Carbon–Phosphorus Heterocycles. A New Route to Tetrahydrophosphinolines, Tetrahydroisophosphinolines, and Related Systems via Cyclization of Alkenyl-Substituted Phosphonium Salts with 115% Polyphosphoric Acid[1]

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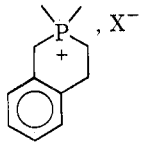
A convenient method of wide scope for the synthesis of the rare tetrahydroisophosphinolinium and tetrahydrophosphinolinium salts has been developed from readily available starting materials. Treatment of a variety of tertiary phosphines (all containing an aryl group and/or an arylmethyl group) with allylic type halides gave phosphonium salts containing a β-alkenyl substitutent. Cyclization of these salts occurred in the presence of 115% polyphosphoric acid (PPA) at 160° for 30 min to give the C–P heterocyclic systems in modest to good yields (24–82%). Work-up of the reaction mixtures simply involved addition to ice water. The resulting *homogeneous* solution was treated with KPF_6 (saturated aqueous solution) which caused the precipitation of the PF_6^- salt of the respective isophosphinolinium or phosphinolinium system. ^1H NMR, ^{31}P NMR, infrared and mass spectral and elemental analyses support the structures of these phosphorus analogs of the corresponding tetrahydroisoquinoline and tetrahydroquinoline heterocycles. Benzyldiphenylvinylphosphonium bromide (**3e**) cyclized at 300° with 115% PPA after 1.25 hr to give, after work-up, 1,2,3,4-tetrahydro-2,2-diphenylisophosphinolinium hexafluorosphate (**4e**, 51%). Thus, formation of the six-membered ring was favored over formation of the phospholane ring system. A mechanism is tentatively put forth to involve a rather classic electrophilic substitution in the cyclization process. The role of the anion(s) of PPA is unknown but probably involves direct association with the phosphonium cation prior to addition of KPF_6.

Carbon–phosphorus (C–P) heterocyclic systems that are the analogs of the quinoline and isoquinoline ring system have rarely been recorded.[3] A paucity of synthetic methods exists for these C–P heterocycles, but the procedures are fraught with tedious manipulations, uncommon starting materials, and long overall reaction times. A number of articles have appeared concerning phosphinolines[4] and isophosphinolines[5] in recent years, but no simple, systematic routes have been published from readily available precursors. We have discovered[6] that 1,2,3,4-tetrahydroisophosphinolines **1** and 1,2,3,4-tetrahydrophosphinolines **2** can be



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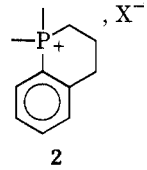

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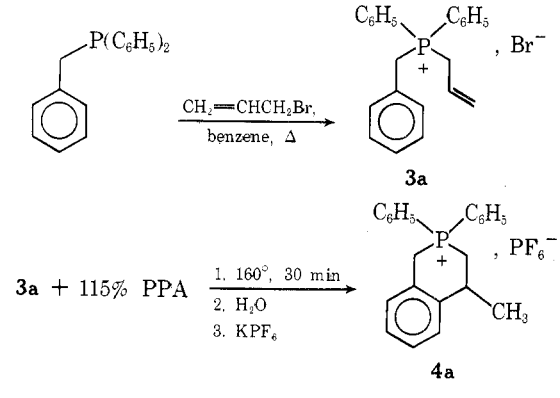
prepared as phosphonium salts from simple open-chain precursors that can easily be synthesized from readily accessible reagents.

To illustrate, benzyldiphenylphosphine can be obtained as shown in an inverse Grignard flask and, without isolation, can be quaternized with allyl bromide to yield allylbenzyldiphenylphosphonium bromide (**3a**). In the presence of 115% polyphosphoric acid (PPA)[7] at 160° for 30 min, phosphonium salt **3a** undergoes ring closure (Scheme I) to produce the 1,2,3,4-tetrahydro-4-methyl-2,2-diphenylisophosphinolinium hexafluorophosphate (**4a**) in good yield (75%) via addition of saturated aqueous KPF_6 to the mixture. Reprecipitation from methylene chloride by the slow addition of ether gave pure **4a**. Other examples of this novel cyclization are shown in Chart I with more detailed information on the properties of compounds listed in Tables I and II.

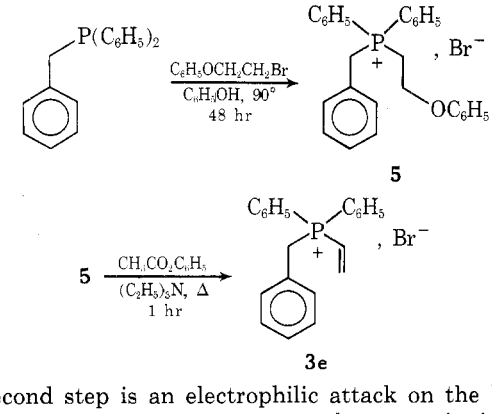
$$(C_6H_5)_2PCl + C_6H_5CH_2MgCl \xrightarrow{\text{ether}} (C_6H_5)_2PCH_2C_6H_5$$

During the cyclization process, a gas is given off, presumably HBr.[8] On the assumption that protonation of **3a** by PPA occurs in such a manner so as to remove Br^- (lost as HBr) and to disrupt the alkene linkage also, the most logical second step is an electrophilic attack on the benzene ring. Loss of a proton to regenerate the aromatic ring could logically follow. The P^+ group is insulated from the aromatic ring by a methylene group and apparently has little effect on the cyclization.

Scheme I



Scheme II



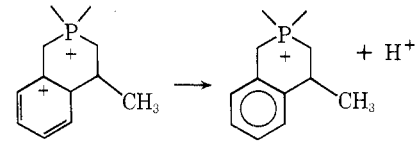
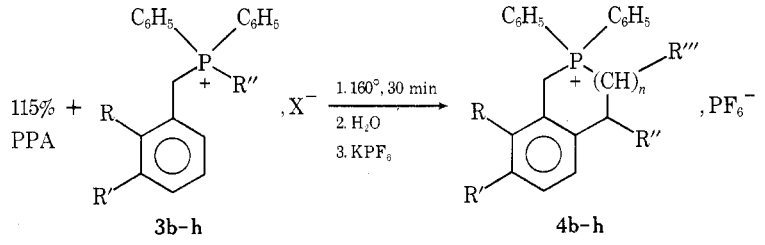


Chart I



Compd	R	R'	R''	X⁻	Compd	R	R'	R''	R'''	n
3b	H	CH_3	$-CH_2CH{=}CH_2$	Br	**4b**[a]	H	CH_3	CH_3	H	1
3c	H	H	$-CH_2CH{=}CHCH_3$	Br	**4c**	H	H	CH_3	H	2
3d	H	CH_3	$-CH_2CH{=}CHCH_3$	Br	**4d**	H	CH_3	CH_3	H	2
3e	H	H	$-CH{=}CH_2$	Br	**4e**[b]	H	H	H	H	1
3f	H	H		Br	**4f**	H	H	$-(CH_2)_3-$		1
3g	Benzo		$-CH_2CH{=}CH_2$	PF_6	**4g**	Benzo		CH_3	H	1
3h	Benzo			Cl	**4h**	Benzo		$-(CH_2)_3-$		1

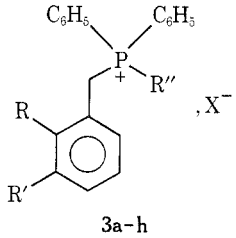
[a] Isolated as the bromide salt and was converted to the hexafluorophosphate derivative. [b] The reaction was performed at 300° for 1.25 hr.

