Tetrahedron Letters No. 48, pp 4179 - 4182, 1977. Pergamon Press. Printed in Great Britain.

THE λ^5-PHOSPHA-6-OXA-INDOLIZINE RING SYSTEM
A NEW PHOSPHORUS HETEROCYCLE

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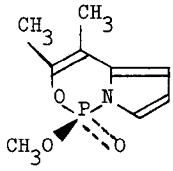
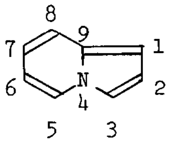
(Received in USA 18 August 1977; received in UK for publication 11 October 1977)

The field of aromatic phosphorus heterocycles is receiving considerable attention, and has been recently reviewed by Märkl[1], Berlin[2], Dimroth[3], and their coworkers. This Communication describes the synthesis of 7,8-dimethyl-5-methoxy-5-oxo-λ^5-5-phospha-6-oxa-indolizine (1)[4], which to our knowledge, represents the first example of a compound with phosphorus and oxygen atoms forming part of the indolizine or pyrrocoline heterocycle[5]. The ring system of 1 provides an opportunity for studies of cyclic delocalization involving the phosphorus atom. The preliminary data furnished below, in particular the mass and ^{31}P nmr spectra, suggest that there is much delocalization and stability present in this heterocycle, which could reflect the ability of the $-\mathrm{O}-\overset{\backslash\,/}{\mathrm{P}}=\mathrm{O}$ unit to transmit electronic effects.

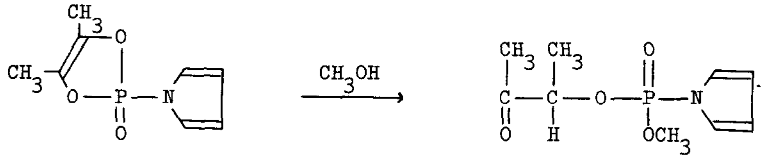


1, δ^{31}P - 8.4



Indolizine

The synthesis of 1 proceeds from N-(1,2-dimethylethenylenedioxyphosphoryl)pyrrole[6] (2), which, upon treatment with methanol, generates the two diastereomers of N-[methoxy(3-oxo-2-butoxy)phosphoryl]pyrrole, 3a,b.

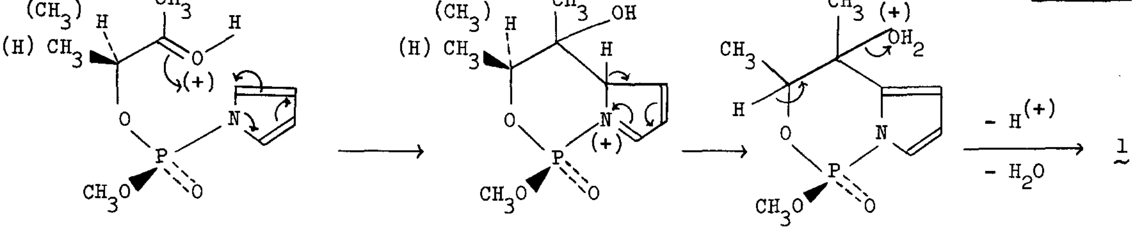


2, $\delta^{31}P$ = +8.8 ppm

3a,b ; $\delta^{31}P$ - 2.0

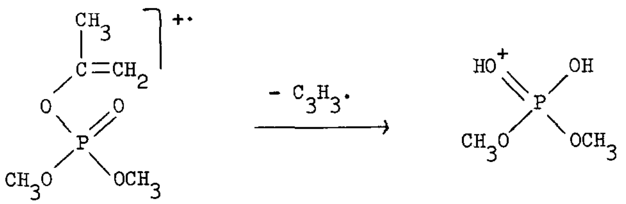
The conversion of the acyclic phosphorylpyrrole, 3a,b, into the heterocycle 1 is achieved in 70% yield under acid catalysis[7], and is assumed to proceed as indicated in Scheme 1. The two diastereomers undergo cyclization at significantly different rates, which is presumably due to a steric effect in the rate-limiting step.

