Inter- and Intramolecular Arylation of the Double Bond in Phospholene Derivatives under Friedel-Crafts Conditions[1]

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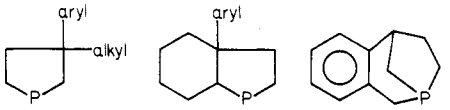
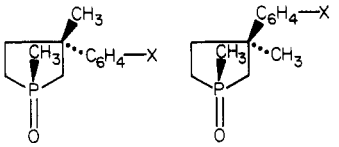
Reaction between benzene or chlorobenzene with the double bond of certain phospholene derivatives occurs in the presence of aluminum chloride at room temperature to yield β-arylated phospholanes. Phospholene derivatives employed in such reactions have included 1,3-dimethyl-3-phospholene oxide, 1-hydroxy-3-phospholene oxide, 1-methylhexahydro-Δ^3-phosphindole oxide and its $\Delta^{3a,7a}$ isomer, 1-methyl-6-methoxyhexahydro-$\Delta^{3a,7a}$-phosphindole oxide, and 1-methylhexahydro-$\Delta^{3a,7a}$-phosphindole. The bicyclic 3a-aryl derivatives were easily nitrated at the para position; the *p*-amino and *p*-methoxy derivatives were also prepared. The benzene ring of 1-benzyl-3,4-dimethyl-3-phospholene oxide participates in intramolecular arylation in the presence of aluminum chloride to form the previously unknown 1-phosphabicyclo[3.2.1]oct-3-ene system. Products were characterized by ^1H, ^{13}C, and ^{31}P NMR spectroscopy.

We have discovered a new property of phospholene derivatives that allows the preparation of structural types unavailable at this time by other approaches: the double bond may be arylated under Friedel–Crafts conditions with remarkable ease. In exploring this new reaction, we have opened access to phospholanes with substitution patterns A and B and to the bridged system C, the latter by intramolecular arylation from a *P*-benzyl substituent. Systems with bridgehead phosphorus, while not unknown,[2,3] are quite rare but of considerable interest for examination of the influence of rigid molecular structure on reactivity of the heteroatom.



A B C

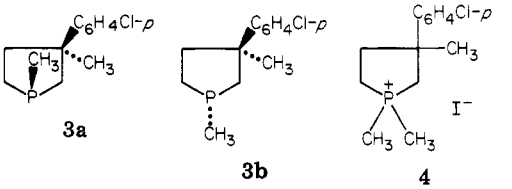
Intermolecular Arylation. The nature of the arylation reaction and its products is well exemplified by results with the 1,3-dimethyl-3-phospholene oxide system. When a sample in benzene was treated with 2 equiv of commercial anhydrous aluminum chloride, an exothermic reaction occurred that was controlled at 25 °C. After 2 h the mixture was quenched with water, and chloroform extraction gave a distillable product (75%) that crystallized on standing. No unreacted starting material was recovered. The presence of cis,trans isomers in the analytically pure reaction product was obvious from the two signals (2:1) in the ^{31}P NMR spectrum and the two PCH_3 and two CCH_3 doublets in the ^1H NMR spectrum. That the minor isomer had the trans orientation of the methyls was evident from the relatively upfield position ($\Delta\delta$ 0.27 ppm) of its ^1H NMR signal for the PCH_3 group, a consequence of positioning in the shielding area of the benzene ring. At the same time, the deshielding effect of phosphoryl causes the C–CH_3 group to fall 0.12 ppm below that of the cis isomer. Both effects are documented in the literature.[4,5] The ^{13}C and ^{31}P NMR chemical shifts were generally similar because of the absence of significant steric compression differences in the isomers and were not useful for structure assignment.



1a, X = H **1b**, X = H
2a, X = *p*-Cl **2b**, X = *p*-Cl

In a similar fashion (75% yield) the *p*-chlorophenyl derivatives **2a** and **2b** were prepared; again the minor isomer in the 2:1 mixture was recognized as **2b** from the anisotropic ^1H NMR effects. The product had no detectable amount of *o*- or *m*-chlorophenyl isomers. A number of attempts to employ the aromatic ethers anisole, phenetole, and veratrole as the arylating agent were unsuccessful due to complications from Lewis salt formation (precipitation or ring deactivation) or from cleavage of the CH_3O group by the aluminum chloride. This prompted a consideration of the use of other Friedel–Crafts catalysts for the arylations, but no reaction occurred with the milder Lewis acids BF_3 and $SnCl_4$ or with anhydrous HCl or polyphosphoric acid. Variations in the conditions employing $AlCl_3$ as catalyst were also made. Best results were obtained with 2 equiv relative to the phosphine oxide, and the preferred solvent was the arylating organic compound in excess. Other common Friedel–Crafts solvents such as nitro compounds failed to give the desired reaction. These solvents probably compete successfully with the phosphoryl group for complexation by $AlCl_3$.

The phospholane oxide mixture **2a,b** was reduced in 67% yield by trichlorosilane in benzene, forming the isomeric phosphines **3a** and **3b**. These gave the same methiodide **4**. Again the steric differences of P–CH_3 are not great in the isomers **3a** and **3b**, causing the ^{13}C and ^{31}P signals to differ insignificantly. However, the usual ^1H phenyl shielding effect on methyl was present (**3b** upfield by 0.18 ppm). The C–CH_3 group also shows an influence to be present, since the shift of isomer **3a** is upfield by 0.34 ppm. A shielding effect has been attributed to proximity to the lone pair electrons in nitrogen heterocycles;[6] it may be operative here, since no other obvious



3a 3b 4

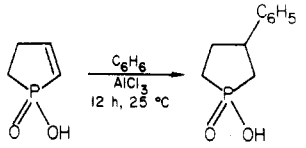
(1) Taken from the Ph.D. Dissertation of J. E. MacDiarmid, Duke University, 1980.
(2) Wetzel, R. B.; Kenyon, G. L. *J. Am. Chem. Soc.* **1974**, *96*, 5189.
(3) Krech, F.; Issleib, K. *Z. Anorg. Allg. Chem.* **1976**, *425*, 209.
(4) Segall, Y.; Alkabets, R.; Granoth, I. *J. Chem. Res. (S)* **1977**, 310; *J. Chem. Res. (M)* **1977**, 3541.
(5) Fitzgerald, A.; Smith, G. D.; Caughlan, C. N.; Marsi, K. L.; Burns, F. B. *J. Org. Chem.* **1976**, *41*, 1155.

