

4-Phosphorinanones. II

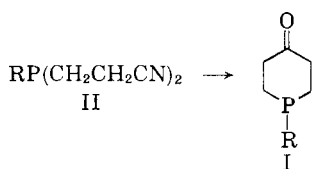
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A series of ring-substituted 4-phosphorinanones was prepared from primary phosphines and dienones. They formed normal ketone and phosphine derivatives. Reduction of the carbonyl group gave good yields of a 4-phosphorinanol and a phosphorinane. Attempted preparation of a heterocyclic phosphorus ylid from a 4-oxophosphorinanium iodide led to ring opening.

We recently reported the preparation of 4-phosphorinanones (I) by the Thorpe-type cyclization of bis(2-cyanoethyl)phosphines (II).¹ Unlike the phosphacyclohexanes described by Grüttner,² Mann,³ and Kosolapoff,⁴ the 4-phosphorinanones bear a ring-carbonyl group. This difference is



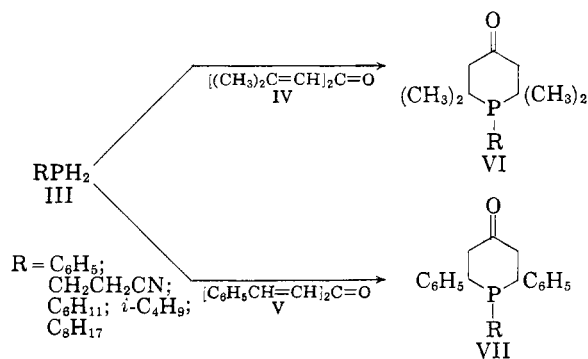
significant because the keto function permits entry by chemical transformation to a difficultly accessible area of organophosphorus chemistry. An important enabling feature in the synthesis of these compounds was the avoidance of organo-metallic reactants capable of side reaction with the carbonyl group.

At this time an alternate, more general approach to 4-phosphorinanones came to mind. The addition of a primary phosphine to a conjugated dienone appeared attractive because these diolefins are readily available, contain activated double bonds, and would lead to products containing the desired ring-carbonyl group.

Results and Discussion

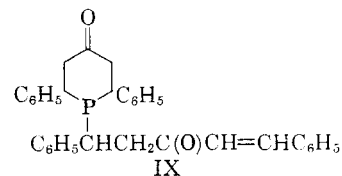
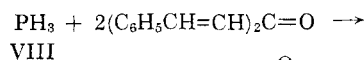
Ten 4-phosphorinanones were prepared from five primary phosphines (III) and two dienones by a two-step procedure, consisting of heating the reactants and distilling the product from the reaction mass. From phorone (IV) and dibenzalacetone (V) were obtained 2,2,6-tetramethyl-4-phosphorinanones (VI) and 2,6-diphenyl-4-phosphorinanones (VII), respectively.

The initial resin-like products from dibenzalacetone before distillation were thought to be polymeric linear or macrocyclic 1:1 adducts, on the strength of analyses, spectra, and molecular weight determinations. In one case the initial product appeared



to be a dimer of the 1:1 adduct, and in another case a tetramer of the 1:1 adduct. The initial products from phorone were not investigated before distillation because small quantities of starting materials were still present. This formation of polymeric adducts is not observed in the addition of primary amines to dienones.⁵

Distillation or sublimation gave the nearly pure monomeric 1:1 adducts in 35–75% yields. Phosphine itself (VIII) did not react with phorone, but reacted completely with dibenzalacetone at all three bonds to form the 1:2 adduct IX.



Although conversion of both the primary phosphine and the dienone was virtually complete in almost every case, there were obvious differences in the rate, dibenzalacetone reacting much more quickly than phorone which has relatively bulky beta substituents. Other experiments, not detailed here, showed that the addition reaction is quite sensitive to the reaction conditions, and that the use of a solvent or free radical catalyst may be undesirable. A similar observation recently

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(2) G. Grüttner and M. Wiernik, *Chem. Ber.*, **48**, 1473 (1915).

(3) F. G. Mann, I. T. Millar, and H. R. Watson, *J. Chem. Soc.*, 2516 (1958).

