TOXIC!)** (0.9 cm^3, 1.30 g, 6.63 mmol) was added to the lithio species **13** (2.96 mmol) in THF (60 cm^3) at −50 °C. The mixture was stirred (2 h), keeping the bath temperature between −50 and −30 °C during which time it became a golden yellow solution. Acetic acid (2.0 cm^3, 2.1 g, 34.2 mmol) was added and the mixture allowed to come to ambient temperature (1 h) during which time it became a deep red. All volatiles were removed at reduced pressure and the residue extracted with CH_2Cl_2. The organics were washed with water, causing another color change to grey-green, dried (Na_2SO_4), and passed through a plug of SiO_2 with an ethyl acetate wash. The green solution was evaporated, causing pure **26** to precipitate as an off-white powder (0.46 g, 42%): mp 239–240 °C (CH_2Cl–EtOAc); IR (KBr) ν 1705 s (C=O), 1271 s (C=C), 1179 m (P=O) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 3.32 (3 H, s, OMe), 3.79 (3 H, s, OMe), 6.87 (1 H, dd, $J_{4,5}$ = 9.0 Hz, J_{PH} = 5.7 Hz, 4-H), 7.10 (1 H, d, $J_{4,5}$ = 9.0 Hz, 5-H), 7.40–7.45 (4 H, m, Ph-*m*), 7.48–7.53 (2 H, m, Ph-*p*), 7.67–7.73 (4 H, m, Ph-*o*), 10.68 (1 H, s, CHO); ^{13}C NMR (62.9 MHz, CH_2Cl_2, external D_2O lock) δ 55.5 (OMe), 56.9 (OMe), 114.0 (d, J_{PC} = 7 Hz, 4-C), 118.0 (5-C), 128.1 (d, J_{PC} = 13 Hz, Ph-*o*), 131.5 (d, J_{PC} = 10 Hz, Ph-*m*), 131.7 (Ph-*p*), 133.4 (d, J_{PC} = 107 Hz, Ph-*i*), 136.3 (d, J_{PC} = 13 Hz, 1-C), 151.7 (d, J_{PC} = 13 Hz, 3-C), 153.6 (6-C); 2-C not apparent; ^{31}P NMR (101.3 MHz, CH_2Cl_2, external D_2O lock) δ 27.4 (P=O); MS 367 $(M + 1)^+$. Anal. Calcd for $C_{21}H_{19}O_4P$: C, 68.85; H, 5.2. Found: C, 68.9; H, 5.35.

(*S*)-[3,6-Dimethoxy-2-(diphenylphosphinoyl)benzyl]-phenylethylamine (27). The amine (*S*)-PhCHMeNH$_2$ (0.2 cm^3, 0.19 g, 1.59 mmol) and active 4A molecular sieves (1.0 g) were added to a solution of the aldehyde **26** (0.47 g, 1.34 mmol) in CH_2Cl_2 (50 cm^3). The mixture was stirred (4 h), after which time a ^1H NMR spectrum of a small sample indicated quantitative formation of the expected imine. The mixture was filtered, the CH_2Cl_2 solvent replaced with EtOH, and $NaBH_4$ (0.51 g, 13.42 mmol) added. The mixture was stirred (1 h) and quenched with water (4 cm^3) and the majority of the EtOH removed. The residue was extracted with CH_2Cl_2–water, and the organics were washed with water and dried (Na_2SO_4). The CH_2Cl_2 was removed, and the resulting oil was crystallized from CH_2Cl_2–hexane (twice) to yield **27** as white needles (0.28 g, 45%): mp 170–171 °C (CH_2Cl_2–hexane); $[\alpha]_D^{25}$ +69.9 (*c* = 2.0, $CHCl_3$); IR (KBr) ν 3479 br (NH), 1271 s (C=C), 1181 m (P=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.31 (3 H, d, J_{HH} = 6.6 Hz, CH*Me*), 3.05 (3 H, s, OMe), 3.69 (3 H, s, OMe), 3.69 (1 H, q, J_{HH} = 6.6 Hz, C*H*Me), 3.90 (1 H, d, J_{HH} = 11.5 Hz, CH_2), 4.03 (1 H, d, J_{HH} = 11.5 Hz, CH_2), 6.70 (1 H, dd, $J_{4,5}$ = 9.0 Hz, J_{PH} = 5.9 Hz, 4-H), 7.00 (1 H, d, $J_{4,5}$ = 9.0 Hz, 5-H), 7.17–7.51 (11 H, m, Ph), 7.57–7.63 (2 H, m, Ph-*o*), 7.68–7.74 (2 H, m, Ph-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 24.8 (CH*Me*), 42.8 (CH_2), 55.5 (OMe), 56.9 (OMe), 58.4 (C*H*Me), 111.5 (d, J_{PC} = 7 Hz, 4-C), 116.0 (5-C), 121.3 (d, J_{PC} = 100 Hz, 2-C), 126.4–131.7 (Ph), 134.9 (d, J_{PC} = 108 Hz, PPh-*i*), 136.2 (d, J_{PC} = 108 Hz, PPh-*i*), 138.0 (br, 1-C), 146.5 (CHPh-*i*), 153.4 (d, J_{PC} = 13 Hz, 3-C), 154.4 (6-C); ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 28.2 (P=O); MS 472 $(M + 1)^+$. Anal. Calcd for $C_{29}H_{30}NO_3P$: C, 73.9; H, 6.4; N, 3.0. Found: C, 73.6; H, 6.5; N, 3.2.