The preference for a five- or six-membered ring being formed was examined with **3e**, although from theoretical principles both would have high-energy intermediate precursors. It was observed that **4e** was produced only when a temperature of 300°C was maintained for 1.25 hr. NMR analysis of the reaction mixture indicated that only a metathesis exchange took place at lower temperatures (160 and 180°, respectively).

Benzyldiphenylvinylphosphonium bromide (**3e**) was obtained from a modification of our procedure and one used by Shutt and Trippett[9] as shown in Scheme II. As before, the benzyldiphenylphosphine produced was not isolated but was allowed to react with β-bromophenetole to make the intermediate benzyl-β-phenoxyethyldiphenylphosphonium bromide (**5**). Compound **5** was then treated with a solution of ethyl acetate–triethylamine to generate **3e**.

Interestingly, compounds **3c** and **3d** underwent ring closure to produce the seven-membered rings, **4c** and **4d**, and *not* the six-membered ring. These cyclic compounds were identified by NMR (and infrared, mass spectral, and elemental analyses) owing to the characteristic doublet seen in the spectra for the methyl group on the saturated ring and not the ethyl substituent. With this in mind, we could assume that protonation had occurred at the γ carbon (in

Table I

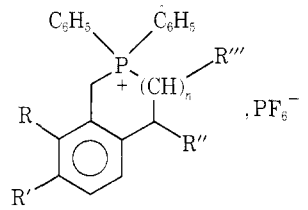


3a-h

Compd	R	R'	R''	X⁻	Mp, °C	Quaternizing solvent (reaction time, hr)	Equiv of halide[a]	Yield, %	Molecular formula	Anal., % P	
3a[b]	H	H	$-CH_2CH{=}CH_2$	Br	201–203	Benzene (24)	2.49	52	$C_{22}H_{22}BrP$	Calcd	7.80
										Found	7.58
3b[b,c]	H	CH_3	$-CH_2CH{=}CH_2$	Br	173–175	Benzene (24)	1.84	48	$C_{23}H_{24}BrP$	Calcd	7.53
										Found	7.50
3c[b,c]	H	H	$-CH_2CH{=}CHCH_3$	Br	177–180	Toluene (24)	1.33	48	$C_{23}H_{24}BrP$	Calcd	7.53
										Found	7.64
3d[b,c]	H	CH_3	$-CH_2CH{=}CHCH_3$	Br	170–173	Ether–benzene (2.75:1) (48)	1.33	35	$C_{24}H_{26}BrP$	Calcd	7.28
										Found	7.19
3e[d]	H	H	$-CH{=}CH_2$	Br	220–222	Phenol (48)	1.0	62	$C_{21}H_{20}BrP$	Calcd	8.08
										Found	8.16
3f	H	H		Br	235–236	Benzene (24)	1.44	70	$C_{24}H_{24}BrP$	Calcd	7.33
										Found	7.20
3g	Benzo		$-CH_2CH{=}CH_2$	PF_6	158–161	Benzene (2.0)	1.1	43	$C_{26}H_{24}F_6P_2$	Calcd	12.10
										Found	11.81
3h	Benzo			Cl	223–226	Benzene (60)	1.41	65	$C_{28}H_{26}ClP$	Calcd	7.23
										Found	7.24

[a] Based on 1 equiv of phosphine. [b] Yield based on starting benzylic halide. [c] When ether is used as the quaternizing solvent, the yields of **3b–d** are decreased to 25, 26, and 29%, respectively. [d] Isolated as benzyl-β-phenoxyethyldiphenylphosphonium bromide and, upon treatment with ethyl acetate–triethylamine, converted to **3e**. Previously reported in ref 9.

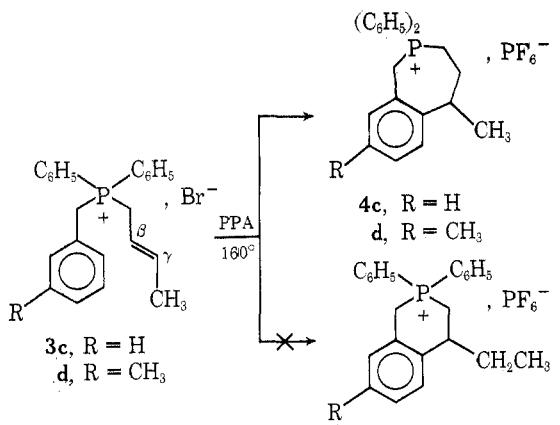
Table II



4a-h

Compd	R	R'	R''	R'''	n	Mp, °C	Yield, %	Molecular formula	Anal., % P
4a	H	H	CH_3	H	1	172.5–174.5	75	$C_{22}H_{22}F_6P_2$	Calcd 13.40
									Found 13.09
4b[a]	H	CH_3	CH_3	H	1	185.5–187	28	$C_{23}H_{24}F_6P_2$	Calcd 13.00
									Found 12.97
4c	H	H	CH_3	H	2	214–216	30	$C_{23}H_{24}F_6P_2$	Calcd 13.00
									Found 12.88
4d	H	CH_3	CH_3	H	2	233–235	24	$C_{24}H_{26}F_6P_2$	Calcd 12.63
									Found 12.69
4e	H	H	H	H	1	174–176	51	$C_{21}H_{20}F_6P_2$	Calcd 13.82
									Found 13.61
4f[b]	H	H	$-(CH_2)_3-$		1	326–328	55	$C_{24}H_{24}BrP$	Calcd 7.33
									Found 7.23
4g	Benzo		CH_3	H	1	219–220	55	$C_{26}H_{24}F_6P_2$	Calcd 12.10
									Found 11.92
4h	Benzo		$-(CH_2)_3-$		1	264–266	25	$C_{28}H_{26}F_6P_2$	Calcd 11.52
									Found 11.33

[a] Isolated as the bromide and converted to the hexafluorophosphate derivative. [b] Isolated as the bromide derivative.

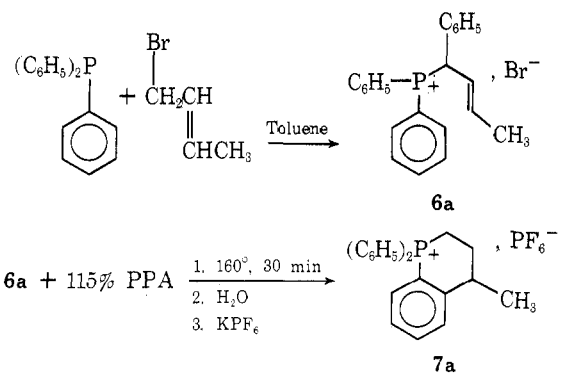


3c, R = H
d, R = CH_3

PPA, 160°

4c, R = H
d, R = CH_3

Scheme III

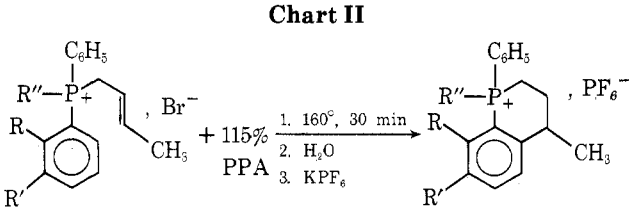


relation to the P atom). The suspected cation formed preferentially can possibly be defended on the grounds of greater hyperconjugative stabilization at the γ carbon because there are five hydrogens available as compared to just four adjacent hydrogens on the β carbon in the cation formed via protonation at the γ carbon in **3c** or **3d**. Moreover, protonation at the β carbon would also place the two positive centers further apart, possibly creating a more stable intermediate owing to less charge repulsion.