(4) G. M. Kosolapoff, *J. Am. Chem. Soc.*, **77**, 6658 (1955).

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has been reported⁶ for additions involving organotin compounds.

Measurement of the basicity of several 4-phosphorinanones showed the 2,6-diphenyl-4-phosphorinanones (VII) less basic than the 2,2,6,6-tetramethyl-4-phosphorinanones (VI). The values are shown in Table I, together with those of some simple tertiary phosphines.

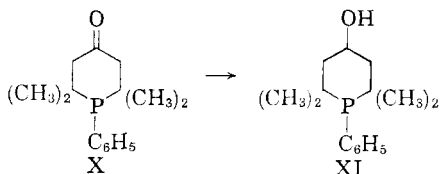
TABLE I
BASICITY OF 4-PHOSPHORINANONES

R	pK_a	pK_a	pK_a
C_6H_{11}	3.86	7.00	9.70
<i>i</i> - C_4H_9	3.58	..	7.97
C_6H_5	1.85	4.61	2.73 ^b
CH_2CH_2CN	0.79	..	1.37

^a See ref. 7. ^b A better compound for comparison is $C_6H_5P(C_2H_5)_2$; $pK_a = 6.25$.

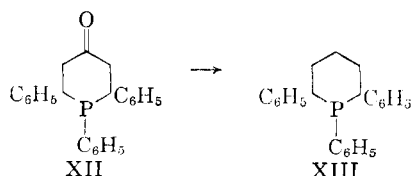
The 4-phosphorinanones formed semicarbazone, methyl iodide, and sulfide derivatives in the manner normal for ketones and tertiary phosphines.

Reduction of 2,2,6,6-tetramethyl-1-phenyl-4-phosphorinanone (X) with lithium aluminum hydride gave the corresponding 4-phosphorinanol (XI), probably a mixture of α - and β -isomers.



The configuration of the purified 4-phosphorinanol was not determined. Under these conditions 4-piperidones give predominantly the α -isomer.⁸

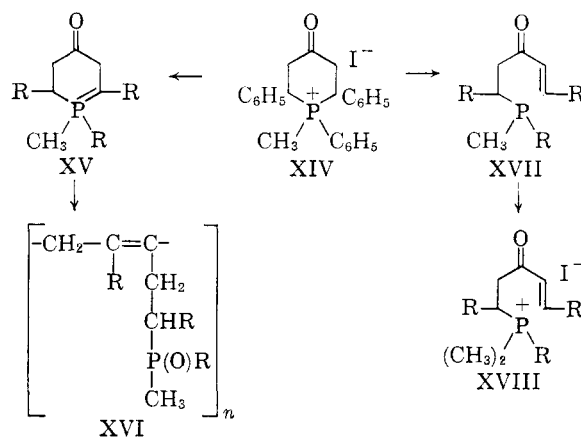
Wolff-Kishner reduction of 1,2,6-triphenyl-4-phosphorinanone (XII) gave 1,2,6-triphenylphosphorinane (XIII) in 82% yield. It formed a normal methyl iodide derivative.



Reduction of 4-phosphorinanones to phosphorinanes is a new approach to these compounds. Although several phosphorinanes were reported

by Grüttner² and Kosolapoff,⁴ none were substituted on ring carbon. Their preparation by the older methods, requiring α,ω -di(secondary halides), would be troublesome.

With the 4-oxophosphorinanium iodide (XIV) at hand we attempted to prepare a heterocyclic phosphonium ylid XV. We were stimulated by both the novelty of such an ylid and our desire to see whether the ylid, containing a keto group also, would undergo an intermolecular Wittig reaction⁹ to give a polyallylic product XVI. Treatment of 1-methyl-4-oxo-1,2,6-triphenylphosphorinanium iodide (XIV) with base gave, not the desired ylid XV but an isomeric product which we believe to be methyl(3-oxo-1,5-diphenyl-4-pentenyl)phenylphosphine (XVII) on the basis of analysis, spectra, and a methyl iodide derivative XVIII. If the



ylid XV was present, formation of the keto olefin XVII was so rapid that the ylid could not be trapped by a Wittig reaction with highly reactive *p*-nitrobenzaldehyde.¹⁰

The reaction is, we think, another example of the base-promoted elimination reaction of a phosphonium salt previously reported for 2-phenylethylphosphonium salts¹¹ and 2-cyanoethylphosphonium salts.¹² The electronegative carbonyl group, like the phenyl and cyano groups, so increases the acidity of the 3-carbon hydrogen that attack occurs there rather than at the 2-carbon hydrogen.