0022-3263/81/1946-1451$01.25/0

structural difference could account for the observed shielding.

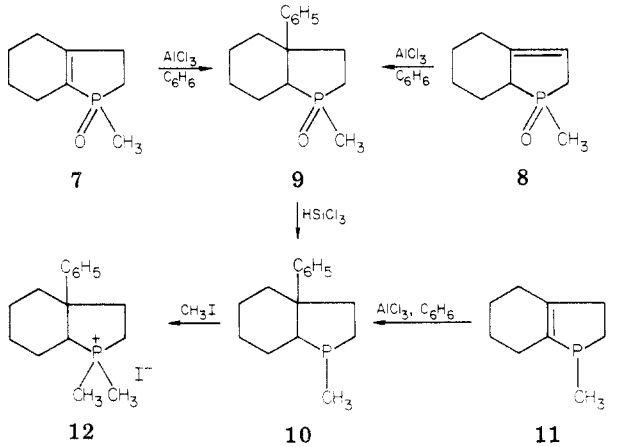
In this series of compounds, the carbon of the C–CH_3 group is coupled through three bonds to ^{31}P; recent studies[7] of the dihedral angle (ϕ) control of this coupling have revealed that the structure around the P atom has a major influence on the curves defining this relation. Thus, for phosphine oxides where the $(CH_3)_2PO$ group is attached to rigid ring systems, minima in $^3J_{PC}$ occur near 90° (~0 Hz), whereas $^3J_{PC}$ in the related phosphines pass through 0 to a minimum at −5 Hz in the region 110–115°. The ϕ values relating CH_3 to P for oxides **1** and **2** and phosphine **3**, in an envelope conformation, would deviate from the 120° for a planar ring by as much as ±20°. If the published curves[7] are examined over the ϕ region 100–140°, it would be predicted that the oxide would have ^3J of 2 to 8 Hz, while that of the phosphine would have 0 to |5| Hz. The observed values fall neatly in these ranges, e.g., oxides **1a** and **1b**, 4.9 Hz, phosphines **3a** and **3b** 2.4 and 3.1 Hz. Other cases need to be considered where the P atom is incorporated in a cyclic structure before it can be concluded that the curves for the noncyclic derivatives are generally useful, but the present work is suggestive of this generality.

The arylation reaction is not limited to phospholene oxides; phosphinic acid **5** also underwent the reaction with benzene, making **6** available in a synthetically useful process.



5 6

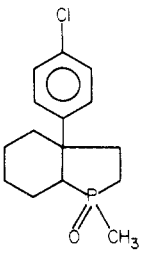
Bicyclic phospholene oxides, readily obtained by the McCormack cycloaddition of 1-vinylcycloalkenes,[8] respond equally well to the arylation. In this system, both of the double bond isomers **7** and **8** were employed successfully,



7 9 8

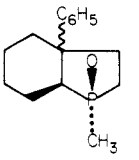
12 10 11

giving the same arylated product **9** as a mixture of isomers (yields 76.4 and 46.7%, respectively). Even the phosphine **11** was found to undergo the arylation in the same facile manner (with the product isolated in 50% yield after oxidation). Chlorobenzene also is useful in this process, although the yield of **13** was only 36%. Once again anisole and veratrole failed to give the arylation product because of complexities mentioned earlier.



13

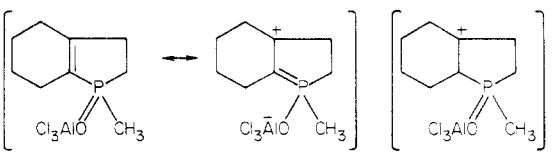
From these arylations, four diastereoisomeric products are possible since three chiral centers are present. The reactions show no pronounced selectivity, and significant amounts of all four isomers of **9** and **13** are formed. In one instance, a fortuitous crystallization of a single isomer of **9** occurred when the mixture, an oil, was allowed to stand. Its steric structure has not been fully assigned, although the relatively downfield position (δ 17.4) of its ^{13}C NMR signal for P–CH_3 indicates a trans (unhindered) relation to ring carbon 7, as in **14**. The isomer mixtures were easily



14

analyzed by ^{31}P NMR, since all members had distinctive values, spread over an 11-ppm range. The phosphine derived from deoxygenation of **9** also consisted of four isomers, but loss of chirality at P in the methiodide **12** caused simplification of that mixture to two isomeric forms.

The mechanism of the arylation has not been studied. The well-known[9,10] presence of HCl and H_2O in "anhydrous" aluminum chloride could suggest a process wherein protonation of the double bond of the $AlCl_3$–phosphine oxide complex provides a reactive electrophilic species to initiate the process. However, it is not necessary for a protonated species to play a role, and direct attack of the $AlCl_3$–oxide complex on the aromatic system could also occur. This mechanism seems more plausible for reactions of 2-phospholene oxides (involving an electrophilic species such as **15a**) than 3-phospholene oxides, where no obvious assistance is provided by oxide complexation. A preliminary double-bond rearrangement (e.g., of **8** to **7**) is a possible event, but no experiments have yet been performed to determine if $AlCl_3$ can effect this rearrangement. That the same ratio of isomers of **9** was obtained from both **7** and **8** could be explained by either the protonation process (forming common intermediate **15b**) or by the preliminary double-bond rearrangement.

