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Diketones from Ozonolysis of Fused 3-Phospholene Oxides: Cyclizations to 3-Phosphorinone and to 1,4-Dihydro-1,4-Azaphosphinine Derivatives†

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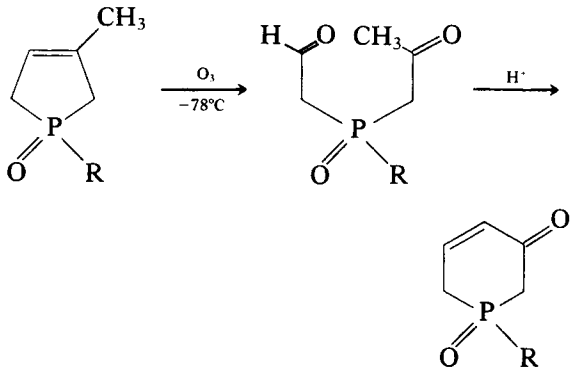
ABSTRACT

1-R-3-Methyl-2,4,5,6,7,7a-hexahydro-1(H)-phosphindole 1-oxide and 1-R-3-methyl-6-methoxy-2,8,9,9a-tetrahydro-1(H)-benzo[e]phosphindole 1-oxide (R = Me or Ph) were prepared and ozonized at −78°C to give diketones in good yield. The intramolecular aldol condensation was performed on certain of these ketones to give multicyclic 3-phosphorinone derivatives. In some cases, double-bond rearrangement into the ring-fusion position was encountered. The 1-phenyl derivative in the benzophosphindole series could not be cyclized due to ready displacement of the P fragment from the tetralone system. The diketones reacted with ammonium acetate to give multicyclic derivatives of the 1,4-dihydro-1,4-azaphosphinine ring system. 1,2,3,4,5,6,7,8-Octahydro-3-oxo-1-phenylphosphinoline 1-oxide was used to demonstrate the value of the bicyclic 3-phosphorinones as precursors of 1-phosphadecalone derivatives. The carbonyl group was protected as the ethylene ketal and the double bond (as well as the benzene ring) was hydrogenated with ease. Hydrolysis gave the 1-phospha-3-decalone derivative. Reduction of the same 3-phosphorinone with $NaBH_4$ gave a mixture of diastereomeric alcohols.

We recently reported [1] a two-step method for converting certain readily accessible 3-phospholene derivatives to 3-phosphorinones, involving ozonolysis to a dicarbonyl compound that could be cyclized by an intramolecular aldol condensation:



(1)

In principle, the method should be extendable to the synthesis of multicyclic 3-phosphorinones by using a cycloalkano-fused 3-phospholene in the ozonolysis. Since there are no reports in the literature on such phosphorus heterocycles, and since these compounds could serve as valuable precursors to other multicyclic compounds, we have explored this possibility, and now report on some of our results. The intermediate dicarbonyl compounds are valuable in the synthesis of other new compounds, and as for the noncyclic dicarbonyl compounds [2] we have also shown their utility in constructing novel cycloalkano-fused 1,4-dihydro-1,4-azaphosphinines. We note also that tricyclic compounds we have prepared have the further potential of conversion to the tetracyclic steroid

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† Experimental work performed at Duke University. Taken from the Doctoral Dissertation of Brian G. Marsi, Duke University, 1986.

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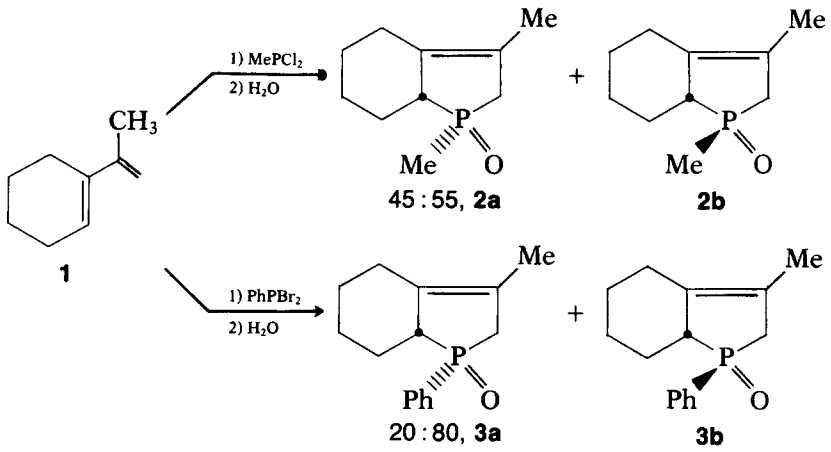


SCHEME 1

system, where phosphorus is present in the A ring. To emphasize this relation, we have included in our model compounds a methoxy group in the potential steroidal C ring, to allow a point of attack for later attachment of the five-membered D ring (as in the method of Nagata et al. [3]).

SYNTHESIS OF MULTICYCLIC 3-PHOSPHOLENE DERIVATIVES

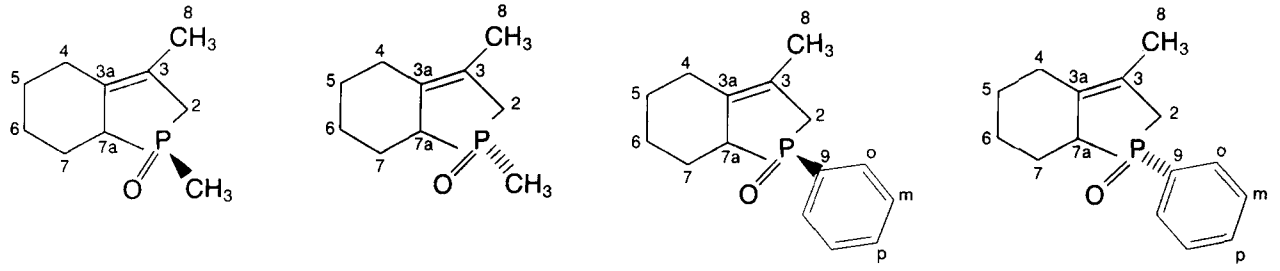
The McCormack cycloaddition of a 1-vinylcyclohexene and a phosphorus(III) halide has been shown in our previous studies [4] to be a useful technique for the construction of bicyclic 3-phospholenes. The use of diene **1** (Scheme 1) provides a phospholene oxide with a methyl group on the double bond, which is needed in the ozonolysis product for the subsequent aldolization to occur. Each of products **2** and **3** consisted of a cis,trans isomer mixture as revealed by the presence of two ^{31}P NMR signals and two sets of ^{13}C NMR signals (Table 1). Using the generalization of previous studies [4], the isomer giving the more upfield ^{13}C NMR signal for the P-CH_3 signal was assigned the structure **2a** with the more sterically crowded methyl (cis to ring carbon 7). It was also previously observed [4] that the cis isomer had the more downfield ^{31}P NMR signal; since the isomer ratio was about 1 : 1 and was not appreciably changed by attempted column chromatography, it was possible to assign the ^{31}P signals to particular forms only by analogy to this generalization. The P-phenyl isomers (**3a** and **3b**) had a similar large difference in ^{31}P NMR shifts, and this was used to assign the structures. The major isomer in the 4 : 1 mixture was assigned the trans structure (**3b**, δ ^{31}P + 48.9), and the minor the cis structure (**3a**, δ ^{31}P + 56.5). Reasonably pure (by NMR) samples of the individual isomers could be obtained by chromatography on silica gel, but they were too hygroscopic to give correct elemental analyses. Their ^{13}C NMR spectra (Table 1) were quite similar and contained no useful features for confirming the assigned isomer structures.

For the synthesis of tricyclic 3-phospholene oxides, diene **4** (Scheme 2) was required and was synthesized from 6-methoxy-1-tetralone [5]. The McCormack cycloadditions with methylphosphonous dichloride and phenylphosphonous dibromide gave the new products **5** and **6**, respectively. Each product again consisted of a mixture of cis, trans isomers, heavily dominated by that isomer giving the more downfield ^{31}P NMR signal and assumed to be the cis form. For the P-CH_3 compounds, the ^{13}C NMR spectra (Table 2) were consistent with this assignment, since the major isomer of the 30 : 1 mixture had the more upfield P-CH_3 signal. The P-phenyl compounds were obtained as 4 : 1 mixture, but the ^{13}C NMR spectrum could be confidently interpreted only for the major isomer (Table 2).

OZONOLYSIS OF MULTICYCLIC 3-PHOSPHOLENE DERIVATIVES

Conditions developed in previous studies [1] were quite satisfactory for the ozonolytic opening of the 3-phospholene ring double bond in the bicyclic compounds **2** and **3**. These reactions were accomplished by passing a dry stream of ozone through a 1 : 1 MeOH–CH_2Cl_2 solution of the 3-phospholene at −78°C. The ozonide was reduced by refluxing with Zn–acetic acid, and the resulting dicarbonyl compounds purified by silica-gel chromatography. The products were obtained as a mixture of diastereoisomers, as detected readily by ^{31}P NMR spectroscopy. The diketone (**7**) (Eq. 1) from 3-phospholene oxide **2** consisted of isomers in the same ratio as in the starting compound (1 : 1), but the uneven ratio (4 : 1) of the P-phenyl isomers **3** was not preserved in the product **8** (1 : 1) (Eq. 2).