The new general synthesis of 4-phosphorinanones reported in this paper has the advantage of using primary phosphines and commercially available dienones. It differs from our earlier method in that phosphorus-carbon bonds are formed, rather than a carbon-carbon bond, but retains the important feature that ring closure is achieved without an organometallic intermediate.

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TABLE II
 PREPARATION OF 4-PHOSPHORINANONES

Structure and Empirical Formula	B.P.	Yield	M.P.	Analysis (Calcd. Found)				Mol. wt.
				C	H	P	N	
VI. R = C ₆ H ₅ (C ₁₈ H ₂₁ OP)	130–140°/0.5 mm. Subl. 100°/0.3 mm.	77	91–92 ^{a,b}	72.54 72.54	8.53 8.61	12.48 12.18
VI. R = C ₆ H ₁₁ (C ₁₈ H ₂₇ OP)	135–140°/1 mm. Subl. 110°/1 mm.	62 ^c	63–65 ^d	70.80 71.00	10.70 10.88	12.18 12.47	254 251
VI. R = CH ₂ CH ₂ CN (C ₁₂ H ₂₀ NOP)	140–150°/1 mm. Subl. 100°/0.8 mm.	71 ^e	48–50 ^f	63.95 64.00	8.95 8.70	13.75 13.65	6.23 6.12	258 237
VI. R = <i>i</i> -C ₄ H ₉ (C ₁₃ H ₂₅ OP)	90–97°/0.3 mm.	57 ^g ^{h,i}	68.30 68.60	11.02 11.14	13.60 13.63	228 237
VI. R = C ₈ H ₁₇ (C ₁₇ H ₃₃ OP)	146–148°/0.8 mm.	67 ^j ^k	71.80 71.56	11.66 11.96	10.89 11.16	284 292
VI. R = H		<i>l</i>						
VII. R = C ₆ H ₅ (C ₂₃ H ₂₁ OP)	Subl. 200°/0.5 mm.	64	176.5–177.5 ^m	80.21 80.43	6.15 6.37	9.00 9.35	344 358
VII. R = C ₆ H ₁₁ (C ₂₃ H ₂₇ OP)	Subl. 190°/1 mm.	57	120–121 ⁿ	78.82 79.23	7.77 8.15	8.84 8.87	350 347
VII. R = CH ₂ CH ₂ CN (C ₂₀ H ₂₀ NOP)	Subl. 180°/0.6 mm.	34 ^o	126–128 ^p	74.75 75.03	6.27 6.28	9.64 9.57	4.36 4.45	321 322
VII. R = <i>i</i> -C ₄ H ₉ (C ₂₁ H ₂₅ OP)	Subl. 150°/1 mm.	57	118–119	77.74 77.29	7.77 7.74	9.55 9.17	324 327
VII. R = C ₈ H ₁₇	Subl. 190°/1 mm.	41	80–81 ^q	78.92 78.86	8.73 8.88	8.13 8.20	381 349
IX (C ₂₄ H ₃₁ O ₂ P) ^r	130–150	81.25 77.67	6.22 6.03	6.16 5.86	502 497