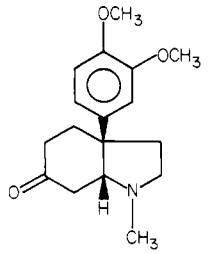


15a 15b

The presence in the arylated bicyclic products of the same skeleton as found in certain alkaloids of the reduced indole type prompted consideration of techniques for increasing the similarity to particular biologically active

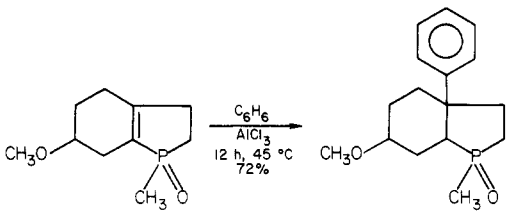
(6) Lambert, J. B.; Keske, R. G. *Tetrahedron Lett.* **1969**, 2023.
(7) Quin, L. D.; Gallagher, M. J.; Cunkle, G. T.; Chesnut, D. B. *J. Am. Chem. Soc.* **1980**, *102*, 3136.
(8) Symmes, C., Jr.; Quin, L. D. *J. Org. Chem.* **1976**, *41*, 238.
(9) Olah, G. A. "Friedel-Crafts and Related Reactions"; Interscience: New York, 1963; Vol. 1, p 205.
(10) Symmes, C., Jr.; Quin, L. D. *J. Org. Chem.* **1978**, *43*, 1250.

alkaloids by introducing functionality at corresponding positions. Mesembrine (16), a member of the group of



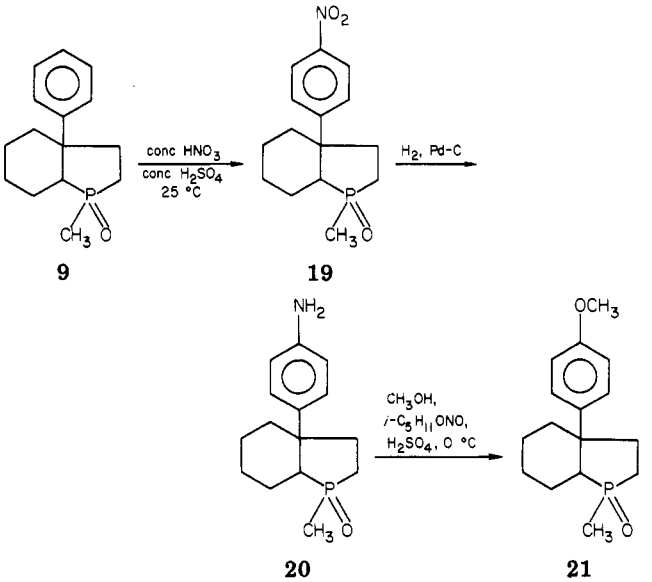
16

Sceletium alkaloids, is an example of such a substance. To approach the *Sceletium* alkaloids, we sought techniques for installing a methoxy group at C-6 of the cyclohexane ring and at the para position of the benzene ring. The first objective was easily accomplished by employing the methoxylated derivative 17[11] of the bicyclic phospholene as the substrate for arylation.



17 18

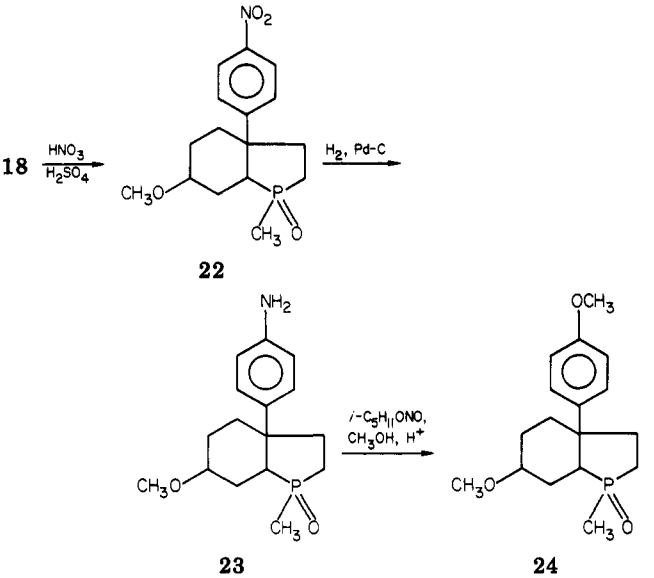
The product (18) was obtained in at least seven of the eight possible diastereoisomeric forms, as judged by the number of ^{31}P NMR signals (δ +60.3 to +73.4). No difficulty was encountered with cleavage of the methoxy group during the reaction. However, the failure of anisole to survive the exposure to $AlCl_3$ prevented accomplishment of the second synthetic objective through the use of this compound as the arylating agent. This problem was circumvented by the longer reaction sequence shown below.



9 19 20 21

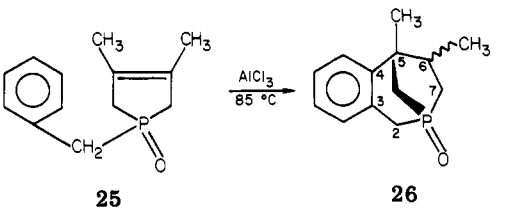
The nitration proceeded smoothly at the para position; NMR analysis did not reveal the presence of isomeric products. The amino derivative was converted to the methoxy in one step by diazotization in a methanol medium. The presence of so many diastereoisomers in each product made crystallization of this series of compounds difficult; however, the amino product was successfully sublimed, and the methoxy distilled by the Kugelrohr technique.

Application of the nitration–reduction–diazotization sequence to the methoxy derivative 18, thus forming a substance (24) with two methoxy functionalities, was complicated by purification problems. NMR spectra of the products suggested success in every step, but thermal instability prevented the use of sublimation or distillation techniques for purification. In this series, all of the eight possible diastereoisomers were present as judged by ^{31}P NMR. Were there sufficient interest in this series to justify the effort, chromatographic techniques should be developed to allow simplification of the complex isomer mixture and crystallization of the product.



18 22 23 24

Intramolecular Arylation. The ease with which arylation of the phospholene double bond occurs suggested that a suitably positioned phenyl group already in the molecule might also participate in the reaction. This proved to be the case for the *P*-benzylphospholene derivative 25; while inert to $AlCl_3$ at room temperature, this compound did undergo internal arylation on being heated at 85 °C for 10 h. The valuable bicyclo derivative 26 was obtained in 30% yield in crystalline form. Mesitylene was



25 26

found to provide a good reaction medium; it dissolves adequate quantities of both the phosphine oxide and $AlCl_3$ and for steric reasons is relatively unreactive itself as an arylating agent. Unlike the intermolecular arylations, this reaction was stereospecific and formed a single isomer.