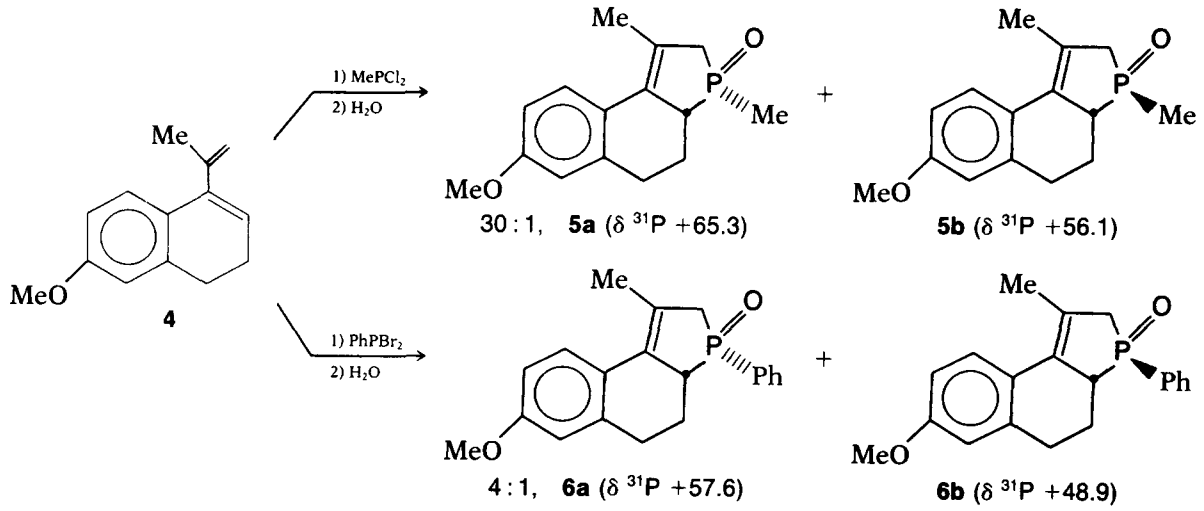
TABLE 1 Carbon-13 NMR[a] Data for 2,4,5,6,7,7*a*-hexahydrophosphindole 1-Oxide Derivatives



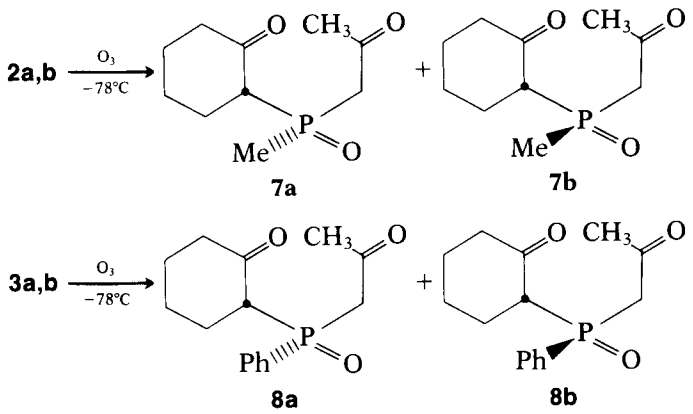
	2a, cis		**2b**, trans		**3a**, cis		**3b**, trans	
C	δ	J_{PC} (Hz)	δ	J_{PC} (Hz)	δ	J_{PC} (Hz)	δ	J_{PC} (Hz)
2	37.8	65.9	36.7	65.9	37.6	68.4	36.8	67.2
3	133.8	9.7	132.2	11.0	124.9	9.7	124.2	9.4
3a	123.2	11.0	122.3	9.8	134.4	10.9	133.5	12.2
4	—[b]	—[b]	—[b]	—[b]	25.1	13.4	26.1	9.4
5	—[b]	—[b]	—[b]	—[b]	25.2	0	24.4	0
6	—[b]	—[b]	—[b]	—[b]	26.9	12.2	24.3	13.4
7	—[b]	—[b]	—[b]	—[b]	26.8	0	25.9	0
7a	43.9	68.4	43.6	70.3	45.2	49.6	44.9	69.8
8	14.9	12.2	15.0	12.2	15.8	12.2	15.0	12.2
9	11.4	62.2	15.1	63.5	131.0	89.1	130.4	88.5
o					128.2	11.0	127.3	12.1
m					130.4	9.8	129.6	8.1
p					131.5	2.4	130.6	2.7

[a] Spectra were obtained in $CDCl_3$ solution. Chemical shifts are downfield of internal TMS.
[b] Unresolved at δ 24.2–26.9.
[c] Assignments are tentative due to overlap.

Without the rigid framework of the bicyclic starting compounds, the diastereoisomers showed little difference in their ^{31}P NMR shifts; the values were similar to those found for noncyclic diketones prepared [1] from monocyclic 3-phospholenes (for **7**, +41.7 and +42.0; for **8**, +32.6 and +33.1; cf. the bis(2-oxopropyl)phosphine oxide noncyclic counterparts with +38.4 (P-Me) and +28.9 (P-Ph). The mixture of isomers could not be easily separated, and the ^{13}C NMR spectra were obtained on the mixture. The signals for the two isomers were very similar but distinct from each other and easily interpreted (Table 3). Noteworthy was the position for the exocyclic carbonyl carbon; as in the noncy-



SCHEME 2



(1)

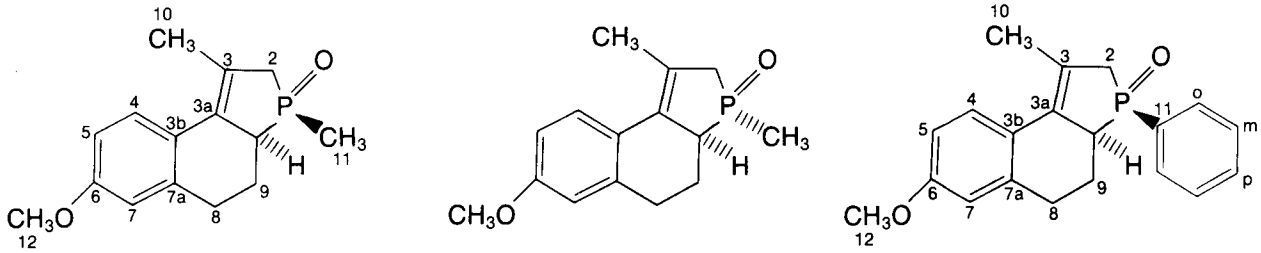
(2)

clic compounds [1], the shifts (δ 200.4–201.9) were several parts per million upfield of the normal position of saturated methyl ketones.

The same conditions were effective for the ozonolysis fo the tricyclic 3-phospholene oxide derivatives **5** and **6** to form diketones **9** and **10**. Structures were confirmed by ^{13}C NMR (Table 4). Since one carbonyl is conjugated to the benzene ring, it gave an infrared stretching band at lower frequency (1685 cm^{-1}) than the nonconjugated one (1710 cm^{-1}).

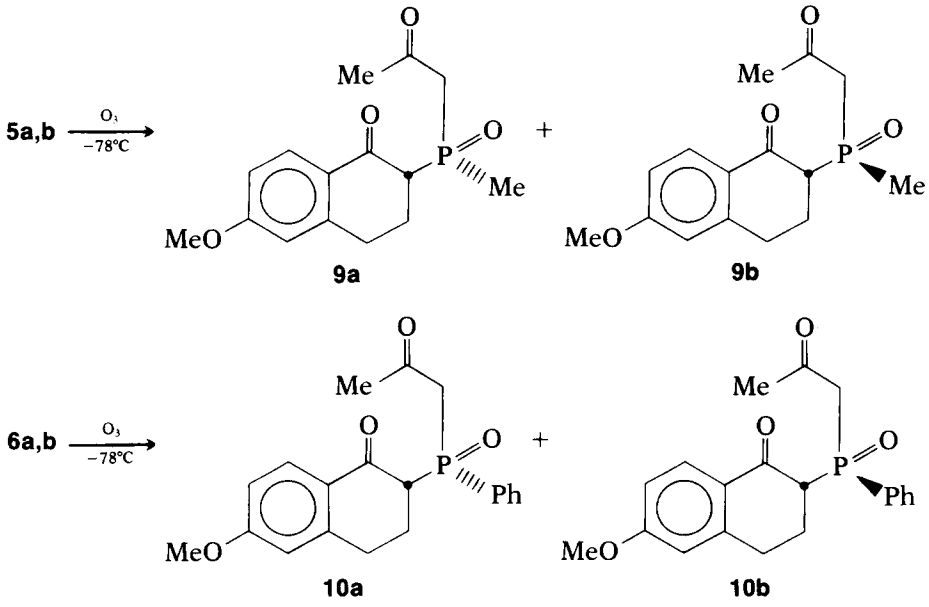
The dicarbonyl compounds made by this approach are of a valuable structural type. Noncyclic bis(2-oxoalkyl) derivatives have been made in this [1] and other laboratories [6], but it is not common to have one carbonyl group incorporated in a ring. The dicarbonyl compounds are useful starting materials in ring-forming reactions, and as will be

TABLE 2 Carbon-13 NMR[a] Data for 2,8,9,9a-Tetrahydro-(1*H*)-benzo[*e*]phosphindole 1-Oxides



	5a, cis[b]		**5b**, trans[b]		**6a**, cis[c]	
C	δ	J_{PC} (Hz)	δ	J_{PC} (Hz)	δ	J_{PC} (Hz)
2	39.0	63.5	41.1	65.3	38.9	65.5
3	125.9	9.8	125.8	7.3	—[d]	
3a	130.3	12.4	131.1	10.4	—[d]	
3b	128.6	4.4	125.9	4.4	—[d]	
4	128.8	—	127.9	—	128.5	—
5	111.5	—	110.7	—	111.3	—
6	158.4	—	157.8	—	158.4	—
7	113.3	—	112.8	—	113.2	—
7a	139.2	—	138.6	—	139.2	—
8	30.3	8.5	29.4	9.7	29.7	8.9
9	22.4	4.0	22.0	4.0	23.0	4.5
9a	42.6	69.5	43.0	70.8	43.8	70.3
10	18.0	12.2	18.7	6.1	18.9	12.1
11	10.2	62.9	15.7	63.5	—[c]	—[c]
12	55.1	—	54.6	—	54.9	—

[a] Spectra obtained on $CDCl_3$ solutions. Chemical shifts are downfield of internal TMS. The basis for the signal assignments is found in an earlier paper on related compounds [16].
[b] Assignments based on observations at 22.5 and 75.4 MHz, and on the INEPT spectrum at 75.4 MHz.
[c] C-*meta* 128.3 (13.2 Hz); C-*ortho* 130.6 (7.7 Hz); C11 and C-*para* not resolved.
[d] Overlapping signals.