Surprisingly, this synthetic procedure was also found to be applicable to the preparation of the isomeric phosphinoline derivatives. For example, it was possible to react triphenylphosphine with halo alkenes, such as 1-bromo-2-butene, to give 2-butenyltriphenylphosphonium bromide[10] (**6a**) in high yield (94%). When treated with PPA (Scheme III), **6a** underwent ring closure to 1,2,3,4-tetrahydro-4-methyl-1,1-diphenylphosphinolinium hexafluorophosphate (**7a**) (82%). Additional examples are listed in Chart II along with more detailed information on the physical properties of the products and precursors in Tables III and IV.

Unlike the isophosphinoline system, the cyclic intermediate precursors suspected for the phosphinoline derivatives are not easily defended. The obvious difficulty with

Chart II



6b-d

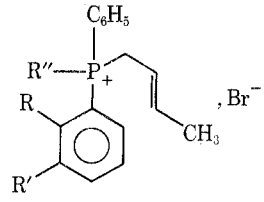
Compd	R = R'	R''
6b	H	CH_3
6c	H	C_2H_5
6d	Benzo	C_6H_5

7b-d

Compd	R = R'	R''
7b	H	CH_3
7c	H	C_2H_5
7d	Benzo	C_6H_5

applying current theory as a rationale is that the benzene ring is already bonded to a positively charged P atom. Intuitively, an intermediate such as represented by 8 seems untenable on the grounds of suspected strong electrostatic repulsion between like charges on adjacent groups. However, PPA anion (PPA^{n-}) very likely stabilizes the intermediate by association, since an excess of this anion is presumably available. This is supported by the observation that the entire reaction mixture is soluble in water. Only upon satura-

Table III

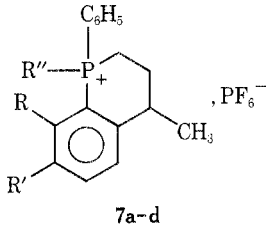


6a-d

Compd	R	R'	R''	Mp, °C	Quaternizing solvent (hr)	Equiv of halide[a]	Yield, %	Molecular formula	Anal., % P
6a[b]	H	H	C_6H_5	241–243	Xylene (19)	0.73	94	$C_{22}H_{22}BrP$	
6b	H	H	CH_3	187–189	Xylene (18)	0.73	88	$C_{17}H_{20}BrP$	Calcd 9.24 Found 9.32
6c	H	H	C_2H_5	198–200	Toluene (12)	1.43	77	$C_{18}H_{22}BrP$	Calcd 8.87 Found 9.15
6d	Benzo		C_6H_5	259.5–261	Benzene (12)	1.81	59	$C_{26}H_{24}BrP$	Calcd 6.92 Found 7.00

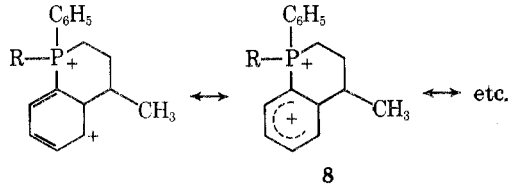
[a] Based on 1 equiv of phosphine. [b] This compound was previously reported in ref 10.

Table IV



7a-d

Compd	R	R'	R''	Mp, °C	Yield, %	Molecular formula	Anal., % P
7a	H	H	C_6H_5	203.5–205	82	$C_{22}H_{22}F_6P_2$	Calcd 13.40 Found 13.42
7b	H	H	CH_3	179.5–182	67	$C_{17}H_{20}F_6P_2$	Calcd 15.48 Found 15.09
7c	H	H	C_2H_5	145–147	42	$C_{18}H_{22}F_6P_2$	Calcd 14.95 Found 14.90
7d	Benzo		C_6H_5	192–194.5	33	$C_{26}H_{24}F_6P_2$	Calcd 12.09 Found 11.99



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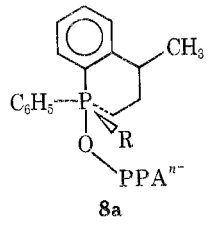


8a

tion of the aqueous solution with the PF_6^- anion did the phosphonium salt precipitate (in the case of **4f**, a saturated solution of NaBr was added). Further speculation seems unwarranted on the mechanism until more data become available, although an intermediate like **8a** is also reasonable.

Structural identification of members of the isophosphinoline and phosphinoline ring systems rests on elemental, infrared, mass spectral,[11] and NMR analyses found in Tables I–V. The most revealing physical data came from extensive ^1H NMR and ^{31}P NMR studies. The NMR spectrum of **4g** showed the methylene protons (attached to the naphthalene group) as a doublet each with geminal coupling. There was also observed a J_{PCH} of 16.0 Hz; apparently the geminal coupling is a result of the electronic arrangement and stereochemistry of the newly formed ring fusion. The methylene group can be characterized as an ABX system[12] (X = P) with values of $\delta_A = 4.61$, $\delta_B = 5.28$, $J_{AB} = 16.0$, $J_{AX} = J_{BX} = 16.0$ Hz. The newly formed methyl group in **4g** appears as a doublet of doubets at δ 1.75 ($J_{PCCCH} = 7$, $J_{HCCH} = 2.0$ Hz) which could be the result of long-range P–H coupling. This phenomenon is not observed in **4c** (or **4d**) as the methyl group appears as a clean doublet at δ 1.48 ($J_{HCCH} = 7$ Hz) in the seven-membered rings. The presence of the methyl group in **4g** also eliminates the possibility of a seven-membered ring. The ^1H NMR spectrum of **4e** showed that the benzylic protons adjacent to phosphorus occurred as a doublet (even at 25-Hz sweep width) which suggests that the two rings are probably close to being coplanar.