The spectral properties fully support the indicated isomerization of 25 to the bicyclic structure. Thus, the ^1H NMR spectrum showed that one methyl was attached to a quaternary carbon (δ 1.58, vicinal H–H coupling absent) and the other to a methine carbon (δ 1.16, $^3J_{HH}$ = 7 Hz). The rigidity of the ring structure brought out nonequivalence in the easily recognized benzylic protons (δ 3.45); the geminal ^1H–^1H and ^{31}P–^1H constants were coincident at about 17 Hz, causing some simplification of the ABX spectrum to give the appearance of a quintet. The ^{13}C

(11) Quin, L. D.; MacDiarmid, J. E. *J. Org. Chem.* **1981**, *46*, 461.

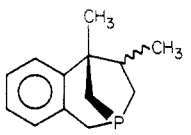
Table I. NMR Spectral Data for 3-Aryl-3-methylphospholane Derivatives[a]

		^{1}H		^{13}C						
compd	^{31}P	PCH_3	CCH_3	PCH_3	C-2	C-3	C-4	C-5	CCH_3	C-7
1a	+66.2[b]	1.70 (13)	1.37	18.7 (62.3)	41.7 (65.9)	45.8 (92)	37.6 (6.1)	27.7 (64.1)	30.4 (4.9)	147.6 (7.3)
1b	+66.5[b]	1.43 (13)	1.49	17.9 (62.9)	41.9 (65.9)	45.8 (9.2)	36.0 (6.7)	27.7 (64.1)	30.4 (4.9)	147.8 (9.2)
2a	+66.5	1.73 (15)	1.37	18.7 (62.9)	41.8 (65.9)	45.7 (7.9)	37.8 (6.7)	27.7 (64.1)	30.5 (5.5)	147.3 (6.7)
2b	+66.5	1.50 (12.5)	1.49	18.0 (64.5)	43.9 (66.5)	45.7 (7.9)	36.2 (6.7)	27.7 (64.1)	30.2 (3.1)	146.9 (10.4)
3a	−32.7	1.17 (3)	1.47	13.9 (18.3)	41.7 (12.8)	49.6 (2.4)	38.8 (4.3)	24.9 (8.6)	29.3 (2.4)	149.1 (3.1)
3b	−35.2	0.99 (2)	1.13	14.5 (18.3)	40.7 (11.0)	50.1 (3.1)	38.8 (4.3)	24.9 (8.6)	30.8 (3.1)	146.8 (s)
4	+48.0	2.10 (15) 2.57 (16)	1.53	12.0 (50.0) 12.3 (49.4)	37.2 (53.1)	48.9 (7.3)	37.3 (3.7)	23.4 (51.3)	30.8 (8.8)	143.3 (5.5)

[a] See ref 15 for details; values in parentheses are coupling constants to ^{31}P, in hertz. [b] May be reversed.

NMR spectrum also showed two different methyl carbons, with only the more downfield (δ 25.6) showing coupling to ^{31}P (16.5 Hz). This signal is attributed to the methyl on the bridgehead carbon; the dihedral angle to ^{31}P is close to 180°, consistent with the large coupling.[7] The lack of coupling to the other methyl at C-6 suggests a much smaller dihedral angle (near 90°), but models show that in an undistorted conformation for the bicyclic structure both exo and endo positions at C-6 have dihedral angles to ^{31}P of 120°. The molecule may have adopted a slightly different conformation to relieve nonbonded interactions and thus achieved a somewhat smaller dihedral angle. Without further information, it is not possible to assign exo or endo location to this methyl. Other spectral features appear in the Experimental Section. The ^{31}P NMR shift (δ + 54.5) was only slightly upfield of values generally found for *P*-alkylphospholane oxides (+60 to +65).

The phosphine (**27**) was readily formed by trichlorosilane reduction of **26** and in turn was converted to the methiodide (**28**). The ^{1}H NMR spectrum of the phosphine



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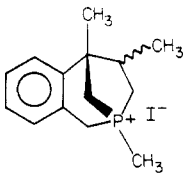

28

had the expected features for the methyl groups (at C-6, δ 0.9, $^3J_{HH}$ = 8 Hz; at C-5, δ 1.54, s). The multiplet for the nonequivalent benzylic protons again showed geminal ^{1}H–^{1}H coupling of about 17–18 Hz in an AB pattern, each line of which was split by vicinal coupling to ^{31}P (6 Hz).

Vicinal ^{13}C–^{31}P coupling constants in phosphines appear to be controlled in rigid systems by the orientation of the lone pair. Thus, in the diphosphatriptycene system,[12] $^3J_{PC}$ can be 1.4 or 13.8 Hz even where both dihedral angles are 180°. The Karplus relation developed[7] from phosphines with rotating $(CH_3)_2P$ groups therefore may not be applicable to a system such as **27**. The rigid geometry in **27** suggests a dihedral angle to the methyl at C-5 of nearly 180°, and the observed coupling of 3.0 Hz does seem small compared to the predicted[7] value of 7 Hz for the $(CH_3)_2P$ series. The ^{31}P NMR value of δ −42.6 again is in a region occupied by certain monocyclic compounds (e.g., stereoisomers of 1,3,4-trimethylphospholane are found at δ −41.6 and −55.4[13]).

The remarkable ease of this new approach to bridgehead-phosphorus compounds makes this system quite readily available for studies of the effect of molecular geometry on chemical and physical properties. So far, attention has only been given to some aspects of the oxides of the 1-phosphabicyclo[2.2.1]heptane and -[2.2.2]octane systems;[2,14] no information is available on the chemistry of phosphines with imposed bridgehead character.

Experimental Section[15]

1,3-Dimethyl-3-phenylphospholane 1-Oxide (1). A slurry of 2.1 g (0.0154 mol) of $AlCl_3$ and 10 mL of benzene was combined with 1,3-dimethylphospholene 1-oxide (1.0 g, 0.0077 mol) and stirred at room temperature for 2 h. Hydrolysis on ice, followed by chloroform extraction and distillation at 140 °C (0.09 mm) gave 1.2 g (75%) of **1** (isomers) as a near colorless oil, which solidified on standing for several days. NMR spectral data are given in Table I.

Anal. Calcd for $C_{12}H_{17}OP$: C, 69.21; H, 8.23; P, 14.88. Found: C, 69.51; H, 8.40; P, 14.63.