(3)

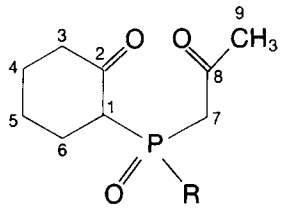
(4)

seen in the next sections, they have allowed the preparation of multicyclic 3-phosphorinones and 1,4-dihydro-1,4-azaphosphinines.

CYCLIZATIONS TO MULTICYCLIC 3-PHOSPHORINONES

Internal aldol condensation of diketone **7** was effected with a variety of reagents (aqueous NaOH, HCl in H_2O–EtOH, *p*-toluenesulfonic acid in benzene or acetic acid). Under all conditions, a secondary reaction followed that converted some of the initial product (*cis*- and *trans*-**11**) to a rearranged form, **12** (Eq. 5). The ratio was generally about 2 : 2 : 1, regardless of conditions, as revealed by ^{31}P NMR analysis, and no technique was found that avoided the rearrangement. Attempted chromatographic separation of the mixture was not success-

TABLE 3 Carbon-13 NMR Data for Diketones **7** and **8**[a]



7, R = CH_3

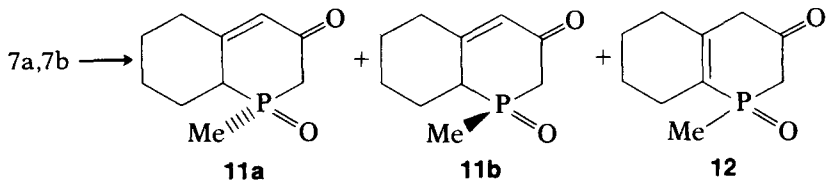
8, R = C_6H_5

	7		8	
Carbon	Isomer A	Isomer B	Isomer A	Isomer B
1	50.7(66.9)	49.8(73.3)	51.4(67.3)	51.3(63.7)
2	207.5(9.4)	207.4(10.7)	206.7(3.9)	206.6(5.0)
3	—[b]	—[b]	41.7	41.4
4,5	—[b]	—[b]	—[b]	—[b]
6	23.9(12.1)	23.4(9.4)	23.1(9.6)	22.3(6.8)
7	—[b]	—[b]	45.4(57.1)	45.0(56.7)
8	201.9(5.3)	201.6(5.4)	201.0(9.6)	200.4(5.6)
9	32.4	32.1	32.2	31.5
R	14.1(69.8)	12.0(69.8)	—[c]	—[c]

[a] As isomer mixtures in $CDCl_3$; relative peak intensities used to recognize isomers. Values in parentheses are J_{CP} (Hz).

[b] Inadequately resolved for measurement.

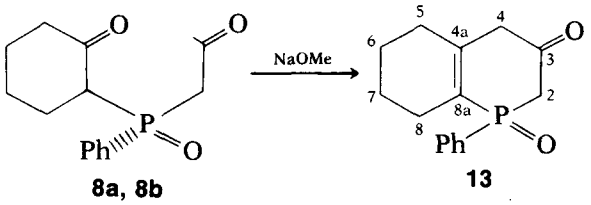
[c] C-*ortho*, 130.8(9.2) and 130.2(9.2); C-*meta*, 128.0(12.4) and 127.7(11.9); C-*para*, 131.5(2.1) and 131.5(2.1); C-*ipso*[b].



(5)

ful. Two of the ^{31}P signals were quite similar (δ +37.6 and δ +37.8) and probably could be assigned to the diastereoisomers of **11**. The lower field signal (δ +41.7) had the lowest intensity and probably arose from the single rearrangement product **12**. The ^{13}C NMR spectrum of the three-component mixture, while quite complex, did possess features supporting structures **11a,b** and **12**; three carbonyl carbons were present, with two showing conjugation (δ 190.8 and 190.9, hence from **11a,b**), and one nonconjugated from **12** (δ 197.6). The olefinic carbon signals were also separated. Their shifts are recorded in the Experimental section.

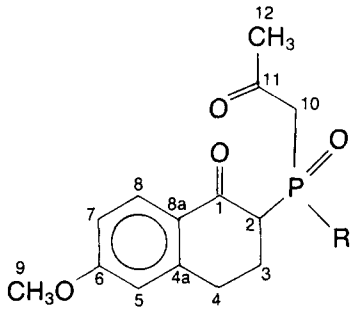
The P-phenyl diketone **8** also was cyclized under a variety of conditions but gave the cleanest product with NaOMe in MeOH. A 77% yield of pure 3-phosphorinone, **13**, the product of the secondary rearrangement, was obtained.



(6)

The structure was confirmed as a nonconjugated ketone from the carbonyl IR value of 1710 cm^{-1}. The ^{13}C NMR signal for C=O (δ 197.9) was also downfield of that expected [1] if the carbonyl were conjugated. One olefinic carbon (δ 124.8) had the

TABLE 4 Carbon-13 NMR Data for Diketones **9** and **10**[a]



9, R = CH_3

10, R = C_6H_5

	9		10	
Carbon	Isomer A	Isomer B	Isomer A	Isomer B
1	192.60(2.5)	192.16(4.2)	192.1(<2)	192.0(3.4)
2	48.56(65.3)	47.48(65.9)	48.3(66.3)	48.2(66.7)
3	22.37(9.8)	22.34(9.7)	22.5	21.8
4	28.60(10.4)	28.40(9.8)	28.3(10.0)	28.0(10.5)
4a	146.2	146.1	146.2	146.1
5	113.25	113.18	113.1	113.1
6	163.74	163.79	163.7	163.7
7	112.79	112.15	111.9	111.8
8	129.62	129.15	—[b]	—[b]
8a	125.38(8.6)	125.0(9.1)	125.5(2.7)	125.3(4.1)
9	55.10	55.07	55.0	54.7
10	47.10(56.8)	44.68(56.8)	46.1(57.3)	45.9(60.9)
11	202.18(5.5)	201.70(6.7)	201.7(6.5)	201.1(5.9)
12	32.8	32.4	32.5	32.0
R	16.99(69.0)	12.89(67.8)	—[b]	—[b]

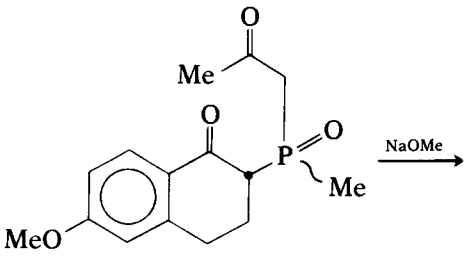
[a] As isomer mixtures in $CDCl_3$; relative peak intensities used to recognize isomers. Values in parentheses are J_{CP} (Hz). Couplings confirmed by measurements at 22.5 and 75.4 MHz. The basis for assignments to ring carbons is found in ref. [16].

[b] Inadequately resolved for measurement.

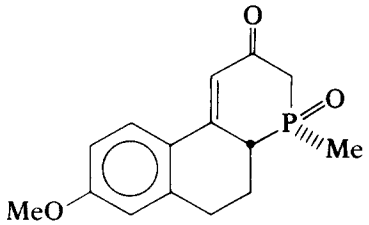
large coupling to ^{31}P (95.3 Hz) expected from a one-bond connection, and no olefinic proton signals appeared in the ^{1}H NMR spectrum.

This tendency for the initial product to rearrange is not observed in the monocyclic system [1] and may be associated with the normal preference for a tetrasubstituted olefinic structure. This rearrangement also occurs, albeit to a smaller extent, with the carbocyclic hexahydronaphthalene counterpart [7], perhaps for the same reason. Interaction of the phosphoryl group with the double bond also is a factor; it is well known that base can cause isomerization of double bonds into a conjugative relation to phosphoryl, as in the well known [8] 3-phospholene oxide to 2-phospholene oxide rearrangement.

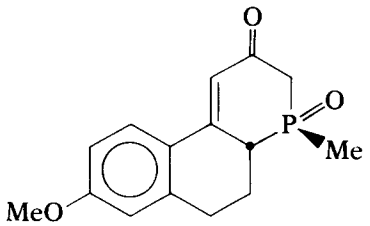
Less satisfactory results were obtained when the bicyclic diketone **9** was used in the aldol condensation. The product mixture from an acid-catalyzed (HCl) condensation gave a complex ^{31}P NMR spectrum, but when 1.5% aqueous NaOH was used, a simpler mixture was obtained from which a major fraction was isolated in 59% yield on silica gel chromatography. This product, however, proved to be a three-component mixture (Eq. 7), as revealed by ^{1}H NMR spectroscopy that showed three P-CH_3 doublets. The ^{13}C NMR spectrum was complex but suggested one component to have a nonconjugated β-carbonyl (δ 199), as in **15**. A signal for conjugated carbonyl appears at δ 191, and may arise from a mixture of diastereoisomers **14a** and **14b**.