[3,6-Dimethoxy-2-(diphenylphosphinoyl)phenyl](2,3-dimethoxyphenyl)methanol (28). Using the method for the synthesis of **19**, addition of 2,3-dimethoxybenzaldehyde (73 mg, 0.44 mmol) to a suspension of the anion **13** (0.44 mmol) in THF (5 cm^3) gave upon crystallization white microneedles of **28** (203 mg, 91%): mp 203–204 °C (CH_2Cl_2–Et_2O); IR (KBr) ν 1264 s (C=C), 1186 s (P=O) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 2.55 (3 H, s, OMe), 3.26 (3 H, s, OMe), 3.26sh (3 H, s, OMe), 3.55 (3 H, s, OMe), 6.27 (1 H, dd, $J_{4,5}$ = 9.0 Hz, J_{PH} = 5.6 Hz, 4-H), 6.36 (1 H, dd, $J_{4',5'}$ = 8.0 Hz, $J_{4',6'}$ = 1.3 Hz, 4-H) 6.66 (1 H, d, $J_{4,5}$ = 9.0 Hz, 5-H); 6.87 (1 H, t, $J_{4',5'}$ = 8.0 Hz, $J_{5',6'}$ = 8.0 Hz, 5′-H), 6.96–7.05 (6 H, m, Ph-*m* + *p*), 7.35 (1 H, d, J_{HH} = 10.7 Hz, C*H*OH), 7.61–7.66 (2 H, m, Ph-*o*), 7.71–7.77 (2 H, m, Ph-*o*), 7.90 (1 H, dd, $J_{5',6'}$ = 8.0 Hz, $J_{4',6'}$ = 1.3 Hz, 6′-H), 8.13 (1 H, d, J_{HH} = 10.7 Hz, CHO*H*, exchanges with D_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 55.0 (OMe), 55.5 (OMe), 57.0 (OMe), 59.8 (OMe), 65.6 (CHOH), 111.0 (4′-C), 111.5 (d, J_{PC} = 7 Hz, 4-C), 117.9 (5-C), 120.3 (d, J_{PC} = 99 Hz, 2-C), 121.1 (CHOH), 122.5 (6′-C), 127.6 (d, J_{PC} = 13 Hz, Ph-*o*), 127.9 (d, J_{PC} = 13 Hz, Ph-*o*), 130.8–131.2 (m, Ph-*m* + *p*), 133.5 (d, J_{PC} = 115 Hz, Ph-*i*), 135.3 (d, J_{PC} = 111 Hz, Ph-*i*), 137.9 (1′-C), 142.3 (d, J_{PC} = 4 Hz, 1-C), 146.1 (2′-C), 151.9 (3′-C), 153.0 (d, J_{PC} = 17 Hz, 3-C), 154.8 (6-C), primed numbers refer to assignments in the 2,3-dimethoxyphenyl group; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 32.8 (P=O); MS 505 $(M + 1)^+$. Anal. Calcd for $C_{29}H_{29}O_6P$: C, 69.0; H, 5.8. Found: C, 69.05; H, 6.0.

2,2′-(Diphenylphosphinoyl)-3,3′,5,5′-tetramethoxybiphenyl (30). Copper powder (0.30 g, 4.72 mmol) was added to a solution of the iodide **21** (100 mg, 0.22 mmol) in DMF (10 cm^3) and the mixture heated to 155 °C (8 h). The mixture was cooled, the pale

