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HETEROCYCLES FROM bis-β-KETOPHOSPHINE OXIDES I:
3,5-DISUBSTITUTED-1-PHENYLPHOSPHORYL-4-AZACYCLOHEXADI-2,5-ENES

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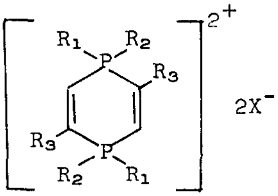
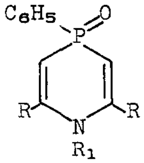
Previous work on the 1,4-diphosphoniacyclohexadiene-2,5 ring system 1 has provided compounds of considerable theoretical interest.[3] Specific biological activity has been observed for two cases of 1.[4] Elucidation of the physical nature of this ring system and synthesis of possibly bio-active new compounds is under way. We wish to report here synthesis of the novel[5] heterocycles, 3,5-disubstituted-1-phenylphosphoryl-4-azacyclohexadi-2,5-enes, 2, (R_1 = H), the first in a series of preparations directed toward heterocycles structurally similar to 1 employing heretofore unknown bis-β-ketophosphine oxides as general precursors.



1



2

R = C_6H_5, t-C_4H_9, n-C_3H_7

Synthesis of 2 is outlined in Scheme I.

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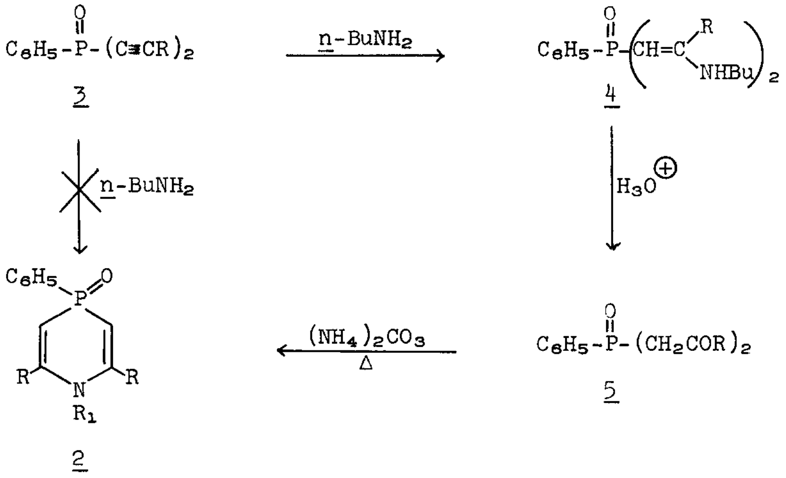

SCHEME I

The convenient preparation of monoenamine phosphine oxides from 1-alkynylphosphine oxides and neat amine has been reported.[6,7] Analogous treatment of the *bis*-alkynylphosphine oxides **3** with *n*-butyl amine at reflux temperature gave the *bis*-enamines in nearly quantitative yields. Prolonged reflux of **3** in neat amine gave no indication of cyclization to **2** (R_1 = *n*-C_4H_9). The *bis*-β-ketophosphine oxides **5** were obtained from two-layer hydrolysis of a 10:1 ether-chloroform solution of the *bis*-enamines[8] **4** with 10% aqueous oxalic acid (Table I).

TABLE I

β-KETO PHOSPHINE OXIDES **5**

	R	Mp °C	Yield[a] %	P-CH_2-	J_{PH}(Hz)[b]
5a	C_6H_5	134-6	67	4.08(d)	15.5
5b	*t*-C_4H_9	150-1	78	3.67(d)	15.0
5c	*n*-C_3H_7	87-8	85	3.42(d)	15.0

a. Overall yield based on preparation from *bis*-alkynylphenylphosphine oxide **3**.

b. nmr were obtained in deuteriochloroform on a Varian A-60 spectrometer and are reported in δ ppm downfield from the internal standard TMS.

Subsequent fusion of the bis-β-ketophosphine oxides 5 with solid ammonium carbonate afforded good yields of 2 (R_1 = H) as listed in Table II.

The cyclic structures assigned to 2a-c are clearly supported by their ir and nmr spectra. Characteristic absorptions are exhibited at 1640 cm^{-1} (C=C) and 1480 cm^{-1} (2° amine). The vinyl protons α to the phosphoryl moiety show a distinct doublet of doublets ($^2J_{PH}$ ~5 Hz; $^4J_{NH-CH}$ ~2 Hz) which collapses into a simple doublet upon double irradiation at the resonance frequency of the amine hydrogen. Exchange of the amine hydrogen with D_2O has the same effect upon the vinyl pattern of 2a and 2c. The failure of 2b to undergo deuterium-hydrogen exchange at nitrogen is attributed to steric interference by the two adjacent tertiary butyl groups.

Elemental analyses, molecular weights, and mass-spectral fragmentation patterns support the assigned structures.

TABLE II

3,5-DISUBSTITUTED-1-PHENYLPHOSPHORYL-4-AZACYCLOHEXADI-2,5-ENES 2

	R	Mp °C	Yield[a] %	δP-CH=	(Hz) $^2J_{PH}$	(Hz) $^4J_{NH-CH}$[b]	^{31}P[c]	λ_{max}	$\epsilon \times 10^3$
2a	C_6H_5	314-6	60	5.62	6	2	-8.7	240	3.01
2b	t-C_4H_9	274-6	62	5.20	5	2	-8.5	220 270	1.94 0.24
2c	n-C_3H_7	262-4	56	5.01	6	1.5	-10.9	221 270	4.15 0.57

a. Based on diketone 5.

b. nmr spectra were obtained in deuteriochloroform on a Varian A-60 spectrometer and are reported in δ ppm downfield from the internal standard TMS.

c. Chemical shifts obtained at 40 MHz on a Varian HR-100 spectrometer and are reported in δ ppm downfield from an external standard of 85% H_3PO_4.

X-ray analysis[9] of 2b has revealed a structure that exhibits all the classical features of a delocalized electronic ground state. The heterocyclic ring is planar and has a mirror plane bisecting the P,N axis with bond lengths: P-C = 1.74 Å; C=C = 1.41 Å; C-N = 1.43 Å; P=O = 1.47 Å. The implications of such a structure with respect to the high field ^{31}P shifts recorded for 2a-c are to be fully discussed in a subsequent paper.

The essential observation is that a delocalized ground state may be inferred for cyclic organophosphorus systems for which the ^{31}P resonance occurs at significantly higher fields than are generally observed for ^{31}P nuclei in a given oxidation state [e.g., for 1 ($R_1 = R_2 = R_3 = C_6H_5$) ^{31}P δ = +3.5, and for 2b ^{31}P δ = -8.5 while the usual range for P(IV) and P(V) species is -15 → -45 and -25 → -35, respectively].

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9. Private communication from Dr. L. M. Trefonas, Department of Chemistry, Louisiana State University, New Orleans, Louisiana.