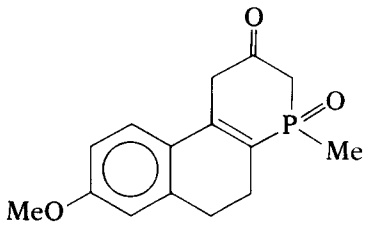
9a,b



14a

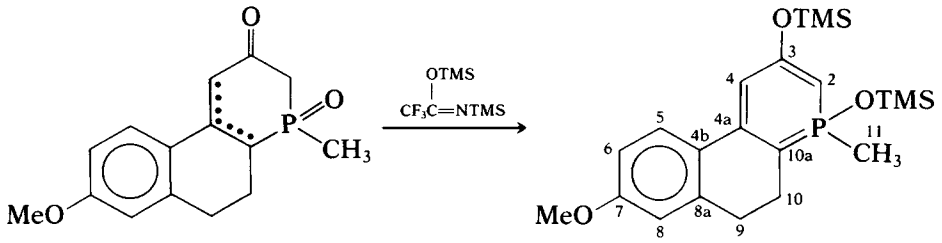


14b



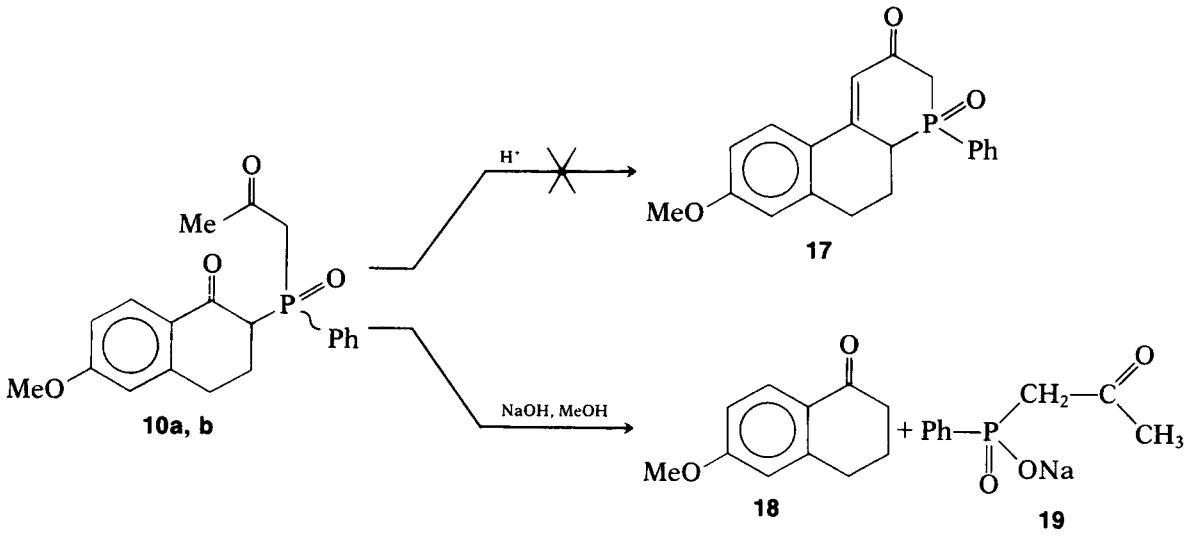
15

Since the overlap of the ^{13}C NMR signals was too severe to allow confirmation of the product as having the tricyclic framework of **14** and **15**, an experiment was performed to simplify the mixture by converting all of the presumed structures **14a**, **14b**, and **15** to the same form. This was accomplished by a silylation reaction. In other work [9] we have found that 3-phosphorinones can be converted to silyl enol ethers, with simultaneous silylation of the oxygen on phosphorus as well. The products are characterized as λ^5-phosphinines. Were this reaction successfully applied to the **14a–14b–15** mixture, a single λ^5-phosphinine (**16**) should result:



14a, 14b, 15 **16**

(8)

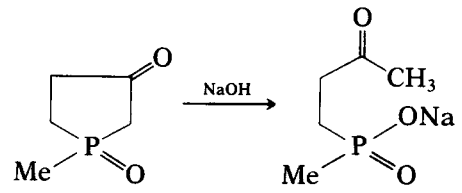


SCHEME 3

This indeed was the case; the product had a single ^{31}P NMR signal at δ +34.4, and after vacuum stripping of the volatile byproduct CF_3CONH–TMS the residue gave a ^{13}C NMR spectrum easily interpreted as arising from **16**. The compound was quite unstable in water and was hydrolyzed to the original mixture of isomers **14a, 14b,** and **15**. The bis(t-butyldimethylsilyl) analog of **16** was also prepared and spectrally characterized, but its hydrolytic stability was not adequately improved for isolation purposes.

With the P-phenyl diketone **10**, no evidence was obtained for the formation of the tricyclic aldol condensation product (**17**) (Scheme 3). Acidic media did not affect **10**, and with base the P fragment was cleaved, presumably as **19** (not observed), giving as an easily recognizable product the tetralone **18**.

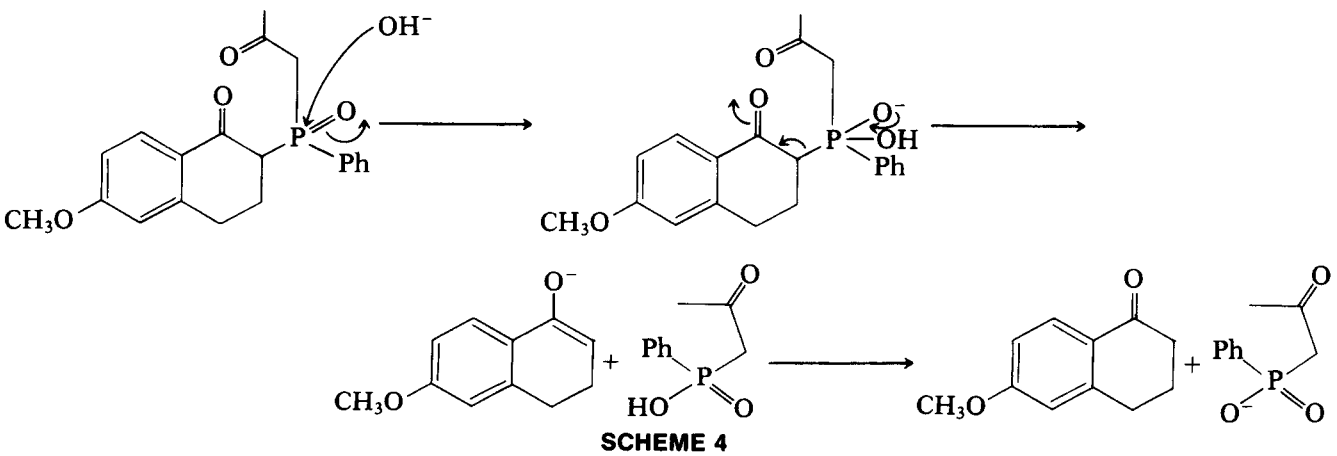
A possible mechanism is shown in Scheme 4. The reaction resembles a cleavage process earlier observed [10] for 3-phospholanones:



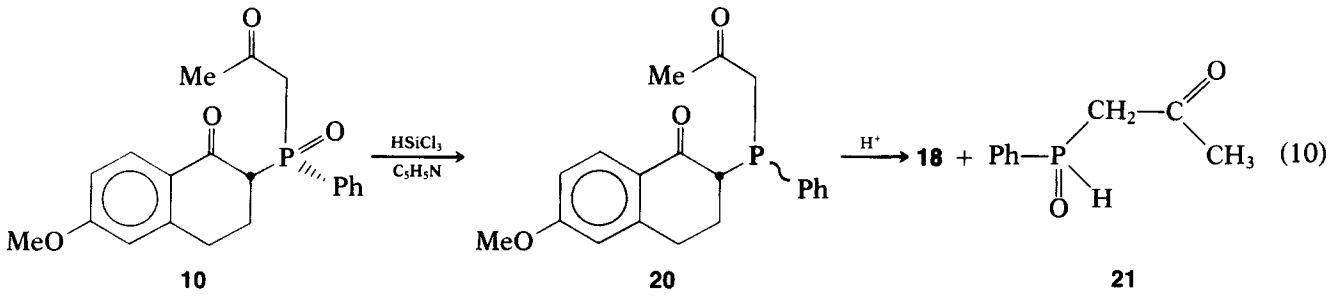
(9)

To lessen the sensitivity of the P function to nucleophilic attack, the oxygen was removed from oxide **10** by reaction with trichlorosilane–pyridine [11] to give the phosphine **20** as a mixture of diastereoisomers with δ ^{31}P NMR −18.3 and −23.4.

With basic reagents, no reaction was observed. With aqueous HCl this mixture also underwent the P cleavage reaction to the tetralone **18**. The acidic reaction medium gave a ^{31}P NMR spectrum with a single signal at δ +20.9, as could arise from a sec-phosphine oxide; that a proton was attached to P was revealed on a proton-coupled spectrum, where the ^{31}P signal was split to a doublet with J = 515 Hz. Presumably this signal arose from the



SCHEME 4



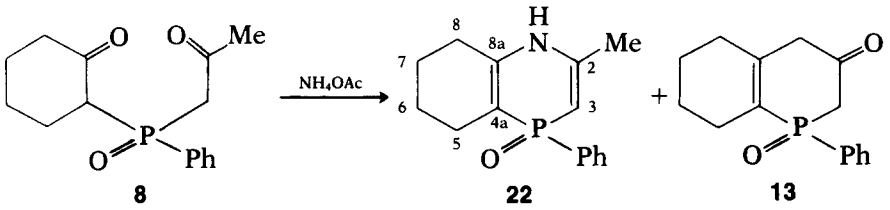
10 20 21 (10)

fragment **21**, and this was supported by a proton NMR spectrum of the aqueous solution, which had saturated CH signals at δ 2.3 (CH_3) and 3.2–3.6 (CH_2).