Scheme 1



Compound 1 is obtained as colorless crystals, m.p. 67-69°, after vacuum distillation. The elemental analysis and molecular weight (by mass spectrometry, see below) conform with the formula given. The U.V. spectrum reveals significant conjugation, with λ max = 269 nm (ε 30,000; CH_3CN). The I.R. spectrum shows absence of carbonyl functions. The ^1H nmr spectrum has singlets at τ= 8.04 and 7.90 ppm, attributed to the methyl groups on the unsaturated carbons, a doublet at τ= 6.28 ppm (J = 12.0 Hz), consistent with the methoxy-group on phosphorus, and multiplets at τ= 3.78, 3.52 and 2.90 ppm, presumably due to aromatic-^1H, all with the expected relative signal intensities (in $CDCl_3$). The ^{13}C spectrum had signals at: 12.77, 16.46 (J = 7.6, d), 54.50 (J = 6.7, d), 106.04 (J = 5.8, d), 108.34 (J = 8.0, d), 114.31 (J = 12.1, d), 119.08 (J = 5.7, d), 134.95 (J = 3.8, d), and 142.27 (J = 11.7, d) (in C_6D_6), which accounts adequately for all the carbons in formula 1. The ^{31}P nmr signal is at significantly higher magnetic field than related compounds, 2 and 3, and reflects a relatively effective shielding of the ^{31}P-nucleus by electrons.

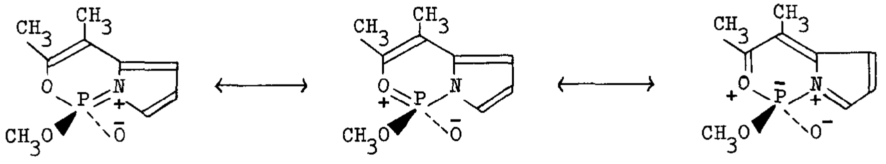
The behavior of 1 in the mass spectrometer is significantly different from that of related phosphates[8-10]. The spectrum of trimethyl phosphate[9] is mainly the result of a loss of formaldehyde from the molecular ion, $(CH_3O)_3PO^{+\cdot}$. The fragmentation of the molecular ion derived from dimethyl(2-propenyl) phosphate[10] involves, exclusively, the loss of the elements of methylacetylene radical and the formation of protonated dimethyl phosphate.



The mass spectra of these phosphate esters are quite complex. In contrast, the spectrum of **1** is extremely simple; the most intense peak corresponds to m/e = 213 and is due to the molecular ion $[C_9H_{12}O_3NP]^{+\cdot}$. In fact, most of the ion current is carried by this ion and by the fragment, m/e = 198, or $[C_8H_9O_3NP]^+$, which results from the loss of a methyl radical. Absence of extensive fragmentation, and strong parent and parent-CH_3 peaks are characteristics of related polycyclic aromatic and heterocyclic compounds.

The 5-cyclopentyloxy and 5-phenoxy analogs of the heterocycle, **1**, have also been prepared by similar reactions; their spectral data (e.g., $\delta^{31}P$ = -11.2 ppm and -14.8 ppm, respectively) are consistent with the assigned structures. This approach to the new P-heterocycle appears to be quite general, and is mechanistically related to the acid-catalyzed cyclization of N-(3-cyanoalkyl)pyrrole[11].

We speculate that compound **1** could derive stabilization from electron-delocalizations of the type depicted in resonance forms **1'**, **1"** and **1'"**. Further work comparing the properties of indolizine with the phosphorus analog will be described in the full paper.



1' **1"** **1'"**

Acknowledgment. This work was supported by Grant CHE 76-16785 from the National Science Foundation and Grant GM 20672 from the National Institutes of Health.

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4. $\delta^{31}P$ values are given in parts per million *vs* 85% H_3PO_4 (positive values refer to signals at lower magnetic field than the reference); τH^1 in parts per million *vs* Me Si = 10. ^1H-decoupled $\delta^{13}C$ in parts per million to low field of Me_4Si = 0; coupling constants, J, are in Hz, d = doublet. Mass spectra were determined on a Hewlett Packard 5980A instrument operating at 70 eV. Samples were introduced via the solid probe at ambient temperature.
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7. Anhydrous HCl was passed through a 0.3 M CH_2Cl_2 solution of **1** at 25° (5 min). The solution was decanted from a trace of insoluble tar, and the solvent was evaporated. The residue was purified by vacuum distillation.
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