pink supernatant liquid decanted off, and CH_2Cl_2 (20 cm^3) added, and the organics were washed repetedly with dilute HCl. The clear CH_2Cl_2 layer was washed with water and dried (Na_2SO_4) and the solvent removed under reduced pressure to give a white solid. Recrystallization from CH_2Cl_2–Et_2O yielded white crystalline **30** (63 mg, 85%): mp >250 °C (CH_2Cl_2–Et_2O); IR (KBr) ν 1255 s (C═C), 1188 s (P═O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.07 (3 H, s, OMe), 3.71 (3 H, s, OMe), 6.79 (1 H, dd, $J_{4,5}$ = 9.0 Hz, J_{PH} = 5.8 Hz, 4-H), 6.91 (1 H, d, $J_{4,5}$ = 9.0 Hz, 5-H), 7.13–7.17 (4 H, m, Ph-*m*), 7.21–7.25 (2 H, m, Ph-*p*), 7.39–7.44 (4 H, m, Ph-*m*), 7.45–7.50 (2 H, m, Ph-*p*), 7.63–7.69 (4 H, m, Ph-*o*), 7.82–7.89 (4 H, m, Ph-*o*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 51.6 (OMe), 53.9 (OMe), 56.2 (OMe), 58.4 (OMe), 110.3 (d, J_{PC} = 7 Hz, 4-C), 112.8 (5-C), 112.9 (d, J_{PC} = 8 Hz, 4-C), 115.3 (5-C), 120.3 (d, J_{PC} = 105 Hz, 2-C), 126.1–135.2 (Ph), 137.6 (d, J_{PC} = 111 Hz, Ph-*i*), 152.1 (br, 3-C), 153.7 (br, 6-C), 1-C not detected, 3:1 mixture of species; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ 26.2 (P═O); MS 675 $(M + 1)^+$. Anal. Calcd for $C_{40}H_{36}O_6P_2$: C, 71.2; H, 5.4. Found: C, 71.0; H, 5.65.

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Registry No. **10**, 13291-46-8; **11**, 72666-56-9; **12**, 136202-00-1; **13**, 136202-01-2; **14**, 136202-02-3; **18**, 85417-48-7; **19**, 136202-03-4; **20**, 136202-04-5; **21**, 136202-05-6; **22**, 136202-06-7; **23**, 136202-07-8; **24**, 136202-08-9; **25**, 136202-09-0; **26**, 136202-10-3; **27**, 136202-11-4; **28**, 136202-12-5; **30**, 136202-13-6; $Ph_2P(O)H$, 4559-70-0; Ph_2S_2, 882-33-7; $Ph_2P(O)Cl$, 1499-21-4; (*S*)-PhCHMeNH$_2$, 2627-86-3; *p*-benzoquinone, 106-51-4; 2-diphenylthiophosphinoylquinhydrol, 54573-03-4; [6-^{2}H](2,5-dimethoxyphenyl)diphenylphosphine, 136201-98-4; [4-^{2}H](2,5-dimethoxyphenyl)diphenylphosphine sulfide, 136201-99-5; 2,3-dimethoxybenzaldehyde, 86-51-1.

Novel Azido-phenylselenenylation of Double Bonds. Evidences for a Free Radical Process

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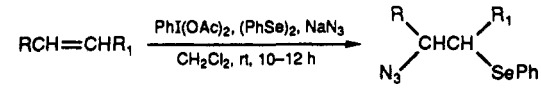
A simple and mild azido-phenylselenenylation of terminal alkenes, which proceeds with complete anti-Markovnikov regioselectivity, has been developed. This reaction occurs when the alkenes are treated with (diacetoxyiodo)benzene, sodium azide, and diphenyl diselenide in dichloromethane at room temperature. The observed regioselectivity can be explained by assuming that the addition process is initiated by azido radicals. This was further supported by the results obtained starting from 1,6-heptadiene and from β-pinene. Under the same conditions, efficient azido-phenylselenenylation of symmetrical olefins, 3,4-dihydro-2*H*-pyran, methyl acrylate, and vinyl crotonate can also be effected.

It is well established that addition to unsymmetrical olefins initiated by electrophilic phenylselenium species proceeds through the formation of seleniranium intermediates which, in the presence of external or internal nucleophiles, usually affords anti adducts with prevalent Markovnikov orientation.[1] We have recently reported the in situ generation of an electrophilic phenylselenenylating agent that reacts with olefins to effect methoxy-, hydroxy-, and amidoselenenylation or selenium-induced ring closure reactions.[2] This strong phenylselenenylating agent is produced when diphenyl diselenide is allowed to react with ammonium peroxydisulfate in different solvents. In some cases, by using an excess of ammonium peroxydisulfate and catalytic amounts of diphenyl diselenide in methanol, the unsaturated compounds undergo alkoxyselenenylation followed by alkoxydeselenenylation reactions.[3]

Scheme I



In all the examples we have described, the trapping of the selenium-containing intermediates and the replacement of the phenylselenium group were always effected by oxygen-centered nucleophiles. An experiment was carried out, using styrene as substrate, and effecting the oxidation of diphenyl diselenide with ammonium peroxydisulfate in the presence of sodium azide in an attempt to extend the use of this methodology to nitrogen nucleophiles. A complex reaction mixture was obtained in this case and the expected product of azido-phenylselenenylation could be obtained in very poor yield. In a parallel investigation we have recently observed that electrophilic phenylselenium species can be produced from diphenyl diselenide, under much milder conditions, by using hypervalent iodine reagents.[4] Application of this procedure to the azido-phenylselenenylation of styrene, using sodium azide, in dichloromethane, gave the expected product in excellent yield. However, careful examination of the spectral data of this compound demonstrated that the addition took place with an unexpected regioselectivity, the azido group being bonded to the terminal carbon atom.

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