We have therefore encountered two complications in the extension of our 3-phosphorinone synthesis to certain multicyclic systems. Some rearrangement of the double bond formed in the aldol condensation was found to occur in all of the reactions, and in one case (**13**) accounted for the entire product. In this sense, the process has utility, since this product is novel and as will be seen can be successfully used in other reactions that give new bicyclic compounds. It can be expected that the rearrangement will always be encountered in such applications, since necessarily the rearrangement can lead to a tetra-substituted olefinic structure. The other complication, that of cleavage of the P-fragment, was encountered in only one structure (**10**) but completely dominated in that case. The structure at P seems to be important to this reaction; with a P-CH_3 group instead of P-C_6H_5, no cleavage was observed for the same molecular framework.

CYCLIZATIONS TO 1,4-DIHYDRO-1,4-AZAPHOSPHININES

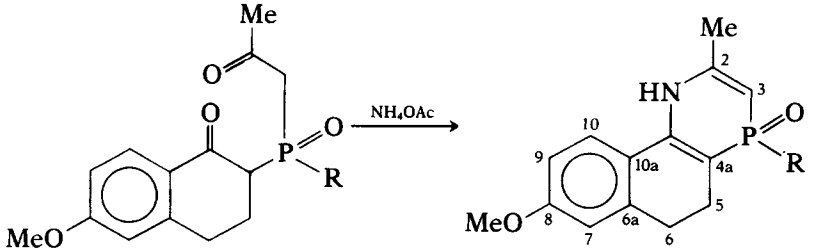
Noncyclic bis(β-oxoalkyl)phosphine oxides are known to react with ammonium acetate to give 1,4-dihydro-1,4-azaphosphinines [2,6]. The ozonolysis products from the multicyclic 3-phospholene oxides offer the first opportunity to prepare cycloalkano-fused dihydroazaphosphinines by this route. When applied to diketone **8**, the desired product **22** was formed but was accompanied by some of the aldol product **13**, even when a large excess of ammonium acetate was used to favor the nitrogen-incorporation reaction:



8 22 13 (11)

However, the two products were easily separated by silica gel chromatography, and a pure specimen of **22** was isolated. The compound is a high-melting (290–291°C) solid, giving ^1H and ^{13}C NMR spectral features like those for the monocyclics previously reported [2].

The bicyclic diketones **9** and **10** were better behaved in this process and provided samples of the dihydrophosphinines **23** and **24** free of the aldol product (Eq. 12), although only **24** could be crystallized and successfully analyzed. The ^{13}C NMR spectra of the products were consistent with the assigned structures.

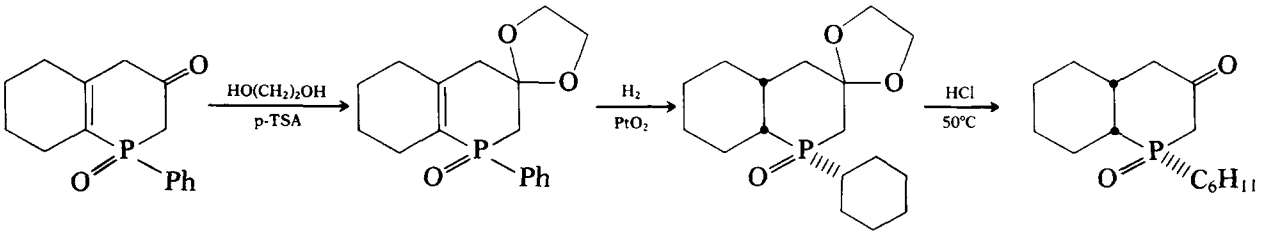


9, R = Me
10, R = Ph

23, R = Me
24, R = Ph (12)

FURTHER REACTIONS OF BICYCLIC 3-PHOSPHORINONE (13)

Since the aldol cyclization with diketone **8** was especially successful and gave a good yield of a pure 3-phosphorinone (**13**), we view this process as having value as an entry to other 1-phosphadecalin derivatives. While several derivatives of this ring system can be found in the literature, none has the functionality at C3 that is a direct consequence of the aldol process. We have found that the carbonyl group of **13** can be protected as the ethylene ketal (**25**), and that the double bond can then be hydrogenated. The conditions used (PtO_2 catalyst at 60 psi of H_2), however, caused simultaneous hydrogenation of the benzene ring, giving a single isomer of the fully saturated ketal **26** in 64% yield. The benzene ring was found to be reduced at about the same rate as the double bond. Other instances are known where P-phenyl groups in P-oxides are surprisingly easily hydrogenated [12]. The stereochemistry of the hydrogenation of a simply monocyclic 2-phospholene oxide has been shown [13] to occur with approach of hydrogen exclusively from the P=O face. If this path (Eq. 13) is followed in the hydrogenation of **25**, the product would have the stereochemistry shown in **26.**

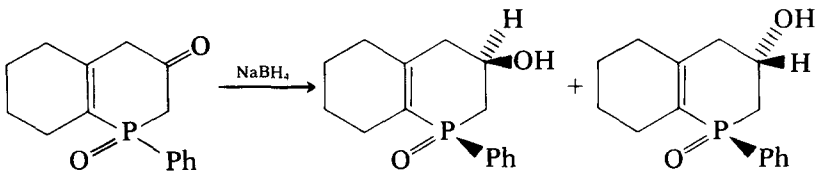


(13)

13 **25** **26** **27**

However, there are no features in the NMR spectra that allow confirmation of this structure. The synthesis of 1-phospha-3-decalone (**27**) was completed by the acid hydrolysis of the ketal group in 77% yield.

Another reaction performed on 3-phosphorinone **13** was the reduction to the alcohol with $NaBH_4$. This provided a mixture (2 : 1) of the diastereomers **28a** and **28b**, which could be separated by chromatography on silica gel:



(14)

13 **28a** **28b**

The ^1H NMR spectra possessed the same useful feature as found [14] for a pair of related monocyclic alcohols; the carbinol proton was more strongly deshielded, presumably by the phosphoryl group, in one isomer (δ 4.5) than in the other (δ 4.1). This allows the assignment of structure **28a** to the former isomer, and **28b** to the latter. There could also be a contribution to the shift difference by some shielding of the carbinol proton of **28b** by the phenyl group.

EXPERIMENTAL

General

Proton NMR spectra were obtained on an IBM NR-80 or a Varian XL-300 spectrometer and are referenced to tetramethylsilane as an internal standard. Carbon-13 NMR spectra (proton decoupled, FT) were obtained on a JEOL FX-90Q spectrometer at 22.5 MHz or a Varian XL-300 spectrometer at 75.4 MHz, and employed tetramethylsilane as an internal standard. Phosphorus-31 NMR (proton decoupled, FT) spectra were obtained on a JEOL FX-90Q at 36.2 MHz and are referenced to 85% phosphoric acid as an external standard, with an internal deuterium lock. Negative shifts are upfield and positive downfield of reference. Mass spectra were obtained on an AEI MS 903 spectrometer at the Research Triangle Mass Spectrometry Center, Research Triangle Park, North Carolina. Melting points were taken on a Mel-Temp apparatus and are corrected. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona or by Galbraith Laboratories, Knoxville, Tennesse. Ozonolyses were accomplished using a Welsbach T-23 laboratory ozonator. All procedures involving

trivalent phosphorus were performed under a nitrogen atmosphere.

1-(1-Methylvinyl)cyclohexene (**1**)

To a stirred solution of 200 mL (0.42 mol) of 2.1 *M* *n*-butyllithium in 400 mL of anhydrous ether was added dropwise 135.7 g (0.38 mol) of methyltriphenylphosphonium bromide over a 30-min period. The mixture was stirred for 4 h, after which 47.4 g (0.38 mol) of 1-acetylcyclohexene was added dropwise. The reaction mixture was refluxed for 24 h, cooled, and then filtered. The filtrate was washed with H_2O until the washings were neutral and then dried over $MgSO_4$. Removal of the solvent by rotary evaporation followed by chromatography on alumina (hexane as eluant) afforded 32.3 g (69%) of **1** in high purity; ^1H NMR and IR match values reported [15]; ^1H NMR ($CDCl_3$, 80 MHz), δ 1.28–1.85 (m, 4H, $-CH_2-CH_2-$), 1.80 (s, 3H, $-CH_3$), 2.05–2.30 (m, 4H, $CH_2C{=}CCH_2$), 4.90 (m, 2H, $=CH_2$), 5.90 (t, $^3J_{HH}$ = 4 Hz, 1H, =C–H); IR (neat) $\nu_{C=C}$ 1634, 1060 cm^{-1}.

1-(1-Methylvinyl)-3,4-dihydro-6-methoxynaphthalene (**4**)

A mixture of 1.9 g (78.1 g-at) of Mg turnings, 50 mL of THF, and 1.0 g (8.2 mmol) of 2-bromopropene was stirred under N_2. A crystal of I_2 was added, and the mixture slowly heated to 40°C. After 15 min, a vigorous reaction ensued, and after it had subsided a solution of 9.0 g (74.4 mmol) of 2-bromopropene in 50 mL of THF was added dropwise. The mixture was then heated for an additional 30 min at 40°C. The mixture was cooled with a water bath to 25°C, and a solution of 9.9 g (56.0 mmol) of 6-methoxy-1-tetralone in 75 mL of THF was added dropwise. The mixture was refluxed for 2 h and then cooled to 5°C. A saturated NH_4Cl solution (80 mL) was added slowly. The resulting layers were separated and the aqueous layer washed (2 × 60 mL) with ether. The organic layers were combined and dried over Na_2SO_4 and then over $MgSO_4$. The solvent was removed by rotary evaporation to yield 12.5 g of a yellow oil, indicated by ^1H NMR to be a mixture of 80% of the desired tetralol and 20% of 6-methoxytetralone. The crude product was dehydrated in benzene (125 mL) containing a crystal of I_2 and 0.2 mL of quinoline by refluxing with a Dean-Stark apparatus. About 1.0 mL of H_2O was collected in the trap. The solvent was removed by rotary evaporation and the residual dark oil chromatographed on silica gel (petroleum ether 35–60°C) to yield 7.5 g (67% based on starting tetralone) of **4** as a colorless liquid. The ^1H NMR ($CDCl_3$, 80 MHz) matched that of Baran [5]; δ 2.05 (s, 3H, CH_3), 2.20–2.41 and 2.60–2.86 (m, 4H, $-CH_2-$), 3.80 (s, 3H, OCH_3), 5.2 (broad, s, 2H, $=CH_2$), 5.95 (t, 1H, $^3J_{HH}$=5 Hz, =CH), 6.70–7.24 (m, 3H, Ar–H).