3-(*p*-Chlorophenyl)-1,3-dimethylphospholane 1-Oxide (2). A slurry of 12.5 g (0.094 mol) of $AlCl_3$ and 25 mL of chlorobenzene was combined with 5 g (0.038 mol) of 1,3-dimethyl-3-phospholene 1-oxide in 5 mL of chlorobenzene, causing the evolution of heat and HCl, and the formation of a red-brown reaction mixture. After the solution was stirred for 12 h, workup as for **1** gave 7.0 g (75%) of **2** (isomers), distilling at 161–175 °C (0.15 mm) as a pale yellow oil; NMR data are given in Table I.

Anal. Calcd for $C_{12}H_{16}ClOP$: C, 59.39; H, 6.65; Cl, 14.61; P, 12.76. Found: C, 59.11; H, 6.74; Cl, 14.41; P, 12.61.

3-(*p*-Chlorophenyl)-1,3-dimethylphospholane (3). A solution of 3.7 g (0.015 mol) of **2** in 50 mL of dry, deoxygenated benzene was cooled in ice. To this solution was added 6.3 mL (8.5 g, 0.06 mol) of $HSiCl_3$ in 15 mL of benzene. The solution was stirred for 1 h at room temperature and 2 h at reflux and then hydrolyzed with 40 mL of deoxygenated 20% NaOH. Separation and extraction of the aqueous phase under N_2 with three 30-mL portions of deoxygenated benzene was followed by drying ($MgSO_4$), filtration under a N_2 stream, and concentration of the combined benzene solutions. Kugelrohr distillation at 81 °C (0.06 mm) yielded 2.3 g (67%) of **3**. NMR spectral data are summarized in Table I.

3-(*p*-Chlorophenyl)-1,1,3-trimethylphospholanium Iodide (4). A solution of 0.6 g (0.003 mol) of **3** and 5 mL of dry, deoxygenated benzene was treated with 0.3 mL (0.7 g, 0.005 mol) of CH_3I, causing rapid precipitation of the salt. After 5 h at room temperature the solids were filtered, washed with several portions of dry benzene, and dried under evacuation to 1.0 g (100%) of **4**, mp 168–171 °C; NMR spectral data are summarized in Table I.

Anal. Calcd for $C_{13}H_{19}ClIP$: C, 42.35; H, 5.20; P, 8.40. Found: C, 42.68; H, 5.25; P, 8.35.

1-Hydroxy-3-phenylphospholane 1-Oxide (6). 1-Hydroxy-2-phospholene 1-oxide (4.0 g, 0.034 mol) in 50 mL of benzene was

(12) Sørensen, S.; Jakobsen, H. *Org. Magn. Reson.* **1977**, *9*, 101.
(13) Breen, J. J.; Engel, J. F.; Myers, D. K.; Quin, L. D. *Phosphorus* **1972**, *2*, 55.
(14) Milbrath, D. S.; Verkade, J. G.; Kenyon, G. L.; Eargle, D. H., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 3167.
(15) Melting points were taken on a Mel-Temp apparatus and are corrected; boiling points are uncorrected. All manipulations of phosphines were conducted in a glovebag with N_2. Spectra were taken as follows: ^{1}H, JEOL MH-100 spectrometer, internal Me_4Si reference, $CDCl_3$ solutions; ^{31}P, Bruker HFX-10 at 36.43 MHz, FT proton decoupled, 85% H_3PO_4 external reference with positive signs downfield, negative upfield, $CDCl_3$ solutions; ^{13}C, JEOL FX-60 at 15.0 MHZ, FT proton decoupled, internal Me_4Si as reference in $CDCl_3$ solutions as lock.

added slowly to a slurry of 15.8 g (0.118 mol) of $AlCl_3$ in 50 mL of benzene. The mixture was stirred overnight at room temperature and then hydrolyzed with ice water. After treatment with concentrated HCl, the solution was extracted several times with $CHCl_3$. The $CHCl_3$ solution was extracted with saturated $NaHCO_3$ solution. Acidification of the aqueous extracts induced the phosphinic acid **6** to precipitate from solution. Later experimentation with the sample indicated a very low solubility in $CHCl_3$ and other organic solvents, thus most of the product was probably discarded with the original aqueous solution. A sample was recrystallized from a large volume of hexane, giving white needles: mp 100.2–100.8 °C; ^1H NMR δ 1.5–3.3 (m, 7 H, phospholane rings), 7.0–7.4 (br s, C_6H_5), 8.8–9.5 (br s, P(O)OH); ^{31}P NMR δ +78.1. The sodium salt in D_2O was prepared for ^{13}C NMR characterization due to the low solubility of the acid in $CDCl_3$; ^{31}P NMR δ +66.4; ^{13}C NMR δ 32.4 (d, 91.6 Hz, C-2), 40.3 (d, 13.4 Hz, C-3), 29.3 (d, 9.8 Hz, C-4), 25.9 (d, 86.7 Hz, C-5).

Anal. Calcd for $C_{10}H_{13}O_2P$: C, 61.22; H, 6.68. Found: C, 61.81; H, 6.76.

1-Methyl-3a-phenyloctahydrophosphindole 1-Oxide (9). (a) **From 1-Methyl-Δ^3-hexahydrophosphindole 1-Oxide.** Aluminum chloride (3.5 g, 0.026 mol) and 10 mL of benzene were slurried together and treated dropwise with 2.2 g (0.013 mol) of **8**. The exothermic reaction was allowed to bring the mixture to reflux. After the reaction had subsided, HCl gas was bubbled in for several minutes. After a period of 22.5 h at room temperature the mixture was hydrolyzed with ice, the aqueous solution was extracted with four 100-mL portions of ether, and the extracts were dried ($MgSO_4$), filtered, and concentrated. The residue was distilled to give 1.5 g (46.7%) of a yellow syrup at 190–220 °C (0.06 mm); ^{31}P NMR δ +72.1, +68.4, +64.4, +61.2. After the syrup stood for 4 days it showed some traces of crystallization. Addition of acetone left some crystalline material: ^{31}P NMR δ +64.4; ^{13}C NMR δ 17.3 (d, 61.0, PCH_3), 22.9 (s, C-5 or C-6), 23.3 (s, C-5 or C-6), 25.6 (d, 5.5, C-7), 26.6 (d, 62.9 C-2), 33.5 (s, C-4), 39.8 (d, 68.4, C-7a), 43.7 (s, C-3), 45.0 (d, 8.5 Hz, C-3a), 145.3 (s, C-8).