The negative ^{31}P chemical shift values for the open-chain phosphonium compounds listed in Table V show the differences to be relatively small. These compare very well with many open-chain compounds,[13] but it should be noted that phosphonium salts have on rare occasions been re-

Table V
NMR Spectral Data for Reaction Products

Compd	Ir absorption spectra in KBr,[a] selected bands, cm^{-1}	^1H NMR spectral assignments, chemical shifts, δ[b]	^{31}P NMR, δ[c]
3a	1443 (s), 1114 (vs), 997 (m), 940 (s), 745 (vs), 691 (vs)	4.26 [d of d (J_{PCH} = 15, J_{HCCH} = 6 Hz), PCH_2CH, 2 H], 4.99 [d (J_{PCH} = 14 Hz), $C_6H_5CH_2P$, 2 H], 5.16–5.80 (m, $-CH{=}CH_2$, 3 H), 7.13 (s, C_6H_5, 5 H), 7.5–8.14 [m, $(C_6H_5)_2P<$, 10 H]	−23.96[i]
3b	1433 (s), 1111 (vs), 999 (m), 942 (m), 745 (s), 694 (s)	2.10 (s, CH_3, 3 H), 4.28 [d of d (J_{PCH} = 15, J_{HCCH} = 6 Hz), PCH_2CH, 2 H], 4.92 [d (J_{PCH} = 15 Hz), $ArCH_2P$, 2 H], 5.14–5.76 (m, $-CH{=}CH_2$, 3 H), 6.78 (s, ArH, 1 H), 6.99 (s, ArH, 3 H), 7.46–8.06 [m, $(C_6H_5)_2P<$, 10 H]	
3c	1443 (s), 1111 (vs), 997 (m), 980 (m), 752 (vs), 690 (vs)	1.24–1.64 (m, CH_3, 3 H), 4.15 [d of d (J_{PCH} = 15, J_{HCCH} = 7 Hz), PCH_2CH, 2 H], 4.91 [d (J_{PCH} = 15 Hz), $C_6H_5CH_2P$, 2 H], 4.90–5.96 (m, CH=CH, 2 H), 7.10 (s, C_6H_5, 5 H), 7.46–8.02 [m, $(C_6H_5)_2P<$, 10 H]	−24.79[i]
3d	1431 (s), 1110 (s), 998 (m), 976 (m), 741 (vs), 688 (vs)	1.24–1.70 (m, $CHCH_3$, 3 H), 2.08 (s, $ArCH_3$, 3 H), 4.17 [d of d (J_{PCH} = 15, J_{HCCH} = 7 Hz), PCH_2CH, 2 H], 4.86 [d (J_{PCH} = 15 Hz), $ArCH_2P$, 2 H], 4.90–6.0 (m, CH=CH, 2 H), 6.77 (s, ArH, 1 H), 6.98 (s, ArH, 3 H), 7.48–8.16 [m, $(C_6H_5)_2P<$, 10 H]	
3e	1433 (s), 1111 (s), 995 (m), 977 (s), 960 (vs), 691 (s)	5.07 [d (J_{PCH} = 15 Hz), $ArCH_2P$, 2 H], 5.91–6.62 (m, $CH{=}CH_2$, 2 H), 6.97–7.40 (m, ArH, $PCH{=}CH_2$, 6 H), 7.46–8.06 [m, $(C_6H_5)_2P<$, 10 H]	
3f	1431 (m), 1111 (s), 746 (s), 698 (s), 690 (s)	1.30–1.80 (m, cyclopentenyl ring, 1 H), 2.00–2.76 (m, cyclopentenyl ring, 3 H), 5.00 (br m, CH, 1 H), 5.06 [d of d (J_{PCH} = 14, J_{HCCH} = 4 Hz), $C_6H_5CH_2P$, 2 H], 5.91 (br s, CH=CH, 2 H), 7.07 (s, $C_6H_5CH_2$, 5 H), 7.44–8.06 (m, $(C_6H_5)_2P<$, 10 H)	
3g[d]	1435 (m), 1114 (s), 933 (m), 836 (vs), 732 (m), 682 (m)	3.79 [d of d (J_{PCH} = 15, J_{HCCH} = 6 Hz), PCH_2CH, 2 H], 4.83 [d (J_{PCH} = 15 Hz), $ArCH_2P$, 2 H], 5.18–5.84 (m, $CH{=}CH_2$, 3 H), 7.12–7.96 (m, ArH, 17 H)	
3h[e]	1437 (m), 1114 (m), 801 (s), 780 (s), 725 (vs), 692 (vs)	1.98–2.74 (m, CH_2CH_2, 4 H), 4.30–4.70 (m, CH, 1 H), 5.17 [d (J_{PCH} = 15 Hz), $ArCH_2P$, 2 H], 5.96 (br m, CH=CH, 2 H), 7.06–8.06 (m, ArH, 17 H)	
4a[f]	1439 (s), 1117 (s), 840 (vs), 743 (s), 689 (s)	1.56–1.80 [d of d (J_{PCCCH} = 6, J_{HCCH} = 2 Hz), CH_3, 3 H], 2.35–2.80 (m, CH, 1 H), 3.10–3.64 (m, CH_2, 2 H), 4.02 [d (J_{PCH} = 14 Hz), ArCHP, 1 H], 4.10 [d (J_{PCH} = 14 Hz), ArCHP, 1 H], 7.22–7.96 (m, ArH, 14 H)	−17.17[j]
4b[f]	1439 (s), 1117 (s), 844 (vs), 743 (s), 690 (s)	1.56–1.80 [d of d (J_{PCCCH} = 6, J_{HCCH} = 2 Hz), CH_3, 3 H], 2.30 (s, $ArCH_3$, 3 H), 2.41–2.80 (m, CH, 1 H), 3.10–3.56 (m, CH_2, 2 H), 3.99 [d (J_{PCH} = 14 Hz), ArCHP, 1 H], 4.05 [d (J_{PCH} = 14 Hz), ArCHP, 1 H], 7.08–7.96 (m, ArH, 13 H)	
4c[f]	1437 (s), 1116 (s), 840 (vs), 746 (s), 690 (s)	1.48 [d (J_{HCCH} = 7 Hz), CH_3, 3 H], 1.66–2.96 (m, CH_2CH_2, 4 H), 3.02–3.42 (m, CH, 1 H), 4.05 [t (J_{PCH} = 15 Hz), CH, 1 H], 4.52 [t (J_{PCH} = 15.0 Hz), CH, 1 H], 7.06–7.98 (m, ArH, 14 H)	−14.22[j]
4d[f]	1435 (s), 1110 (s), 838 (vs), 745 (s), 690 (s),	1.47 [d (J_{HCCH} = 7 Hz), CH_3, 3 H], 1.64–2.94 (m, CH_2CH_2, 4 H), 2.30 (s, CH_3, 3 H), 3.04–3.38 (m, CH, 1 H), 3.98 [t (J_{PCH} = 15 Hz), CH, 1 H], 4.47 [t (J_{PCH} = 15.0 Hz), CH, 1 H], 6.96 (s, ArH, 1 H), 7.24–8.02 (m, ArH, 12 H)	
4e[f]	1437 (s), 1116 (s), 840 (vs), 758 (s), 746 (s), 691 (s)	2.90–3.56 (m, CH_2CH_2, 4 H), 4.12 [d (J_{PCH} = 14 Hz), CH_2, 2 H], 7.20–7.88 (m, ArH, 14 H)	
4f[g]	1437 (s), 1115 (s), 758 (s), 683 (m)	1.69–2.82 [m, $-(CH_2)_3-$, 6 H], 3.30 (m, ArCH, 1 H), 4.05 [t (J_{PCH} = 16 Hz), ArCHP, 1 H], 4.5 (m, PCH, 1 H), 5.34 [t (J_{PCH} = 16, J_{HCH} = 1 Hz), ArCHP, 1 H], 6.7–8.3 (m, ArH, 14 H)	
4g[e]	1441 (m), 1406 (s), 1114 (s), 835 (vs), 742 (m), 685 (m)	1.75 [d of d (J_{PCCCH} = 7, J_{HCCH} = 2 Hz), CH_3, 3 H], 3.00–3.14 (m, CH, 1 H), 3.50–3.98 (m, CH_2, 2 H), 4.61 [t (J_{PCH} = 16.0 Hz), CH, 1 H], 5.28 [t (J_{PCH} = 16.0 Hz), CH, 1 H], 7.06–8.52 (m, ArH, 16 H)	