^a Product showed polymorphism on heating, with melting point depending on rate of heating. The NMR proton spectrum showed a quartet in the 7–7.5- τ region, caused by nonequivalence of the two methylene protons. In addition, the two protons were not equally coupled to P as shown by further splitting of the quartet. ^b Derivatives: 1. 2,2,6,6-Tetramethyl-1-phenyl-4-phosphorinanone, semicarbazone, m.p. 198.5–199.5°, from ethanol-water. Calcd. for C₁₈H₂₄N₂OP: C, 62.93; H, 7.92; N, 13.76; P, 10.15. Found: C, 63.19; H, 8.18; N, 13.70; P, 9.99. 2. 1,2,2,6,6-Pentamethyl-1-phenyl-4-phosphorinanone iodide, m.p. 229–230°, from acetonitrile. Calcd. for C₁₆H₂₄OPI: C, 49.24; H, 6.20; P, 7.94; I, 32.52. Found: C, 49.54; H, 6.32; P, 7.78; I, 32.35. 3. 2,2,6,6-Tetramethyl-1-phenyl-4-phosphorinanone-1-sulfide, m.p. 138.5–139°, from methanol. Calcd. for C₁₈H₂₁OSP: C, 64.25; H, 7.55; S, 11.44; P, 11.05. Found: C, 64.58; H, 7.78; S, 11.52; P, 11.10. ^c Reaction time 28 hr.; 20 hr. found inadequate. ^d Methyl iodide derivative, m.p. 275–278°, from acetonitrile. Calcd. for C₁₈H₃₀OPI: C, 48.50; H, 7.63; P, 7.80; I, 32.00. Found: C, 48.27; H, 7.93; P, 8.02; I, 32.11. ^e Reaction complete after 20 hr., not after 10 hr. ^f Methyl iodide derivative, m.p. 290–295° dec. Calcd. for C₁₈H₂₉NOPI: C, 42.50; H, 6.30; N, 3.82; P, 8.43; I, 34.80. Found: C, 42.50; H, 6.28; N, 3.93; P, 8.35; I, 32.79. ^g In autoclave, conversion complete in 6 hr. at 125°. ^h *n*_D²⁰ 1.4962. ⁱ Methyl iodide derivative, m.p. 263–265°. Calcd. for C₁₄H₂₃OPI: C, 45.40; H, 7.63; P, 8.36; I, 34.30. Found: C, 45.62; H, 8.05; P, 7.96; I, 33.50. ^j Conversion incomplete after 17 hr. at 130°. ^k Methyl iodide derivative, m.p. 150–152°. Calcd. for C₁₈H₃₃OPI: C, 50.80; H, 8.53; P, 7.25; I, 29.70. Found: C, 51.11; H, 8.71; P, 7.05; I, 29.42. ^l Phorone and excess phosphine, in autoclave 18 hr. at 125°; no reaction occurred. ^m Semicarbazone derivative, m.p. >270°, from acetonitrile. Calcd. for C₂₄H₂₄N₂OP: C, 71.80; H, 6.03; N, 10.47; P, 7.72. Found: C, 72.06; H, 6.30; N, 10.36; P, 7.86; methyl iodide derivative, m.p. 137° dec. Calcd. for C₂₄H₂₄OPI: C, 59.27; H, 4.97; P, 6.37; I, 26.10. Found: C, 59.03; H, 5.06; P, 6.30; I, 26.02. ⁿ From methanol-water. ^o Reaction time was 1 hr. at 130–155°, followed by 30 min. at 175–200°. Analysis of product before sublimation: Calcd. for (C₂₀H₂₀NOP)₂: C, 74.75; H, 6.27; N, 4.36; P, 9.64; mol. wt., 1284. Found: C, 74.08; H, 6.24; N, 4.08; P, 9.08; mol. wt., 1344. ^p From ethanol. ^q From methanol-water. ^r Excess phosphine and dibenzalacetone, in autoclave 1 hr. at 170°; product an amorphous resin, nonsublimable, no longer containing P—H bond (infrared spectrum).

Experimental¹³

Materials.—Phosphine and mono(2-cyanoethyl)phosphine (*n*_D²⁰ 1.4821) were prepared in the usual manner.¹⁴ Phenylphosphine (*n*_D²⁰ 1.5748–1.5755) was prepared from phenylphosphonous dichloride.¹⁵ The remaining phosphines were obtained by the usual procedure.¹⁶ Phorone (2,6-dimethyl-2,5-heptadiene-4-one) came from the K and K Laboratories; *n*_D²⁰ 1.4912; and dibenzalacetone from Eastman Chemical Co. The ethanol used was 2B alcohol (anhydrous ethanol containing 0.5% benzene).