(b) From 1-Methyl-$\Delta^{3a(7a)}$-hexahydrophosphindole 1-Oxide (7). Aluminum chloride (36.4 g, 0.27 mol) was slurried with 150 mL of benzene and treated with a solution of 22.1 g (0.13 mol) of **7** in 50 mL of benzene. After 4.5 h at room temperature the mixture was poured over ice. The solution was extracted with several portions of $CHCl_3$ and the extracts were dried ($MgSO_4$), filtered, and concentrated. The residue was distilled to give 24.6 g (76.4%) of yellow syrup which was then redistilled at 170–175 °C (0.05 mm) to yield 19.9 g (61.8%) of a nearly colorless syrup of **9**.

Anal. Calcd for $C_{15}H_{21}O_2P$: C, 72.56; H, 8.53; P, 12.48. Found: C, 72.65; H, 8.68; P, 12.31.

(c) From Phosphine 11. $AlCl_3$ (5.6 g, 0.042 mol) was slurried under N_2 with 20 mL of dry, deoxygenated benzene. To this stirred suspension was added a solution of 3.1 g (0.020 mol) of **11** in 10 mL of benzene, causing mild warming of the reaction flask and separation of two solid-free liquid layers in the flask. After 20 h at ambient temperature, hydrolysis over ice was performed, followed by treatment of the aqueous solution with several milliliters of 10% H_2O_2–H_2O solution. A gold oil separated. The aqueous solution was extracted with three 50-mL portions of $CHCl_3$ and the extracts were dried ($MgSO_4$), concentrated, and then distilled under vacuum to give 1.3 g of **7** and 2.5 g (50%) of **9** at 160–175 °C (0.05 mm). The ^1H and ^{31}P NMR of this sample of **9** matched those for **9** prepared from the phosphine oxides **7** and **8**.

1-Methyl-3a-phenyloctahydrophosphindole (10). A solution of 6 g (0.024 mol) of **9** in 50 mL of dry deoxygenated benzene at 0 °C was treated with a solution of 10.1 mL (13.5 g, 0.1 mol) of $HSiCl_3$ in 20 mL of dry, deoxygenated benzene. The mixture was stirred for 2 h at ambient temperature, brought to reflux for 2 h, and then allowed to stand overnight under N_2. The solution was then cooled in ice and hydrolyzed by slow addition of 65 mL of deoxygenated 20% aqueous NaOH. The layers were carefully separated under N_2, and the aqueous portion was extracted with three 40-mL portions of deoxygenated benzene. The combined benzene solutions were dried ($MgSO_4$), filtered under a stream of N_2, concentrated, and Kugelrohr distilled to yield 5.1 g (91%) of **10** as a pale yellow liquid: ^1H NMR δ 1.04 (several overlapping d, J = 2–3 Hz, PCH_3), 0.9–3.0 (m, ring CH_2), 7.25 (br s, C_6H_5); ^{31}P NMR δ −15.4, −17.1, −28.8, −34.8.

Anal. Calcd for $C_{15}H_{21}P$: C, 77.55; H, 9.11; P, 13.33. Found: C, 77.29; H, 9.27; P, 13.21.

1,1-Dimethyl-3a-phenyloctahydrophosphindolium Iodide (12). Phosphine **10** (1 g, 0.0043 mol) was dissolved in 15 mL of dry, deoxygenated benzene under N_2 and treated dropwise with 0.3 mL (0.64 g, 0.0045 mol) of CH_3I in 10 mL of dry, deoxygenated benzene. Rapid formation of a white precipitate occurred. After the mixture had been stirred for 14 h, the solid was filtered, washed with fresh benzene, and dried to yield 1.6 g (100%) of **12**: mp 227 °C; ^{31}P NMR δ +52.3, +47.5.

Anal. Calcd for $C_{16}H_{24}IP$: C, 51.35; H, 6.47; P, 8.28. Found: C, 51.42; H, 6.45; P, 8.41.

3a-(*p*-Chlorophenyl)-1-methyloctahydrophosphindole 1-Oxide (13). To a slurry of 1.65 g (0.012 mol) of $AlCl_3$ in 5 mL of chlorobenzene was added 1 g (0.006 mol) of **7** in 5 mL of chlorobenzene. The exothermic reaction brought the mixture to reflux. After 18 h at ambient temperature the mixture was hydrolyzed in ice. $CHCl_3$ extraction and drying ($MgSO_4$), filtration, and concentration of the extract gave 0.8 g of a dark yellow oil. This was taken up in warm ether, leaving about 0.1 g of dark gum behind. The solution was decolorized with Norit-A charcoal, filtered, and reconcentrated to 0.6 g of a pale yellow syrup. Kugelrohr distillation at 180 °C (0.05 mm) yielded 0.6 g (36.1%) of a pale yellow glass; ^1H NMR δ 1.5–1.75 (overlapping d, J = 12–13 Hz, PCH_3), 1.0–3.4 (m, 16 H, all aliphatic plus PCH_3), 7.0–7.3 (m, 4H, C_6H_4Cl).

Anal. Calcd for $C_{15}H_{20}ClOP$: C, 63.71; H, 7.14; Cl, 12.54; P, 10.96. Found: C, 63.55; H, 7.19; Cl, 12.37; P, 10.71.

6-Methoxy-1-methyl-3a-phenyloctahydrophosphindole 1-Oxide (18). A slurry of 5.9 g (0.044 mol) of $AlCl_3$ in 50 mL of dry benzene was slowly treated with a solution of 2.1 g (0.011 mol) of 6-methoxy-1-methyl-$\Delta^{3a(7a)}$-hexahydrophosphindole 1-oxide (**17**) and 15 mL of dry benzene. The reaction mixture was heated at 45 °C for 11 h and then hydrolyzed over ice to give a cherry-red mixture. The solution was extracted with 300 mL of $CHCl_3$ in several portions, all color being extracted into the organic phase. Drying ($MgSO_4$), filtration, and concentration of the extract gave 3.4 g of a dark red syrup. Thin-layer chromatography on silica gel plates with acetone eluent showed two colored components, deep red at R_f 0.3 and orange-pink at R_f 0.05. The crude material was chromatographed on a silica gel column, using acetone as eluent first to remove a deep red component (0.4g), which has not been identified. The column was then eluted with methanol to remove the product and the orange-red colored component. The orange eluate was treated with Norit-A charcoal and filtered to give a colorless solution, which was concentrated under vacuum to 2.1 g (72%) of **18** as a light-gold oil. A small sample was Kugelrohr distilled at 150 °C (0.08 mm): ^{31}P NMR δ +73.4, +69.6, +67.1, +65.7, +65.4, +62.1, +60.3; ^1H NMR δ 1.59 (d, J = 13 Hz, PCH_3), 3.43 (s, OCH_3), 3.5 (br s, >CHOR), 7.24 (br s, C_6H_5).