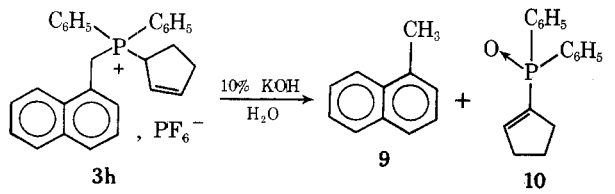
Table V
(Continued)

Compd	Ir absorption spectra in KBr,[a] selected bands, cm^{-1}	^1H NMR spectral assignments, chemical shifts, δ[b]	^{31}P NMR, δ[c]
4h[h]	1441 (s), 1397 (m), 1111 (s), 838 (vs), 731 (m), 686 (m)	2.04–3.00 [m, $-(CH_2)_3-$, 6 H], 3.64–3.96 (m, ArCH, 1 H), 4.06–4.40 (m, PCH, 1 H), 5.00 [t (J_{PCH} = 17 Hz), ArCHP, 1 H], 5.62 [t (J_{PCH} = 17 Hz), ArCHP, 1 H], 7.06–9.00 (m, ArH, 16 H)	
6a	1433 (s), 1110 (vs), 998 (m), 968 (m), 749 (s), 691 (s)	1.50–1.70 (m, CH_3, 3 H), 4.42–4.76 [d of d (J_{PCH} = 15, J_{HCCH} = 7 Hz), PCH_2CH, 2 H], 5.08–6.12 (m, CH=CH, 2 H), 7.54–8.0 (m, $(C_6H_5)_3P-$, 15 H)	−21.14[i]
6b	1433 (s), 1119 (vs), 996 (m), 977 (s), 760 (vs), 691 (s)	1.44–1.74 (m, $CHCH_3$, 3 H), 2.82 [d (J_{PCH} = 14 Hz), PCH_3, 3 H], 4.82 [d of d (J_{PCH} = 15, J_{HCCH} = 8 Hz), PCH_2CH, 2 H], 5.06–6.38 (m, CH=CH, 2 H), 7.54–8.2 (m, $(C_6H_5)_2P<$, 10 H)	−21.84[i]
6c	1433 (s), 1119 (vs), 975 (s), 767 (vs), 738 (vs)	1.06–1.48 [d of t (J_{PCCH} = 20, J_{HCCH} = 7 Hz), PCH_2CH_3, 3 H], 1.50–1.74 (m, $CHCH_3$, 3 H), 3.12–3.56 [s[i] (J_{PCH} = 13, J_{HCCH} = 7 Hz), PCH_2CH_3, 2 H], 4.25 [d of d (J_{PCH} = 15, J_{HCCH} = 7 Hz), PCH_2CH, 2 H], 5.02–6.2 (m, CH=CH, 2 H), 7.58–8.24 [m, $(C_6H_5)_2P<$, 10 H]	
6d	1431 (m), 1111 (s), 971 (s), 777 (s), 690 (s)	1.36–1.64 (m, CH_3, 3 H), 4.72 [d of d (J_{PCH} = 14, J_{HCCH} = 7 Hz), PCH_2CH, 2 H], 5.0–6.14 (m, CH=CH, 2 H), 7.34–8.46 (m, ArH, 17 H)	
7a[f]	1437 (s), 1115 (s), 840 (vs), 750 (s), 693 (s)	1.47 [d (J_{HCCH} = 7 Hz), CH_3, 3 H], 1.85–3.56 [m, (CH_2CH_2, CH), 5 H], 7.22–8.0 (m, ArH, 14 H)	−10.74[k]
7b[f]	1437 (m), 1119 (s), 840 (vs), 767 (s), 749 (s), 687 (s)	1.47 [d (J_{HCCH} = 6 Hz), CH_3, 3 H], 2.32–2.50 [2 d (J_{PCH} = 14 Hz), PCH_3, 3 H], 1.88–3.18 (m, CH_2CH_2, 4 H), 3.18–3.56 (m, CH, 1 H), 7.42–7.92 (m, ArH, 9 H)	−9.77[k]
7c[f]	1437 (m), 1114 (s), 840 (vs), 722 (s), 741 (s), 689 (s)	1.12–1.46 (m, PCH_2CH_3, 3 H), 1.45 [d (J_{HCCH} = 7 Hz), CH_3, 3 H], 1.98–3.10 [m (CH_2CH_2, PCH_2CH_3), 6 H], 3.18–3.52 (m, CH, 1 H), 7.42–7.92 (m, ArH, 9 H)	
7d[f]	1437 (m), 1111 (s), 840 (vs), 773 (s), 739 (s), 720 (m), 690 (s)	1.28 [d (J_{HCCH} = 7 Hz), CH_3, 3 H], 2.04–3.58 [m (CH_2CH_2, CH), 5 H], 7.03–8.38 (m, ArH, 16 H)	

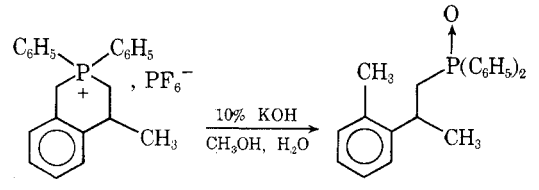
[a] The spectra were obtained on samples (4 mg) with KBr (400 mg) pellets. All compounds displayed medium to strong absorption in the regions 1431–1443 and 1110–1119 cm^{-1} which have often been assigned to the C_6H_5–P bond. Many examples are reported to support the assignment ranges but little definitive evidence is available to substantiate the correctness of the assignment; see L. C. Thomas, "Interpretation of the Infrared Spectra of Organophosphorus Compounds," Heyden, London, 1974. Chapter 15. [b] Spectra obtained on $DCCl_3$ solution of each compound with Me_4Si as internal standard; peak positions quoted in the case of doublets are measured from the approximate center, and relative peak areas are given as whole numbers. [c] ^{31}P resonance is relative to 85% H_3PO_4. [d] ^1H NMR spectra obtained in $DCCl_3$ with 4–5 drops of acetone-d_6 added. [e] NMR data was on the PF_6^- derivative in acetone-d_6. [f] ^1H NMR spectra obtained on $DCCl_3$ solution with 4–5 drops of CF_3CO_2H added. [g] Time averaged for 200 scans. [h] ^1H NMR spectra obtained in pyridine-d_5. Heteronuclear ^{31}P decoupling caused the collapse of the triplets at δ 5.00 and 5.62 to doublets (J = 17 Hz). Homonuclear decoupling gave a J_{PCH} = 17 Hz. [i] The spectra were obtained on samples (1.0 g) in $DCCl_3$ (4 ml). [j] The spectra were obtained on samples (1.0 g) in $DCCl_3$ (3 ml) and CF_3CO_2H (1 ml). [k] The spectra were obtained on samples (1.0 g) in CH_3CN (4.0 ml) with 5 drops of CF_3CO_2H added. The PF_6^- moiety has a value of δ +144.35 and δ +144.32 in **7a** and **7b**, respectively, compared to KPF_6 in H_2O (all compared to 85% H_3PO_4 standard external) which has a value of δ +144.68. [l] Appears as a sextet.

ported to have positive δ values. The cyclic derivatives also show expected shifts, but the variations could possibly be due to angular strain at phosphorus which could influence the symmetry around P and thus the shielding characteristics. Further work is obviously needed in this area before any quantitative judgments can be made.