2,2,6,6-Tetramethyl-1-phenyl-4-phosphorinanone (VI. R = C₆H₅).—A mixture of 7.0 g. of phorone and 5.6 g. of phenylphosphine, heated under nitrogen for 6 hr. at 115–

130°, crystallized on cooling. Infrared spectrum showed that all P—H and C=C bonds were gone, and that carbonyl absorption had shifted from 1650 to 1700 cm.⁻¹. Vacuum distillation followed by sublimation gave the pure product VI; see Table II for melting point and analysis. When 5 mole % of α,α' -azobisisobutyronitrile was present, reaction was incomplete after 5 hr. at 80°.

1,2,6-Triphenyl-4-phosphorinanone (VII. R = C₆H₅).—A mixture of 4.4 g. of phenylphosphine and 9.4 g. of dibenzalacetone became quite viscous after heating at 120–125° for 13 min. under nitrogen. The hard white glass obtained on cooling was converted into a cream-colored powder by dissolving in benzene and freeze-drying. It melted gradually to a sirup above 95°; it was soluble in cold acetonitrile, dioxane, ethyl acetate, benzene, and chloroform, partly soluble in hot methanol and ethanol, and insoluble in hot hexane and water. It was purified by reprecipitation from benzene-hexane system.

Anal. Calcd. for (C₂₃H₂₁OP)₂: C, 80.21; H, 6.15; P, 9.00; mol. wt., 688. Found: C, 71.9–74.3; H, 5.5–6.3; P, 8.76; mol. wt. 682. A portion was sublimed, and the

(13) All melting points are corrected; molar weights were determined by ebullioscopic method unless otherwise indicated.

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yellowish sublimate, in benzene solution, passed through a column of alumina. Freeze-drying and recrystallization from acetonitrile gave white crystals, m.p. 176.5–177.5°; "now" soluble in *hot* acetonitrile, dioxane, and ethyl acetate. The sublimed material can also be effectively decolorized by washing with ether.

Reaction of phenylphosphine and dibenzalacetone was incomplete after 1.5 hr. in refluxing toluene, and also after 4 hr. at 85° with α, α' -azobisisobutyronitrile.

The preparation and characterization of the other 4-phosphorinanones are summarized in Table II.

Derivatives.—The semicarbazones were prepared in the conventional manner. Methyl iodide salts were prepared using either ether or excess methyl iodide as the solvent. The sulfide was prepared by refluxing in benzene with elemental sulfur. Other details are shown in Table I.

Basicity.—The basicities of six 4-phosphorinanones were determined by titration with standard perchloric acid in nitromethane as the solvent.⁷ The results are shown in Table I.

2,2,6,6-Tetramethyl-1-phenyl-4-phosphorinanol (XI).—A solution of 5 g. of 2,2,6,6-tetramethyl-1-phenyl-4-phosphorinanone (VI. R = C₆H₅) in 75 ml. of tetrahydrofuran was added to a slurry of 1.5 g. of lithium aluminum hydride in 200 ml. of tetrahydrofuran during 15 min. at room temperature under a nitrogen atmosphere. The mixture was heated at 50° for 2 hr., cooled, and cautiously decomposed with 20 ml. of water. After filtration and extraction of the precipitate with ether, the combined filtrates were dried and freed of solvent. The residue was sublimed and recrystallized from hexane giving 2.8 g. (56%) of waxy solid melting at 98–100°. Repeated recrystallization from hexane and acetonitrile raised the m.p. to 123–124.5°.

Anal. Calcd. for C₁₈H₂₈OP: C, 71.97; H, 9.26; P, 12.38. Found: C, 71.92; H, 9.10; P, 12.32. Analysis of the lower melting (98–100°) material was also satisfactory. Calcd.: mol. wt., 250. Found: mol. wt., 259.

1,2,6-Triphenylphosphorinane (XIII).—In accord with the general procedure,¹⁷ a mixture of 5.6 g. of 1,2,6-triphenyl-4-phosphorinanone (VII. R = C₆H₅) 3.5 g. of 85% aqueous hydrazine, 3.0 g. of sodium hydroxide, and 50 ml. of diethylene glycol was refluxed under nitrogen for 2 hr. at 168°, then for 3 hr. at 197°. After neutralization, extraction with benzene, and freeze-drying, a 6.3 g. residue was obtained, free of carbonyl groups (infrared spectrum). Recrystallization from ethanol and aqueous acetonitrile gave an 82% yield of white crystals, m.p. 167–168°.