1,3-Dimethyl-2,4,5,6,7,7a-hexahydro-1(H)-phosphindole 1-Oxide (**2**)

To a wide-mouth, screw-cap bottle was added 50 mL of hexane, 9.7 g (0.079 mol) of diene **1**, 15.1 g (0.13 mol) of methylphosphonous dichloride, and 50 mg of copper stearate. The bottle was sealed and allowed to stand for 2 weeks. The resulting solid was filtered and washed with hexane (2 × 50 mL). The solid was slowly added to 60 mL of cold H_2O. After 30 min of stirring the solution was neutralized by addition of solid $NaHCO_3$; the aqueous solution was filtered and extracted with three 100-mL portions of $CHCl_3$. The solvent was evaporated in vacuo from the combined organic solutions to give a yellow oil. Chromatography (3% methanol in chloroform) followed by Kugelrohr distillation (76–81°C, 0.2 mm) afforded 9.9 g (68%) of **2** as a colorless oil consisting of a 45 : 55 mixture of diastereomers **2a** and **2b**, not readily separable by chromatography; ^{31}P NMR ($CDCl_3$), δ +62.8 (**2a**) and +56.1 (**2b**); ^{13}C NMR, Table 1. Elemental analysis was performed on the isomer mixture. Analysis calculated for $C_{10}H_{17}OP \cdot 1/2\ H_2O$; C, 62.16; H, 9.39; found, C, 62.14; H, 9.17.

3-Methyl-1-phenyl-2,4,5,6,7,7a-hexahydro-1(H)-phosphindole 1-Oxide (**3**)

This compound was prepared by the general procedure described for **2**, using phenylphosphonous dibromide. There was obtained a 4 : 1 mixture of diastereomers of **3** with ^{31}P NMR δ +48.9 and +56.5 respectively. Chromatography on silica gel (4% methanol in chloroform) afforded 25.1 g (78%) of the mixture as a colorless oil. Repeated chromatography afforded the minor isomer **3a** as a very hygroscopic solid, mp 126–132°C, that could not be successfully analyzed; ^{31}P NMR ($CDCl_3$), δ +56.5; ^{13}C NMR, Table 1. For **3b** ^{31}P NMR ($CDCl_3$), δ +48.9; ^{13}C NMR, Table 1.

1,3-Dimethyl-6-methoxy-2,8,9,9a-tetrahydro-1(H)-benzo[e]phosphindole 1-Oxide (**5**)

A mixture of 6.8 g (34.0 mmol) of diene **4** and 3.4 mL (37.0 mmol) of methylphosphonous dichloride in 100 mL of ligroin was reacted in the same manner as described for the preparation of **2.** After 2 weeks, the solid adduct was filtered and washed with ligroin (2 × 50 mL). The solid was then added to 50 mL of ice water and stirred vigorously for 1 h. The aqueous solution was extracted with $CHCl_3$ (3 × 50 mL), and the combined organic portions dried over $MgSO_4$. Solvent was removed by rotary evaporation, and the residual oil was chromatographed (3% methanol in chloroform) to afford 8.0 g (90.0%) of a diastereomeric mixture of **5a** and **5b** in a 30 : 1 ratio. Repeated chromatography resulted in isolation of pure **5a.** When the adduct was left to stand 4

weeks before hydrolysis, the diastereomer ratio changed to 4:1. For **5a** ^{31}P ($CDCl_3$), δ +65.3; ^{13}C, Table 2; ^1H NMR ($CDCl_3$, 300 MHz), δ 1.52 (d, $^2J_{PH}$ = 11.9 Hz, 3H, P—CH_3), 1.82–3.10 (m, CH, CH_2), 2.02 (s, 3H, C—CH_3), 3.77 (s, 3H, OCH_3), 6.66–7.8 (m, 2H, Ar-H), 7.36 (d, $^2J_{HH}$ = 8.0 Hz, 1H, Ar-H). The compound was pure by chromatography and NMR spectroscopy but gave low values on elemental analysis due to its retention of water.

For **5b** ^{31}P NMR ($CDCl_3$), δ +56.1; ^{13}C NMR, Table 2; ^1H NMR ($CDCl_3$, 80 MHz), δ 1.65 (d, $^2J_{PH}$ = 14.1 Hz, P–CH_3), 2.05 (s, C–CH_3), 3.86 (s, OCH_3).

6-Methoxy-3-methyl-1-phenyl-2,8,9,9a-tetrahydro-1(H)-*benzo*[e]*phosphindole 1-Oxide* (**6**)

A mixture of 15.7 g (78.4 mmol) of diene **4**, 11.8 mL (82.4 mmol) of phenylphosphonous dibromide, and 50 mL of hexane was reacted in the same manner as described for the preparation of **2.** After 2 weeks, the solid adduct was filtered and washed with hexane (2 × 50 mL). The solid was then added to 100 mL of a 1:3 mixture of chloroform and H_2O. The resultant mixture was stirred vigorously for 2 h; the layers were separated and the aqueous phase extracted with chloroform (2 × 50 mL). The organic extracts were combined, dried ($MgSO_4$), and concentrated to give a gummy solid. Chromatography on silica gel (2% CH_3OH–$CHCl_3$) afforded 16.3 g (64%) of **6a** and **6b** as a 4:1 mixture; ^{31}P NMR ($CDCl_3$), δ +57.6 (**6a**), and +48.9 (**6b**); ^{13}C NMR, Table 2.

Ozonolysis of 1,3-Dimethyl-2,4,5,6,7,7a-hexahydro-1(H)-*phosphindole 1-Oxide* (**2**)

A solution of 1.1 g (6.0 mmol) of **2** in 50 mL of methanol–dichloromethane (1:1) was treated with ozone at −78°C until the light blue color of excess ozone appeared. Nitrogen was passed through the solution to remove excess ozone. The solution was concentrated to about 10 mL and then added to 200 mL of an acetic acid–H_2O (1:1) solution containing 200 mg of zinc dust. The solution was refluxed for 30 min and then filtered to remove solids. The solvent was removed by rotary evaporation and the resultant oil chromatographed on silica gel (3% methanol in chloroform) to yield 0.70 g (55%) of a clear oil containing only **7** as a 1:1 mixture of diastereomers; ^{31}P NMR ($CDCl_3$), δ +41.7, 42.0; ^{13}C NMR, Table 3; IR (neat) $\nu_{C=O}$ 1708 cm^{-1} (br). The mixture was used immediately for other reactions.

Ozonolysis of 3-Methyl-1-phenyl-2,4,5,6,7,7a-hexahydro-1(H)-*phosphindole* (**3**)

A solution of 1.9 g (7.7 mmol) of **3** in 50 mL of dichloromethane–methanol (1:1) was ozonized according to the procedure for **2.** Chromatography on silica gel (3% methanol in chloroform) afforded 1.7 g (79%) of a clear oil containing only **8** as a 1:1 mixture of diastereomers; ^{31}P NMR ($CDCl_3$), δ +32.6, +33.1; ^{13}C NMR, Table 3; IR (neat) $\nu_{C=O}$ = 1710 cm^{-1} (br). The mixture was used immediately in other reactions.

Ozonolysis of 1,3-Dimethyl-6-methoxy-2,8,9,9a-tetrahydro-1-(H)-*benzo*[e]*phosphindole 1-Oxide* (**5**)

A solution of 0.89 g (3.0 mmol) of **5** in 50 mL of methanol–dichloromethane (1:1) was ozonized exactly as described for the ozonolysis of **2.** Chromatography on silica (3% methanol in chloroform) afforded 0.6 g (68%) of a clear oil shown to be a 1:1 mixture of isomeric diketones **9a** and **9b;** ^{31}P NMR ($CDCl_3$), δ +50.9, +51.4; ^{13}C NMR, Table 4; ^1H NMR ($CDCl_3$, 80 MHz), δ 1.48 (d, $^2J_{PH}$ = 13.2 Hz, P–CH_3), 1.75 (d, $^2J_{PH}$ = 13.2 Hz, P–CH_3), 2.2 (s, C–CH_3), 2.25 (s, C–CH_3), 3.90 (s, both OCH_3); IR (neat) $\nu_{C=O}$ (cyclic) 1685 cm^{-1}, (acyclic) 1710 cm^{-1}. The mixture was used immediately in other reactions.

Ozonolysis of 6-Methoxy-3-methyl-1-phenyl-2,8,9,9a-tetrahydro-1(H)-*benzo*[e]*phosphindole 1-Oxide* (**6**)

A solution of 2.64 mg (0.8 mmol) of **6** in 50 mL of methanol–dichloromethane (1:1) was ozonized exactly as described for the ozonlysis of **2.** Chromatography (4% methanol in chloroform) led to 208 mg (71%) of a 1:1 mixture of diastereomers **10a** and **10b;** ^{31}P NMR ($CDCl_3$), δ +38.4, +39.9; ^{13}C NMR, Table 4; ^1H NMR ($CDCl_3$, 80 MHz), δ 2.25 (s, C–CH_3), 2.35 (s, C–CH_3), 3.82 (s, OCH_3), 3.88 (s, OCH_3); IR (neat) $\nu_{C=O}$ (cyclic) 1685, (acyclic) 1710 cm^{-1}. The mixture was used directly in other reactions.