Additional support for the structure identification of compounds **3h** and **4a** resulted from identification of the base hydrolysis products in each case. As a model for base hydrolysis, phosphonium salt **3h** gave 1-methylnaphthalene (**9**) and 1-cyclopentenyldiphenylphosphine oxide (**10**) in modest yields. Thus C—P bond cleavage at the benzylic position was found to take precedence as expected.[14] Similar results were observed in the preparation of **11**. Compound **9** was compared to the known compound while **10** and **11** were identified by elemental analyses and spectral data.



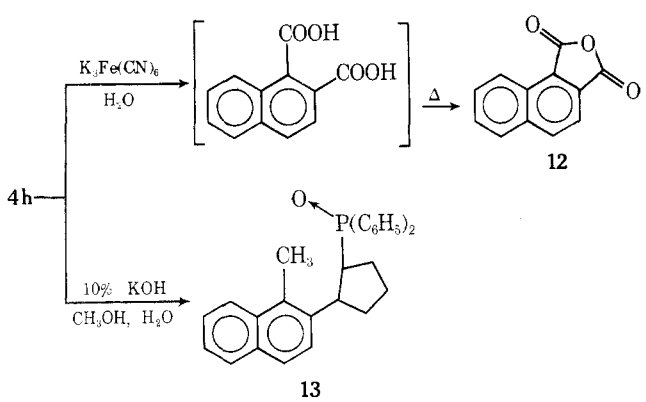
3h **9** **10**



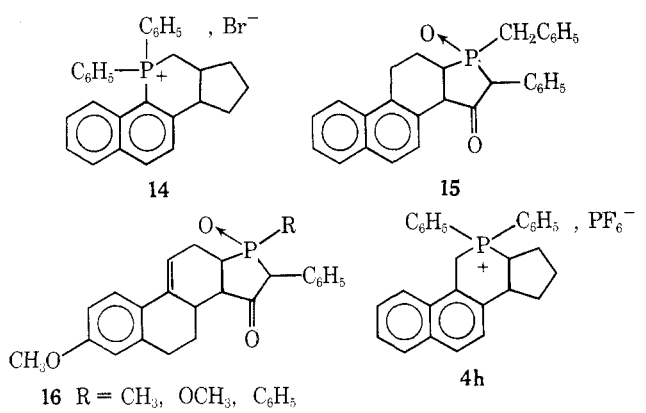
4a **11**

Oxidative degradation of **4h** with potassium ferricyanide and dehydration of the resulting diacid (Scheme IV) gave the known 1,2-naphthalene dicarboxylic anhydride (**12**), establishing that the new ring juncture was formed at the 2 position of the naphthalene ring. Further structural information came from hydrolysis of **4h** in 10% KOH (4:1 methanol–water), which cleaved the naphthylic C–P bond to give **13** in good yield. The NMR spectrum, infrared spectrum, and elemental analysis of **13** support the expected structure.

Scheme IV



Interest in heterosteroids as possible regulatory antagonists in metabolism has made the synthesis of new representatives of this class desirable. Although several attempts[15] to synthesize phosphasteroids (where carbon is replaced by phosphorus in the steroid skeleton) are recorded, only three examples have been reported in the literature to date. The synthesis of **14** (an 11-phosphasteroid)[16] and similar structures **15**[17] and **16**,[18] both possessing the



17-phosphasteroidal skeleton, were only very recently advanced. We report herein the synthesis of a fourth phosphasteroid, **4h**, where P is incorporated in the 12 position and several model compounds. The utility of heterophenanthrenes as precursors and model compounds for the synthesis of heterosteroids has been well recognized. However, few examples of C–P heterophenanthrenes are known[19] and the routes to these are often very tedious. Work is continuing on the extention of the method for the preparation of novel phosphorus heterocycles.

Experimental Section

General Data. Melting points were obtained with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-5A unit as KBr pellets. ^1H NMR and ^{31}P NMR spectra were obtained with a XL-100(15) Varian spectrometer and run in $DCCl_3$ with tetramethylsilane as an internal standard unless otherwise indicated. Mass spectral analyses were performed on a CEC Model 21 HR unit. Elemental analyses were carried out by Galbraith Laboratories, Knoxville, Tenn. Anhydrous solvents such as ether, benzene, toluene, and xylene were dried over sodium and filtered prior to use.

Starting Materials. The tertiary phosphines were either prepared by the classic Grignard reaction as described in the text (phosphines **3a–e**) or via a lithium cleavage process.[20c] One exception was 1-naphthyldiphenylphosphine, which was obtained by the reaction of 1-naphthylmagnesium chloride and diphenylphosphinous chloride and isolated and identified.[20a] Triphenylphosphine was commercially available. The 115% PPA was obtained from FMC Corp.[7]

The benzyl-substituted phosphonium salt **3f** was prepared from 3-cyclopentenyldiphenylphosphine[20c] and benzyl bromide. Standard apparatus used was a 300-ml, three-necked, inverse Grignard flask, addition funnel, mechanical stirrer, condenser, and a N_2 inlet. To this was attached a 300-ml, three-necked, round-bottomed flask, condenser, and a N_2 inlet. The preparation of allylbenzyldiphenylphosphonium bromide (**3a**) will be described as a general procedure.

Allylbenzyldiphenylphosphonium Bromide (3a). To 1.09 g (0.045 g-atom) of Mg in 20 ml of anhydrous ether was added a catalytic amount of iodine and ethyl bromide. After the reaction began, 5.7 g (0.045 mol) of benzyl chloride in 40 ml of ether was slowly added dropwise over a 15-min period followed by a 30-min period at reflux. To the Grignard mixture was slowly added 9.92 g (0.045 mol) of diphenylphosphinous chloride in 40 ml of ether over a 20-min period. This mixture was boiled for 1 hr after the final addition. In the lower, attached flask was placed 8.0 g (0.066 mol) of allyl bromide in 100 ml of anhydrous benzene. The benzene solution was heated to almost reflux, and the contents in the upper flask were added dropwise over a 2.5-hr period. When all the liquid in the upper flask had drained, it was rinsed with 25 ml of ether. The ether, via continued heating and a steady rate of N_2, was expelled from the lower flask. Allyl bromide (5.6 g, 0.046 mol) in 25 ml of benzene was added to the lower flask. The upper flask was removed, and the solution was boiled with stirring for 24 hr under N_2. A precipitate formed and was collected by vacuum filtration, dissolved in a minimum amount of H_2CCl_2, and then reprecipitated by the dropwise addition of ether until the solution became cloudy. After 24 hr, a white precipitate was collected by filtration and dried in vacuo to give 9.3 g (52%) of **3a**, mp 201–203°. Infrared, NMR, and analytical data are given in Tables I and V.

Ring Closures to Produce the Isophosphinolinium Salts. The general procedure will be illustrated with the preparation of **4a** (the most typical), **4b**, and **4e**.