Anal. Calcd. for C₂₂H₂₂P: C, 83.61; H, 7.01; P, 9.38. Found: C, 83.41; H, 6.87; P, 9.51.

Its methyl iodide derivative, 1-methyl-1,2,6-triphenylphosphorinanium iodide, was prepared in ether; m.p. 240° dec.

Anal. Calcd. for C₂₄H₂₈PI: C, 61.02; H, 5.55; P, 6.56; I, 26.87. Found: C, 61.32; H, 5.97; P, 6.68; I, 25.95.

Methyl(3-oxo-1,5-diphenyl-4-pentenyl)phenylphosphine (XVII).—Addition of 150 ml. of 1 *N* sodium hydroxide to a

cold solution of 6.2 g. of 1-methyl-4-oxo-1,2,6-triphenylphosphorinanium iodide (XIV) in 45 ml. of ethanol under nitrogen immediately gave a flocculent precipitate. After standing for 1.5 hr. it was dried at reduced pressure, giving 4.2 g. (90%) of cream-colored solid, m.p. 119–121°.

Anal. Calcd. for C₂₄H₂₂OP: C, 80.42; H, 6.47; P, 8.64; mol. wt. 358. Found: C, 80.35; H, 6.34; P, 8.56; mol. wt., 377 (isopiestic method¹⁸ with methylene chloride as the solvent, but see below). The compound showed new infrared bands at 1650 cm.⁻¹ (conjugated ketone), and 1630 cm.⁻¹ (C=C), but no absorption at 1710 cm.⁻¹ (saturated ketone). The ultraviolet spectrum showed maximum absorptivity $a = 48.0$ at 289 m μ (ϵ 17,200) suggesting a conjugated ketone. The NMR phosphorus spectrum showed a single peak at +17 p.p.m., referred to 85% H₃PO₄, in the range expected for a tertiary phosphine of the postulated structure.

The same keto olefin was obtained by addition of 8.0 ml. of 0.32 *N* lithium ethoxide solution to a solution of 0.85 g. of the phosphonium salt in 10 ml. of absolute ethanol. After an induction period of 5 sec., the clear yellow solution deposited a heavy flocculent precipitate (64% yield).

In solubility tests on a very small scale the keto olefin was soluble in cold benzene, chloroform, and acetonitrile (amber solutions), soluble in hot methanol and ethanol (yellow solutions depositing white crystals on cooling), and insoluble in hot water and hexane. On longer heating, as in attempted recrystallization from methanol or ethanol, the yellow solution became wine-red and no longer deposited on cooling. Removal of the solvent gave a brown resin-like solid, showing infrared bands corresponding to both saturated and unsaturated ketone, and a large amount of phosphine oxide.

On prolonged standing at room temperature under nitrogen, dilute solutions of keto olefin in carbon disulfide, chloroform, and methylene chloride acquired an orange-red color and deposited small quantities of a colorless gelatinous solid. This behavior cast some doubt on the validity of the molecular weight determination.

Reaction of the phosphonium salt XIV and lithium ethoxide in the presence of an equivalent of *p*-nitrobenzaldehyde gave only the same keto olefin.

The keto olefin reacted with excess methyl iodide to form a yellow solid, m.p. 90° dec.

Anal. Calcd. for C₂₂H₂₆OPI: C, 60.01; H, 5.23; P, 6.19; I, 25.37. Found: C, 58.56; H, 5.20; P, 5.80; I, 25.96.

The ultraviolet spectrum showed a peak, $a_{291} = 43$ (ϵ 21,500) assigned to conjugated ketone. Its infrared spectrum showed bands at 1665 and 1615 cm.⁻¹ assigned to conjugated ketone and olefin, respectively.

Acknowledgment.—We thank Dr. Sheldon Buckler and Dr. Neil McKelvie for their helpful discussion, and Dr. C. A. Streuli for the basicity measurements.

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