Aldol Cyclization of **7**

A mixture of 0.40 g (1.85 mmol) of **7**, 7 mL of ethanol, and 7 mL of 12*N* HCl was refluxed for 48 h. The mixture was cooled, the solvent removed in vacuo, and the resultant oil dissolved in 25 mL of $CHCl_3$. The solution was washed with 10 mL of H_2O and then dried over $MgSO_4$. Removal of the solvent by rotary evaporation afforded 0.22 g (60%) of a yellow oil. Phosphorus-31 NMR ($CDCl_3$) analysis showed three components, δ +37.6 and +37.8 (**11a,b**), and +41.7 (**12**) in a 2:2:1 ratio, respectively. Attempts to separate these compounds by chromatographic methods were not successful. Partial ^{13}C NMR ($CDCl_3$), C=O, for **11a, 11b,** 190.8 and 190.9 (J_{PC} = 3.7 Hz); for **12,** 197.6 (4.0); C=C–CO for **11a, 11b,** 123.6 and 125.3 (2.7); C=C–CO for **11a, 11b,** 157.7, 160.1; C=C–P for **12,** 124.9 (94.0); C=C–P for **12,** 142.2 (8.0).

1,2,3,4,5,6,7,8-Octahydro-3-oxo-1-phenylphosphinoline 1-Oxide (**13**)

To 50 mL of methanol was added 1.1 g (4.5 mmol) of **8** and 0.4 g (9.0 mmol) of sodium methylate. After the mixture had been stirred overnight at room temperature, 6 mL of concentrated HCl was added and the resultant mixture stirred an additional 24 h. The solvent was removed in vacuo and the residue redissolved in chloroform, filtered, and chromatographed on silica gel (5% methanol in chloroform) to yield 0.8 g (77%) of **13** as a colorless oil; ^{31}P NMR ($CDCl_3$), δ +32.0; ^{13}C NMR ($CDCl_3$), C2, 47.8 (J_{PC} 33.6 Hz); C3, 197.9 (4.0); C4, 48.9 (18.8); C4a, 145.5 (8.1); C5, 31.7 (14.8); C6, 21.6; C7 (or C8), 21.5 (10.7); C8 (or C7), 22.9 (8.1); C8a, 124.8 (95.3); C-*ipso*, 130.9 (107.4); C-*ortho*, 130.2 (107.4); C-*meta*, 128.6 (12.1); C-*para*, 132.1 (2.6); ^{1}H NMR ($CDCl_3$, 80 MHz), δ 1.4–3.80 (m, 12H, CH_2), 7.25–7.80 (m, 5H, Ar-H); IR (neat) $\nu_{C=O}$ 1710 cm^{-1}. Analysis calculated for $C_{15}H_{17}O_2P \cdot H_2O$: C, 65.20; H, 6.75; P, 11.42; found, C, 64.77; H, 6.88; P, 11.13.

Aldol Cyclization of **9**

A solution consisting of 0.1 g (0.34 mmol) of a 1 : 1 mixture of diketones **9a** and **9b**, 5 mL of H_2O, 5 mL of methanol, and 0.140 g (3.5 mmol) of NaOH was refluxed for 3 h. The mixture was cooled, and 5% HCl was added until the solution became slightly acidic. The aqueous phase was then extracted with dichloromethane (3 × 30 mL); the organic portions were combined and dried over $MgSO_4$. Chromatography on silica gel (3% methanol in chloroform) afforded 55 mg (59%) of a mixture giving three P–CH_3 signals for **14a, 14b,** and **15** in the ^{1}H NMR spectrum ($CDCl_3$, 300 MHz), δ 1.50, 1.64, and 1.74 (all d, $^2J_{PH}$ = 12.7 Hz, ratio 6 : 3 : 1, respectively); partial ^{13}C NMR ($CDCl_3$), δ 199.0 (C=O, **14a, 14b**), 191.4 (C=O, **15**). Analysis calculated M^+ for $C_{15}H_{17}O_3P$, 276.0912; found, *m/z*, 276.0916.

Silylations of the Aldol Condensation Products **14a** *and* **15** *from Diketone* **9**

To 0.4 g (1.44 mmol) of the mixture of **14a,b** and **15** from diketone **9** in 0.3 mL of $CDCl_3$ was added 0.3 mL (1.73 mmol) of bis(trimethylsilyl)trifluoroacetamide. A slight warming was observed upon the addition. The crude product **16** had ^{31}P NMR ($CDCl_3$), δ +34.4; ^{13}C NMR ($CDCl_3$, numbering in text), C2, 68.0 (117.8 Hz); C3, 161.8 (4.2); C4, 88.8 (9.8); C4a, 139.2 (4.9); C5 or C8a (or both), 125.6; C6, 111.6; C7, 158.7; C8, 113.0; C9, 30.3 (7.4); C10, 38.7; C10a, 83.4 (122.5); C11, 17.6 (110.4); C12 (54.9). The compound could not be isolated due to ease of hydrolysis. Similarly, a 0.1-g (0.36-mmol) mixture of **14a,b** and **15** in 0.5 mL of $CDCl_3$ was treated with 0.17 mL (0.72 mol) of *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide. A slight warming was observed upon addition. The product had a single ^{31}P NMR ($CDCl_3$) signal at +34.5 and a ^{13}C NMR spectrum closely matching that of **16.** The compound could not be isolated due to water sensitivity.

P-Deoxygenation of Oxide **10** *and Reaction of Phosphine* **20** *with HCl*

To a solution of 0.63 mL (6.19 mmol) of trichlorosilane in 50 mL of dry benzene was added 1.80 mL of pyridine. To this was added 1.10 g (3.09 mmol) of an equal mixture of **10a** and **10b** in 5 mL of dry benzene. The mixture was refluxed for 1.5 h and then cooled in an ice bath for addition of 20 mL of 5% NaOH. The mixture was stirred for 15 min and the layers were separated. The aqueous layer was extracted with benzene (2 × 15 mL). The organic portions were combined, dried ($MgSO_4$), and rotary evaporated to yield 0.72 g (65%) of **20a** and **20b** (1 : 1) as a clear oil; ^{31}P NMR ($CDCl_3$), δ −18.3 and −23.4. Portions of the isomer mixture were used directly in tests of aldol cyclization. With basic reagents (aqueous NaOH, NaOH in MeOH, NaOMe in MeOH), no reaction occurred. On treatment of a chloroform solution of the phosphines with aqueous HCl, the phosphines were decomposed in about 30 min. The mixture was extracted with water and the layers were separated. The organic layer contained 6-methoxytetralone, according to the ^{1}H NMR spectrum. The aqueous layer contained the phosphorus product **21**; ^{31}P NMR = δ +20.9, $^1J_{PH}$ 515 Hz; ^{1}H NMR, δ 2.3 (s, CH_3), 3.2–3.6 (m, CH_2CH_2), 7.5 (ArH), 7.7 (d, $^1J_{PH}$ 490 Hz, P–H).

Attempted Aldol Cyclization of Diketone **10**

A 0.375-g sample of phospholene oxide **6** was ozonized as described and after the reduction of the ozonide and removal of solvents, the residual diketone **10** was dissolved in a solution of 10 mL of water and 10 mL of MeOH containing 160 mg of NaOH. The mixture was stirred overnight, and then the MeOH was removed on a rotary evaporator. Water (20 mL) was added and the solution neutralized with 10% HCl. The solution was extracted with three 10-mL portions of chloroform. Solvent was removed and a portion of the residue (200 mg) was dissolved in $CDCl_3$. Both the ^{1}H and the ^{13}C NMR spectra showed the product to be primarily 6-methoxytetralone.

1,4,5,6,7,8-Hexahydro-2-methyl-4-phenyl-1,4-benzazaphosphinine 4-Oxide (**22**)

A mixture of 0.72 g (2.6 mmol) of **8,** 1.0 g (0.013 mol) of NH_4OAc, and 100 mL of acetic acid was refluxed for 16 h. Removal of the solvent by rotary, evaporation followed by chromatography on silica gel (5% methanol in chloroform) gave 0.6 g of a mixture of

ketone **11** and **22** (^{31}P NMR, δ +37.6 and +12.4, respectively). Chromatography on silica gel (2% methanol in chloroform) afforded 100 mg (15%) of **22** in high purity, mp 290–291°C (decomp); ^{31}P NMR ($CDCl_3$), δ +10.8; ^{13}C NMR ($CDCl_3$, numbering in text), C2, 147.8; C3, 88.8 (J_{CP} 106.8 Hz); C4a, 100.9 (103.9); C5, C6, C7, P–CH_3 unresolved at 22–23; C8 (tentative) 28.3 (8.0); C8a, 143.6 (3.5); C-*ipso*, 135.6 (118.5); C-*ortho*, 132.3 (10.8); C-*meta*, 127.9 (12.7); C-*para*, 130.5 (2.4); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 1.30–1.90 (m, 7H, –CH_2–$\underline{CH_2}$–$\underline{CH_2}$–CH_2, CH_3), 2.30–2.52 (m, 4H–$\underline{CH_2}$–CH_2–$\underline{CH_2}$), 5.82 (d, $^2J_{PH}$ = 7.9 Hz, 1H, =C–H), 7.35–7.72 (m, 5H, Ar–H), 8.0 (s, 1H, N–H). Analysis calculated M^+ for $C_{15}H_{18}NOP$, 259.1110; found, *m/z*, 259.1118.