Anal. Calcd for $C_{16}H_{23}O_2P$: C, 69.04; H, 8.33; P, 11.13. Found: C, 69.11; H, 8.12; P, 11.43.

1-Methyl-3a-(*p*-nitrophenyl)octahydrophosphindole 1-Oxide (19). A solution of 12.7 g (0.051 mol) of **10** and 15 mL of glacial acetic acid was cooled in ice and treated slowly with a mixture of 15 mL of concentrated HNO_3 and 10 mL of concentrated H_2SO_4. The reaction mixture was stirred for 20 h and then poured over ice. The aqueous solution was extracted with four 50-mL portions of $CHCl_3$. The extract was stirred with solid $NaHCO_3$ until no further evolution of CO_2 was visible, then dried ($MgSO_4$), and concentrated under vacuum to remove most of the acetic acid. This material was used without further purification in the synthesis of **20**: ^{31}P NMR δ +78.9, +74.7, +70.7, +67.6; ^1H NMR possessed the characteristic multiplet for para substitution at δ 7.1–8.3.

3a-(*p*-Aminophenyl)-1-methyloctahydrophosphindole 1-Oxide (20). The nitro compound **19** in 60 mL of ethanol was hydrogenated at 50 psi over 0.5 g of 10% palladium-on-carbon for 40 h. The mixture was filtered and evaporation of solvent left 16.4 g of an oil. This was taken up in $CHCl_3$ and decanted from a small quantity of black solids. Kugelrohr distillation gave 10.4 g (77% overall from nitration and reduction of **10**); a sample sublimed at 195 °C (0.05 mm) gave a powdery solid: mp 191–193 °C; ^1H NMR δ 1.55 (d, $^2J_{PH}$ = 12.5 Hz, PCH_3), 3.3 (br s, NH_2), 6.4–7.0 (m, aromatic H); ^{31}P NMR δ +69.2, +66.7, +64.9, +61.7.

Anal. Calcd for $C_{15}H_{22}NOP$: C, 68.42; H, 8.42; N, 5.32; P, 11.76. Found: C, 68.49; H, 8.65; N, 5.07; P, 11.89.

3a-(*p*-Methoxyphenyl)-1-methyloctahydrophosphindole 1-Oxide (21). A sample of amine **20** (3.0 g, 0.0114 mol) in 50 mL of methanol at 0 °C was treated with a solution of 1.86 mL (0.0342 mol) of concentrated sulfuric acid in 25 mL of methanol. Amyl nitrite (2.67 g, 0.0288 mol) in 25 mL of methanol was added from a dropping funnel to the stirred amine salt solution, causing an immediate darkening. The mixture was stirred in an ice bath for 4 h and then refluxed for 1 h. After the solution had cooled, it was neutralized with powdered $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to 10.2 g of a solid–oil mass. This was taken up in $CHCl_3$, and filtered to remove inorganic salts, and then reconcentrated. Kugelrohr distillation at 156–157 °C (0.1 mm) yielded 2.2 g (68.8%) of **21** as an orange syrup. The color was not removed by successive redistillations, charcoal decolorization, or column chromatography: ^1H NMR δ 1.57 (d, $^2J_{PH}$ = 13 Hz, PCH_3), 3.80 (s, OCH_3), 6.6–7.3 (m, aromatic H); ^{31}P NMR δ +73.2, +69.3, +65.1, +61.9.

Anal. Calcd for $C_{16}H_{23}O_2P$: C, 69.04; H, 8.33; P, 11.13. Found: C, 69.16; H, 8.22; P, 11.33.

Conversion of 18 to the 4-Methoxyphenyl Derivative (24). A sample of **18** (2.9 g, 0.01 mol) in 12 mL of glacial acetic was treated at 0 °C with a solution of 12 mL of HNO_3 and 8 mL of H_2SO_4. After the mixture has been stirred for 1 h in the ice bath, it was poured into ice. The aqueous solution was extracted with 150 mL of $CHCl_3$ in several small portions. The extract was swirled with powdered $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue of **22**, still containing some acetic acid, had ^1H NMR δ 1.70 (d, J = 13 Hz, PCH_3), 3.41 (s, OCH_3), 3.6 (br s, >CHOR), 7.1–8.5 (m, *p*-$C_6H_4NO_2$) and ^{31}P NMR δ +79.0, +74.8, +73.7, +72.2, +71.0, +67.0, +66.3, +65.1. The sample was dissolved in 50 mL of methanol and hydrogenated at 50 psi over 0.6 g of 10% palladium-on-carbon catalyst. After 24 h, the solution was filtered through Celite and concentrated to 3.6 g of a brown glassy material. This hygroscopic material could be transformed to a granular powder in acetone and was filtered in a glovebag. A methanol solution was treated with Norit-A, filtered, reconcentrated, and stirred in acetone to generate the granular form. After the solid **23** was filtered from acetone under a nitrogen atmosphere, it was held under vacuum to a constant weight (1.9 , 62.3% from **18**): ^1H NMR (D_2O, shifts are approximate as no standard was used) δ 1.6 (d, $^2J_{PH}$ = 13 Hz, PCH_3), 3.4 (s, OCH_3), 7.0–7.6 (m, $C_6H_4NH_2$); ^{31}P NMR (D_2O) δ +85.7, +81.3, +80.2, +78.7, +74.7, +73.7, +72.8.