1,2,3,4-Tetrahydro-4-methyl-2,2-diphenylisophosphinolinium Hexafluorophosphate (4a). In a 100-ml beaker was placed 60 ml of 115% PPA which was heated to 160°. Compound **3a** (2.0 g, 5 mmol) was added over a 10-min period followed by an additional 30 min of stirring. During the addition, a gas was given off, probably HBr.[8] The solution was cooled to 110–115° and slowly poured into 500 ml of ice water which resulted in a *homogeneous solution* upon stirring for 15 min. Precipitation of crude **4a** resulted upon the addition of 50 ml of a saturated KPF_6 solution. The crude, wet solid was collected by filtration and dissolved in a minimum amount of H_2CCl_2, and the water layer was separated. The solid was reprecipitated by the dropwise addition of ether until the solution became cloudy. A second reprecipitation from H_2CCl_2–ether gave 1.70 g (75%) of **4a**, mp 172.5–174.5°. Infrared, NMR, and analytical data are given in Tables II and V.

1,2,3,4-Tetrahydro-4,7-dimethyl-2,2-diphenylisophosphinolinium Hexafluorophosphate (4b). Phosphonium salt **3b** was slowly added to 120 ml of 115% PPA at 160° and, when the addition was complete, a stirring period of 45 min followed. When cooled to 110°, the solution was poured into 500 ml of ice water and stirring produced a homogeneous solution. A saturated NaBr solution (100 ml) was added, and the mixture was extracted with three 200-ml portions of H_2CCl_2 and dried ($MgSO_4$). The H_2CCl_2 solution was reduced to ca. 50 ml, and the dropwise addition of ether produced the crude bromide **4b**. The bromide proved exceptionally tedious to purify with much loss of product. Thus, this salt was dissolved in 90 ml of anhydrous methanol and addition of 30 ml of a saturated solution of KPF_6 with stirring produced a heavy precipitate. Purification by reprecipitation from H_2CCl_2–ether gave 1.30 g (28%) of **4b**, mp 185.5–187°. Infrared, NMR, and analytical data are given in Tables II and V.

1,2,3,4-Tetrahydro-2,2-diphenylisophosphinolinium Hexafluorophosphate (4e). To 70 ml of 115% PPA at 300° was added 2.0 g (5 mmol) of **3e** over a 10-min period followed by an additional

1.25 hr of stirring. The very dark solution was cooled to 120° and slowly poured into 250 ml of ice water. Continued stirring gave a clear solution that was filtered through a small piece of glass wool to remove a small amount of insoluble material. Upon addition of 35 ml of saturated KPF_6, a heavy precipitate separated that was extracted (owing to slow filtration) with two 200-ml and one 100-ml portions of H_2CCl_2. The solution was concentrated to ca. 40 ml followed by treatment with ether to produce crude **4e**. Infrared, NMR, and analytical data are given in Tables II and V.

Ring Closure to Produce the Phosphinolinium Salts. The general procedure will be illustrated with **7a**, which was typical of all systems studied.

1,2,3,4-Tetrahydro-4-methyl-1,1-diphenylphosphinolinium Hexafluorophosphate (7a). Compound **6a** (2.0 g, 5 mmol) underwent cyclization when treated with 60 ml of 115% PPA at 160° for 30 min. The crude heterocyclic salt **7a** was precipitated from 300 ml of water upon addition of 500 ml of a saturated KPF_6 solution. Two reprecipitations from H_2CCl_2–ether produced 1.9 g (82%) of **7a**, mp 203.5–205°. Infrared, NMR, and analytical data are given in Tables IV and V.

Base Hydrolysis of 3-Cyclopenten-1-yl(1-naphthylmethyl)-diphenylphosphonium Hexafluorophosphate (3h). The phosphonium compound **3h** (400 mg, 0.74 mmol) was boiled for 16 hr in 50 ml of methanol–water (4:1) containing 5 g of KOH. The mixture was cooled and 50 ml of water was added. The water layer was extracted with ether and then chloroform and, after drying ($MgSO_4$), gave 280 mg of residue. This residue was chromatographed over neutral alumina (benzene) to give 80 mg (76%) of 1-methylnaphthalene (**9**), identical with an authentic sample, and 130 mg (65%) of 1-cyclopentenyldiphenylphosphine oxide (**10**);[20c] ir ν 1600 (C=C), 1437, 1122 (P–C_6H_5), 1186 cm^{-1} (P → O); ^1H NMR (CCl_4) δ 2.00 [quartet (J = 7 Hz), CH_2, 2 H], 2.50 [m, $-(CH_2)_2-$, 4 H], 6.21 [d (J = 10 Hz), CH, 1 H], 7.20–7.80 (m, 2 C_6H_5, 10 H); mass spectrum (70 eV) m/e 268 (M^+).

Base Hydrolysis of 1,2,3,4-Tetrahydro-4-methyl-2,2-diphenylisophosphinolinium Hexafluorophosphate (4a). Compound **4a** (400 mg, 1 mmol) was heated in 40 ml of methanol–water (4:1) with 4 g of KOH for 12 hr. The solution was cooled and 50 ml of water was added. This was extracted with $HCCl_3$ and dried ($MgSO_4$). The residue was chromatographed an acidic alumina (Merck activity I) using benzene to give 217 mg (65%) of **11**: ir (film) ν 3450 (hydrate), 1439, 1121 (P–C_6H_5), 1188 cm^{-1} (P → O); ^1H NMR ($DCCl_3$) δ 1.34 [d (J = 7 Hz), CH_3, 3 H], 2.12 (s, CH_3, 3 H), 2.50 [d of d (J_{HCCH} = 6, J_{PCH} = 11 Hz), PCH_2CH, 2 H], 3.55 (m, CH, 1 H), 7.00–7.90 (m, aromatic H, 14 H); mass spectrum (70 eV) m/e 334 (M^+).

Anal. Calcd for $C_{22}H_{23}OP$: C, 79.02; H, 6.93. Found: C, 78.50; H, 7.36.

Oxidative Degradation of 4h. Preparation of 1,2-Naphthalenedicarboxylic Anhydride (12). The procedure was essentially that of Cope with some modifications.[21] The cyclic product **4h** (0.125 g, 0.23 mmol), 7.0 g of $K_3Fe(CN)_6$, and 1.25 g of KOH were heated at 70–75° 60 hr in 25 ml of water. The reaction mixture was filtered, carefully acidified (concentrated HCl), and extracted with ether. The residue from the ether solution was sublimed at 160° (0.2 mm) to give 5 mg (11%) of anhydride **12**, mp 162–165° (lit.[22] mp 168°). The low solubility of **4h** in water could explain the low yield of **12**.

Base Hydrolysis of 6,6a,7,8,9,9a-Hexahydro-6,6-diphenyl-5*H*-benzo[*h*]cyclopent[*c*]isophosphinolinium Hexafluorophosphate (4h). Compound **4h** (300 mg, 0.56 mmol) was heated for 14 hr in 40 ml of methanol–water (4:1) containing 4 g of KOH under N_2. An additional 20 ml of water was added and the mixture was extracted (3 × 25 ml of $HCCl_3$). The organic layer was dried ($MgSO_4$), and the residue from the chloroform solution was chromatographed over neutral alumina (benzene) to yield 180 mg (79%) of **13**: mp 168–169°; ir (KBr) ν 1429, 1116 (P–C_6H_5), 1174 cm^{-1} (P → O); ^1H NMR ($DCCl_3$) δ 2.10 [m, $-(CH_2)_3-$ 6 H], 2.62 (s, CH_3, 3 H), 2.95 (m, CH, 1 H), 3.60 (m, CH, 1 H), 7.30–8.00 (m, aromatics, 16 H); mass spectrum (70 eV) m/e 410 (M^+).

