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SYNTHESIS OF A PHOSPHOLECARBOXYLIC ESTER

Louis D. Quin and Stephen G. Borleske
Paul M. Gross Chemical Laboratory, Duke University
Durham, N. C. 27706, U.S.A.

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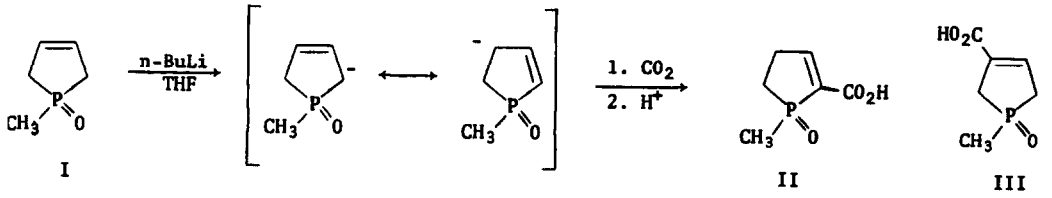
The phosphole ring system has been known for over a decade, and a number of alkyl and aryl derivatives have been reported. However, no phosphole has yet been synthesized where a reactive group is situated on the ring. We have accomplished the first synthesis of such a compound; methyl 1-methylphosphole-3-carboxylate (VIII) has been prepared and characterized, and indications are that the 4-methyl derivative can be obtained by the same method. The availability of such compounds opens up for study a new aspect of the chemistry of this ring system.

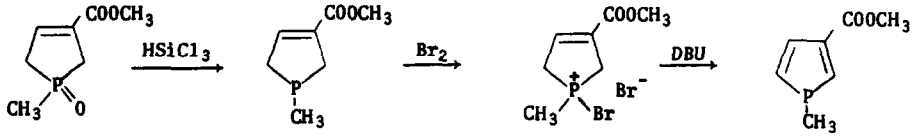
The carboxy group was first installed on the phospholene oxide ring. The anion from



I II III

1-methyl-3-phospholene oxide[1](I) was formed at -75°[2]. After 30 min, the solution was carbonated and then passed through a Dowex 50-H+ ion exchange column. On evaporation of the aqueous eluate, a mixture of acids II (65%) and III (35%) was obtained in 50% combined yield. That the double bond had rearranged into conjugation with the acid group was readily apparent from the nmr spectrum; each isomer had only one olefinic proton (δ8.42, doublet of triplets, J_{PCCH} = 36 Hz, J_{HCCH} = 2.6 Hz; δ7.52, broad doublet, J_{PCCH} = 32 Hz). The very strong deshielding of the olefinic proton in the former isomer permitted the assignment to it of structure II, where the combined effect of carbonyl and phosphoryl on the β-proton is present. The 3-phospholene oxide structure III was assigned to the other isomer on the basis of the simplicity (approaching a 4H doublet) of the methylene signals; the 2-phospholene oxide system gives a more complicated nmr spectrum[1]. Acid II was obtained in pure form (mp 214° dec) by fractional crystallization of the mixture from methanol.

The acid mixture was subjected to Fischer esterification. The ester (V) derived from acid II proved to be particularly easily polymerized, a property allowing its removal from the desired ester IV. Polymerization of V occurred in benzene solution at room temperature, but was accelerated by an amine such as morpholine. Addition of ether precipitated the polymer as a gum; evaporation of the filtrate left a residue of IV of sufficient purity for continuation of the synthesis.



IV VI VII VIII

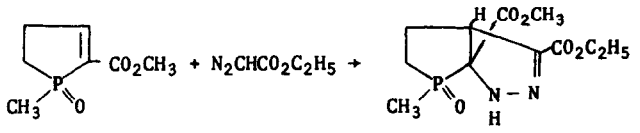
Trichlorosilane reduction gave phosphine VI, the first known ester of the phospholene family, in 30-40% yield, bp 45-46° (0.1 mm). The ester had the expected proton nmr and ir spectra and formed a methiodide, mp 188.4-190.4°, giving the correct analysis. The ^{31}P nmr signal of VI (+33.5 ppm relative to 85% H_3PO_4 reference) provided confirmation of the presence of the 3-phospholene ring, for the 2-phospholene would have a more deshielded phosphorus atom[3]. VI rapidly consumed 1 mole of bromine, forming bromophosphonium bromide VII, whose structure (verified by nmr) at phosphorus is the same as that of a diene-phosphonous dihalide cycloadduct. This permitted the application of the dehydrohalogenation method of Mathey and Mankowski-Favelier[4] for the synthesis of phosphole VIII. The bromide was treated in benzene-CH_2Cl_2 with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) at 0°. The hydrobromide of DBU was removed by filtration after 3 hrs; the filtrate was washed with water to remove DBU, and then stripped of solvent. The residue was rapidly distilled directly into a receiver chilled in a Dry Ice-acetone bath. The bp of the colorless liquid was not measured accurately but was about 40-50° (0.2 mm). The purity of the product so obtained was at least 95% as indicated by gas chromatography.

The carbomethoxy group introduces considerable instability into the phosphole system; VIII is markedly less stable than 1-methylphosphole[5] and 1-benzylphosphole[6]. It decomposes at room temperature, forming a dark resinous mass, but can be preserved in a Dry Ice-acetone bath

Phosphole VIII had its ^{31}P nmr signal at -3.0 ppm; the downfield shift relative to 1-methylphosphole (+8.57) is indicative of electron withdrawal from the ring due to conjugation

with the carbomethoxy group. The ^1H nmr spectrum at 60 MHz contained the P-CH_3 signal (singlet) at $\underline{\delta}1.92$ and the OCH_3 signal at $\underline{\delta}4.26$. The olefinic region was examined at 90 MHz and was analyzable by inspection: $\underline{\delta}7.3$ (1H, m, H_5, $^2J_{PH}$ = 38, $^3J_{H_5H_4}$ = 7.5, $^4J_{H_5H_2}$ = 2.5 Hz), $\underline{\delta}7.8$ (1H, m, H_4, $^3J_{PH}$ = 17, $^3J_{H_4H_5}$ = 7.5, $^4J_{H_4H_2}$ = 1.5 Hz), $\underline{\delta}8.3$ (1H, m, H_2, $^2J_{PH}$ = 34.5, $^4J_{H_2H_5}$ = 2.5, $^4J_{H_2H_4}$ = 1.5 Hz). Of particular note are the large coupling constants of phosphorus with the α-protons, entirely consistent with the value (38 Hz) for the α-protons of 1-methylphosphole[5], and the strong deshielding by the carbomethoxy group on the protons of adjacent carbons, especially that at C-2 (δ8.3). This deshielding effect is also seen in the spectrum of methyl thiophene-3-carboxylate[7], to which the spectrum of VIII bears a strong similarity. The mass spectrum had the expected molecular ion (m/e 156.0339; calcd for $C_7H_9O_2P$, 156.0341), which was the base peak. The UV maximum (307 mμ) was considerably shifted, as expected, from that of 1-methylphosphole (285 mμ[5]).

We would also like to point out synthetic utility for 3-carbomethoxy-1-methyl-2-phospholene oxide(V); this substance is reactive to 1,3-dipoles, and is therefore a valuable intermediate for the preparation of phospholane derivatives with 5-membered rings fused in the 2,3-positions. As one example of several reactions studied, ethyl diazoacetate reacted readily with V to yield the pyrazoline IX, mp 174.5-176°, having the correct analysis and the expected nmr spectrum.



V IX

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