2,4-Dimethyl-8-methoxy-1,4,5,6-tetrahydronaphth[1,2-b]-1,4-azaphosphinine 1-Oxide (**23**)

To 1.0 g (3.8 mmol) of **9** dissolved in 30 mL of acetic acid was added 3.0 g (38 mmol) of ammonium acetate. The mixture was refluxed for 20 h and then concentrated by rotary evaporation. Chromatography on silica gel (8% methanol in chloroform) led to isolation of 400 mg (38%) of **23** as a brown oil; ^{31}P NMR ($CDCl_3$), δ +11.8; ^{13}C NMR ($CDCl_3$, numbering in text), C2, 147.7; C3, 89.9 (J_{CP} 105.2 Hz); C4a, 99.7 (102.1); C5, 20.0 (9.4); C6, 28.4 (10.3); C6a, 140.1; C7, 113.4, C8, 159.8; C9, 111.3; C10, 124.2; C10a, 121.9 (10.6); C10b, 140.0; C–$\underline{CH_3}$, 22.7 (9.7); O–CH_3, 55.0; P–CH_3, 18.3 (88.6); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 1.47 (d, $^2J_{PH}$ = 13.9 Hz, 3H, P-CH_3), 2.10 (s, 3H, CH_3), 2.20–3.60 (m, 4H, –CH_2–CH_2–), 3.71 (s, 3H, OCH_3), 4.78 (d, $^2J_{PH}$ = 7.92 Hz, 1H, =C–H), 6.65 (m, 2H, Ar–H), 7.48 (d, $^2J_{HH}$ = 7.1 Hz, 1H, Ar–H), 8.55 (s, 1H, N–H). Satisfactory analyses were not obtained.

8-Methoxy-2-methyl-4-phenyl-1,4,5,6-tetrahydronaphth[1,2-b]-1,4-azaphosphinine 1-Oxide (**24**)

To a solution of 1.0 g (2.8 mmol) of **10** in 30 mL of acetic acid was added 1.0 g (13.0 mmol) of ammonium acetate. The mixture was refluxed overnight and then concentrated by rotary evaporation to afford a black oil. Chromatography on silica gel (5% methanol in chloroform) led to 300 mg of **24** as a tan solid; mp 240°C (decomp); ^{31}P NMR ($CDCl_3$), δ +9.36; ^{13}C NMR ($CDCl_3$, numbering in text), C2, 147.3; C3, 90.8 (J_{CP} 106.4 Hz); C4a, 99.6 (105.9); C5, 20.2 (9.8); C6, 28.3 (6.5); C6a, 140.0; C7, 113.5; C8, 159.5; C9, 111.3; C10, 122.7; C10a, 121.6 (7.2); C10b, 140.3 (4.1); C–CH_3, 22.5 (12.1); O–CH_3, 54.8; C-*ipso*, 135.8 (120.7); C-*ortho*, 132.0 (13.3); C-*meta*, 127.5 (15.2); C-*para*, 130.3 (2); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 2.22 (s, 3H, CH_3), 2.5–2.8 (m, 4H, –CH_2–CH_2–), 3.80 (s, 3H, OCH_3), 5.02 (d, $^2J_{PH}$ = 7.4 Hz, 1H, =C–H), 6.75 (m, 2H, Ar–H), 7.2–7.8 (m, 6H, Ar–H), 7.45 (s, 1H, N–H). Analysis calculated for $C_{20}H_{21}NO_2P \cdot 1/2\ H_2O$, C, 69.35; H, 6.11; N, 4.04; P, 8.94; found, C, 69.77; H, 6.11; N, 3.96; P, 9.09.

3,3-Ethylenedioxy-1,2,3,4,5,6,7,8-octahydro-1-phenylphosphinoline 1-Oxide (**25**)

A mixture of 190 mg (0.73 mmol) of ketone **13**, 65 mg (1.0 mmol) of ethylene glycol, 20 mg of *p*-toluenesulfonic acid, and 30 mL of toluene was refluxed for 18 h. The mixture was then washed with saturated $NaHCO_3$ (2 × 25 mL) and dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the residue chromatographed on silica gel (3% methanol in chloroform) to yield 151 mg (68%) of **25** as a colorless oil; ^{31}P NMR ($CDCl_3$), δ +28.3; ^{1}H NMR ($CDCl_3$, 80 MHz), δ 1.45–2.65 (m, 12H, CH_2), 3.72–4.15 (m, 4H, O–CH_2–CH_2–O), 7.32–7.90 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$), C2, 38.1 (J_{CP} 61.0 Hz); C3, 106.5 (2.4); C4, 43.0 (7.3); C4a, 147.7 (9.9); C5, 32.4 (12.2); C6, 21.8; C7 (or C8), 21.7 (8.5); C8 (or C7), 22.5 (8.5); C8a, 123.0 (95.2); $O(CH_2)_2O$, 64.5 and 64.3; C-*ipso*, 132.4 (101.3); C-*meta*, 128.2 (12.2); C-*ortho* and -*para*, 131–132 (overlapped). The ketal was used without further purification in the synthesis of **26**.

cis-*1-Cyclohexyl-1,2,3,4,4a5,6,7,8,8a-decahydro-3,3-ethylenedioxyphosphinoline 1-Oxide* (**26**)

A mixture of 150 mg (0.5 mmol) of ketal **25**, 50 mL of methanol, and 50 mg of PtO_2 was placed in a Parr pressure bottle and shaken under H_2 (60 psi) for 28 h. The solution was filtered through Celite and the solvent removed in vacuo to give a pale yellow oil. The oil was chromatographed on silica gel (3% methanol in chloroform) to yield 100 mg (64%) of **26** as a colorless oil. Crystallization with cyclohexane gave white needles, mp 186–188°C; ^{31}P NMR ($CDCl_3$), δ +46.8; partial ^{13}C NMR ($CDCl_3$), δ 63.9, 65.4 (s, –O$\underline{CH_2}$–$\underline{CH_2}$–O), 108.0 (d, $^2J_{PC}$ = 2.6 Hz, C—3); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 1.10–2.28 (m, 24H, CH, CH_2), 2.22 (m, 1H, fusion (P–CH), 3.85–4.15 (m, 4H, OCH_2CH_2O). Analysis calculated for $C_{17}H_{29}O_2P \cdot H_2O$, C, 61.80; H, 9.46; P, 9.37; found, C, 61.30; H, 9.52; P, 9.66.

cis-*1-Cyclohexyl-1,2,3,4,5,6,7,8-octahydro-3-oxophosphinoline 1-Oxide* (**27**)

A mixture of 6 mg (0.02 mmol) of ketal **26**, 1 mL of methanol, and 1 mL of 3*N* HCl was heated for 2 h at 50°C. The mixture was cooled and 10 mL of H_2O was added. The solution was extracted with chloroform (3 × 10 mL) and the combined organic layers dried over Na_2SO_4. Removal of the solvent by

rotary evaporation gave 4 mg (77%) of a clear oil. Analysis by ^{31}P NMR showed only one phosphorus component (**27**); ^{31}P NMR ($CDCl_3$), δ +54.2; ^{13}C NMR ($CDCl_3$), δ 209.8 (s, C=O); ^1H NMR ($CDCl_3$, 300 MHz) showed only aliphatic protons, δ 1.2–3.05. Analysis calculated M^+ for $C_{15}H_{25}O_2P$, 268.1591; found *m/z*, 268.1591.

3-Hydroxy-1,2,3,4,5,6,7,8-octahydro-1-phenylphosphinoline 1-Oxide (**28**)

To a mixture of 18 mg (0.5 mmol) of $NaBH_4$ in 4.0 mL of ethanol was added a solution of 100 mg (0.8 mmol) of **27** in 4.0 mL of ethanol. The reaction mixture was stirred 3 h at room temperature and then treated with 5 drops of acetone. The solvent was removed by rotary evaporation and the residue redissolved in 10 mL of $CHCl_3$. The mixture was washed with $NaHCO_3$ (2 × 5 mL) and then once with 5 mL of 10% HCl. Chromatography on silica gel (4% methanol in chloroform) afforded 116 mg (57%) of **28** as a 2:1 mixture of isomers with ^{31}P NMR shifts of +28.3 and +30.1 ppm, respectively. Repeated chromatography on silica gel (4% ethanol in chloroform) gave pure samples of each isomer.

For **28a**, ^{31}P NMR ($CDCl_3$), δ +28.3; partial ^{13}C NMR ($CDCl_3$), C2, 38.5 (J_{PC} 62.5 Hz); C3, 62.6; C4, 42.4 (6.3); C4a, 149.6 (10.1); C5, 32.3 (8.5); C8, 22.8 (7.6); C8a, 123.4 (92.7); ^1H NMR ($CDCl_3$, 300 MHz), 1.20–2.65 (m, 12H, CH_2), 4.50 (m, 1H, CH), 4.8 (s, 1H, OH), 7.35–7.70 (m, 5H, Ar–H); IR (CCl_4) ν_{O-H} 3410 cm^{-1} (br).

For **28b**, ^{31}P NMR ($CDCl_3$), δ +30.1; partial ^{13}C NMR ($CDCl_3$), C2, 37.5 (64.9); C3, 64.0; C4, 41.9 (7.9); C4a, 149.1 (10.0); C5, 32.5 (8.5); C8, 22.8 (7.8); C8a, 122.4 (98.7); ^1H NMR ($CDCl_3$, 300 MHz), 1.10–2.45 (m, 12H, CH_2), 4.05 (m, 1H, CH), 3.95 (s, 1H, OH), 7.30–7.70 (m, 5H, Ar–H); IR (CCl_4), ν_{O-H} 3410 cm^{-1} (br). Analysis, calculated M^+ for $C_{15}H_{19}O_2P$, 262.1121; found, *m/z*, 262.1121.

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