Anal. Calcd for $C_{28}H_{27}PO$: C, 81.91; H, 6.63; P, 7.56. Found: C, 81.84; H, 6.61; P, 7.72.

Registry No.—**3a**, 53201-22-2; **3b**, 54229-88-8; **3c**, 54229-89-9; **3d**, 54229-90-2; **3e**, 23901-74-8; **3f**, 54229-91-3; **3g**, 54229-93-5; **3h**, 54229-94-6; **4a**, 54229-96-8; **4b**, 54229-98-0; **4c**, 54230-00-1; **4d**, 54230-02-3; **4e**, 54230-04-5; **4f**, 54230-05-6; **4g**, 54293-27-5; **4h**, 54230-07-8; **5**, 23901-73-7; **6a**, 28975-45-3; **6b**, 54230-08-9; **6c**, 54230-09-0; **6d**, 54230-10-3; **7a**, 54230-12-5; **7b**, 54293-29-7; **7c**, 54230-14-7; **7d**, 54230-16-9; **10**, 38868-18-7; **11**, 54230-17-0; **12**, 5343-99-7; **13**, 54230-18-1; 1-naphthyl chloride, 90-13-1; 3-cyclopentenyldiphenylphosphine, 54230-19-2; benzyl bromide, 100-39-0; benzyl chloride, 100-44-7; diphenylphosphinous chloride, 1079-66-9; allyl bromide, 106-95-6; 1-bromo-2-butene, 4784-77-4; 3-methylbenzyl chloride, 620-19-9; 1-naphthylmethyl chloride, 86-52-2; β-bromophenetole, 589-10-6; ethyl acetate, 141-78-6; triphenylphosphine, 603-35-0; diphenyl-1-naphthylphosphine, 1162-90-9.

References and Notes

(1) We gratefully acknowledge support of this work by the U.S. Public Health Service, National Cancer Institute, Grant CA 11967.
(2) (a) Predoctoral Candidate, 1970–1974; Research Associate, 1974; (b) Research Associate, 1971–1973.
(3) (a) D. M. Hellwege and K. D. Berlin, *Top. Phosphorus Chem.*, **6**, 1–186 (1969); (b) F. G. Mann, "The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, and Bismuth", 2nd ed, Wiley-Interscience, New York, N.Y., 1970, pp 3–354; (c) T. E. Snider, C. H. Chen, and K. D. Berlin, *Phosphorus*, **1**, 81 (1971).
(4) (a) G. Märkl, A. Merz, and H. Rausch, *Tetrahedron Lett.*, 2989 (1971); (b) C. E. Griffin and W. L. Bryant, *Phosphorus*, **2**, 49 (1972); (c) G. Märkl and K. H. Heler, *Angew. Chem., Int. Ed. Engl.*, **11**, 1016 (1972); (d) ibid., **11**, 1017 (1972); (e) W. Schaefer, A. Schweig, G. Märkl, and K. H. Heler, *Tetrahedron Lett.*, 3743 (1973); (f) L. E. Rowley and J. M. Swan, *Aust. J. Chem.*, **27**, 801 (1974); (g) D. J. Collins, L. E. Rowley, and J. M. Swan, ibid., **27**, 815 (1974).
(5) (a) G. Märkl and H. Baier, *Tetrahedron Lett.*, 4439 (1972); (b) H. G. de Graaf, J. Dubbeldam, H. Vermeer, and F. Bickelhaupt, ibid., 2397 (1973).
(6) Preliminary results of this work were reported in part at the 165th National Meeting of the American Chemical Society, Dallas, Tex., April 10, 1973, Abstracts, No. ORGN-49, and at the 20th Tetrasectional Meeting of the Oklahoma Section of the American Chemical Society, Stillwater, Okla., March 2, 1974.
(7) We gratefully acknowledge the encouragement and generous sample of 115% PPA from Mr. J. P. Cassidy, FMC Corp., Inorganic Division. The 115% PPA used contained a minimum of 83.2% P_2O_5.
(8) C. K. Bradsher and L. S. Davies, *J. Org. Chem.*, **38**, 4167 (1973). In strong acid solution, HBr was reported to have been evolved in the preparation of 11-aminoacridizinium perchlorate by the action of concentrated H_2SO_4 on 1-benzyl-2-cyanopyridinium bromide. It is not unreasonable to assume that an analogous situation occurs in our reaction.
(9) J. R. Shutt and S. Trippett, *J. Chem. Soc. C*, 2038 (1969).
(10) F. Bohlmann and H. Mannhardt, *Chem. Ber.*, **89**, 1307 (1956).
(11) The complete mass spectral data for all compounds reported herein are available upon request.
(12) F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy", Academic Press, New York, N.Y., 1969, pp 103, 206.
(13) (a) V. Mark, C. H. Dungan, M. M. Crutchfield, and J. R. Van Wazer, *Top. Phosphorus Chem.*, **5**, 227 (1967); (b) G. Mavel, *Annu. Rep. NMR Spectrosc.*, **5B**, 1 (1973).
(14) Cleavage of benzylphosphonium salts resulted in the formation of a phosphine oxide and toluene. The mechanistic implications of this reaction are discussed by W. E. McEwen, *Top. Phosphorus Chem.*, **2**, 1 (1965).
(15) (a) Y. Kashman and M. Sprecher, *Tetrahedron*, **27**, 1331 (1971); (b) Y. Kashman and E. D. Kaufman, ibid., **27**, 3437 (1971).
(16) C. H. Chen and K. D. Berlin, *Phosphorus*, **1**, 49 (1971).
(17) R. Bodalski and K. Pietrusiewicz, *Tetrahedron Lett.*, 4209 (1972).
(18) Y. Kashman and O. Awerbouch, *Tetrahedron Lett.*, 3217 (1972).
(19) (a) E. R. Lynch, *J. Chem. Soc.*, 3729 (1962); (b) E. A. Cookson and P. C. Crofts, ibid., 2003 (1966); (c) E. M. Richards and J. C. Tebby, *Chem. Commun.*, 957 (1967); D. W. Allen and I. T. Millar, *J. Chem. Soc. C*, 252 (1969); (e) C. H. Chen and K. D. Berlin, *J. Org. Chem.*, **36**, 2791 (1971).
(20) (a) K. Issleib and R. Volker, *Chem. Ber.*, **94**, 392 (1961); (b) D. Wittenberg and H. Gilman, *J. Org. Chem.*, **23**, 1063 (1958); (c) T. E. Snider, D. L. Morris, W. R. Purdum, G. A. Dilbeck, and K. D. Berlin, *Org. Prep. Proceed. Int.*, **6**, 221 (1974).
(21) A. C. Cope, *J. Am. Chem. Soc.*, **78**, 2551 (1956).
(22) E. F. Bradbrook and R. P. Linstead, *J. Chem. Soc.*, 1739 (1936).