A sample of 1.7 g of **23** (0.006 mol) was dissolved in 50 mL of methanol. The flask was cooled in ice, and a solution of 1 mL (0.017 mol) of H_2SO_4 and 25 mL of methanol was added. With the solution maintained at 0 °C, a solution of 2 mL (1.7 g, 0.015 mol) of amyl nitrite in 20 mL of methanol was added at a moderate rate. The reaction was kept in ice for 3 h and brought rapidly to reflux (1 h). At room temperature it was treated with powdered $NaHCO_3$, dried ($MgSO_4$), and concentrated until inorganic salts began precipitating. The mixture was taken up in $CHCl_3$ and filtered, treated with Norit-A with warming, and concentrated to 1.6 g of brown oil. The product was column chromatographed on silica gel with $CHCl_3$, losing some color; recovery was only 1.2 g. This material was taken up in a moderate quantity of ethyl ether, leaving some dark brown oils undissolved. Reconcentration of the ether solution yielded 1.1 g of a light brown oil. An attempt to Kugelrohr distill the product resulted in some decomposition (especially loss of methoxyl). No sample was adequately purified for characterization by elemental analysis: ^1H NMR δ 1.62 (d, J = 12.5 Hz, PCH_3), 3.40 (s, OCH_3), 3.6 (br s, >CHOR), 3.80 (s, OCH_3), 6.4–7.6 (m, C_6H_4OR); ^{31}P NMR δ +60.9, +61.3, +62.4, +65.8, +67.3, +69.7, +73.6.

3,4-Benzo-5,6-dimethyl-1-phosphabicyclo[3.2.1]oct-3-ene 1-Oxide (26). A slurry of 12.1 g (0.091 mol) of $AlCl_3$ in 35 mL of mesitylene was warmed to 85 °C and treated dropwise with a solution of 5 g (0.023 mol) of 1-benzyl-3,4-dimethyl-3-phospholene 1-oxide in 35 mL of mesitylene. The mixture was stirred at 85 °C for 10 h and then hydrolyzed with ice. The aqueous solution was extracted with $CHCl_3$ to give a green-brown fluorescing solution. This extract was partially decolorized by treatment with Norit-A, filtered, dried ($MgSO_4$), and concentrated by rotary evaporation. The mesitylene was distilled from the crude product at about 80 °C under vacuum. The hot brown oil remaining was taken up in warm hexane, leaving some dark insoluble oils. The hexane solution was slowly cooled and the product crystallized (1.6 g, 32%). A sample recrystallized from hexane had the following: mp 110–111.5°C; ^{31}P NMR δ +54.5; ^1H NMR δ 1.16 (d, $^3J_{HH}$ = 7 Hz, CH_3C-6), 1.58 (d, $^4J_{PH}$ = 2 Hz, CH_3-C-5), 3.45 (apparent quintet, $^3J_{HH} \simeq {}^2J_{PH} \simeq$ 17 Hz, H_2-C-2); ^{13}C NMR δ 19.8 (s, CH_3-C-6), 25.6 (d, J = 16.5 Hz, CH_3-C-5), 31.7 (d, J = 64.7 Hz, C-7), 34.0 (d, J = 61.6 Hz, C-8), 36.1 (d, J = 59.5 Hz, C-2), 44.6 (d, J = 4.3 Hz, C-6), 46.7 (d, J = 9.8 Hz, C-5), 126.1–146.7 (aromatic C).

Anal. Calcd for $C_{13}H_{17}OP$: C, 70.89; H, 7.78; P, 14.06. Found: C, 70.67; H, 7.61; P, 13.80.

3,4-Benzo-5,6-dimethyl-1-phosphabicyclo[3.2.1]oct-3-ene (27) and its Methiodide (28). To a solution of 0.5 g (0.0023) mol) of oxide **26** in 15 mL of benzene was added a solution of 1 mL of trichlorosilane in 5 mL of benzene. The mixture was stirred at room temperature for 1 h and then refluxed for 2 h. While being cooled in an ice bath, the mixture was treated with 20 mL of 20% NaOH. The organic layer was collected and combined with three 20-mL benzene extracts of the aqueous layer. The benzene solution was dried ($MgSO_4$) and evaporated, and the residue distilled by the Kugelrohr technique to yield a small specimen of the phosphine **27** for characterization: ^1H NMR δ 0.90 (d, $^3J_{HH}$ = 8 Hz, CH_3C-6), 1.54 (s, CH_3C-5), 1.2–2.1 (m, H_2C-7), 1.8 (d, $^2J_{PH}$ = 7 Hz, H_2C-8), 2.3 (q, $^3J_{HH}$ = 8 Hz, HC-6), 2.4–3.2 (apparent AB with $^2J_{HH}$ = 18 Hz, also $^2J_{PH}$ = 6 Hz, H_AH_BC-2); ^{13}C NMR δ 19.3 (CH_3-C-6), 24.0 (d, $^3J_{PC}$ = 3.1 Hz, CH_3C-5), 31.2, 32.7, 32.8 (overlapping d, C-2, C-7, C-8), 48.0 (d, J_{PC} = 4.3 Hz, C-5 or C-6), 49.8 (d, J_{PC} = 3.7 Hz, C-5 or C-6), 125.7–148.8 (aromatics); ^{31}P NMR δ –42.6.

Anal. Calcd for $C_{13}H_{17}P$: C, 76.44; H, 8.39; P, 15.16. Found: C, 76.34; H, 8.56; P, 15.27.

The methiodide (**28**), prepared in benzene, had mp 208.5–210 °C.

Anal. Calcd for $C_{14}H_{20}IP$: C, 48.57; H, 5.82; P, 8.95. Found: C, 48.74; H, 5.95; P, 9.19.

Registry No. 1a, 76232-55-8; **1b**, 76232-56-9; **2a**, 76232-57-0; **2b**, 76232-58-1; **3a**, 76232-59-2; **3b**, 76232-60-5; **4**, 76232-61-6; **5**, 694-24-6; **6**, 76232-62-7; **6** sodium salt, 76232-63-8; **7**, 57065-64-2; **8**, 76232-64-9; **9**, 76232-65-0; **10**, 76232-66-1; **11**, 70610-55-8; **12**, 76232-67-2; **13**, 76232-68-3; **17**, 76232-69-4; **18**, 76232-70-7; **19**, 76232-71-8; **20**, 76232-72-9; **21**, 76232-73-0; **22**, 76232-74-1; **23**, 76250-72-1; **24**, 76232-75-2; **25**, 76232-76-3; **26**, 76232-77-4; **27**, 76232-78-5; **28**, 76232-79-6; 1,3-dimethyl-3-phospholene 1-oxide, 15450-79-0; benzene, 71-43-2; chlorobenzene, 108-90-7.