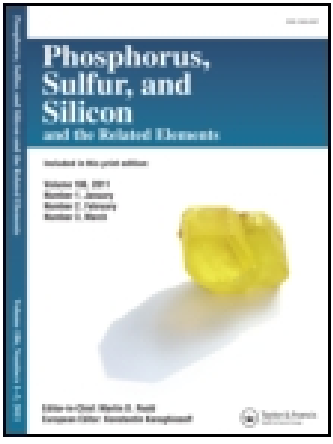

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The Synthesis of Phosphonyl Pyrazoles

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The Synthesis of Phosphonyl Pyrazoles

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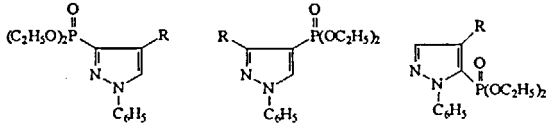
Phosphonyl hydrazones react with DMF/$POCl_3$ to afford 3-phos-phonyl pyrazoles.Phospho-nyl methylene hydrazones react with DMF/$POCl_3$ to provide 4-phosphonyl pyrazoles. 5-phosphonyl pyrazoles are obtained from the reaction of phosphonyl chlorovinylaldchydes with phenylhydrazine.

Keywords: Phosphonyl pyrazole; Vilsmeier reagent; Hydrazone

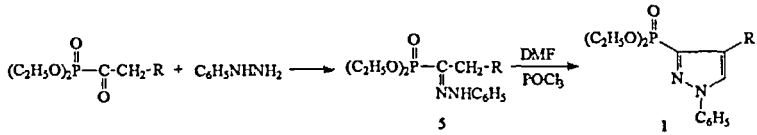
Pyrazoles have recently been exploited as herbicides, acaricides and insecticides, in which many compounds have commercially been produced[1]. To a large degree, the biological activity is attributed to the nature of substituents in pyrazole ring. Furthermore, it is known that the phosphonyl group could regulate important biological functions[2]. It is conceivable that molecular modification of pyrazole rings introducing organophosphorus functionalities might be expected to exhibit the potential pesticide activity. Although some synthetic approaches to phosphonyl pyrazoles have been reported[3-5], there is still much active research in this area. In this note we report about an efficient and facile strategy for the synthesis of phosphonyl pyrazoles. Depending on the position of the phosphonyl group in pyrazole ring, it is necessary to develop respective synthetic approach.



1 2 3

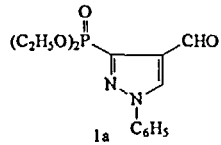
R= H, CH_3, C_6H_5

Compounds 1-3 were prepared as representative examples of phosphonyl pyrazoles.The reaction of phosphonyl hydrazones 5 with the Vilsmeier reagent ($DMF/POCl_3$) in equimolar ratio affords 1-phenyl-3-diethoxyphosphonyl pyrazoles 1 (Scheme 1).

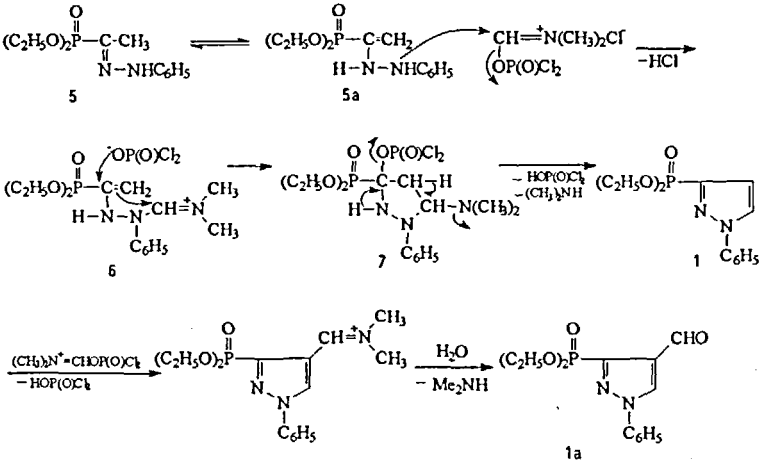


Scheme 1

When R=H, the byproduct of this reaction is compound 1a.



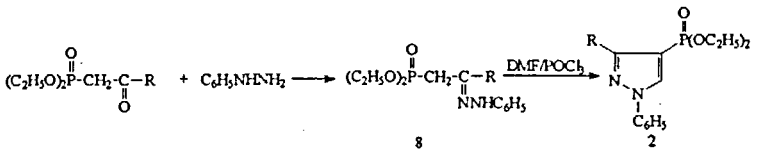
After completion of the reaction , the reaction mixture is directly separated by plate chromatography to give the compound 1 (R = H). If the reaction mixture is hydrolyzed first, the compounds 1, 1a, are isolated respectively by plate chromatography. A more plausible pathway for the above reaction is shown in scheme 2.



scheme 2

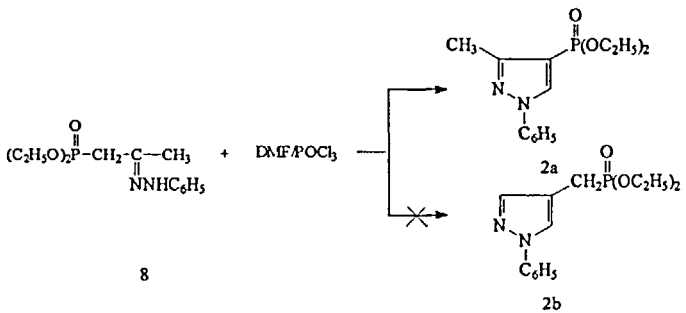
Phosphonyl hydrazone 5 in tautomeric form 5a acts as a nucleophile towards reactive intermediate obtained from DMF/$POCl_3$ to give 6. Addition of $^-OP(O)Cl_2$ to carbon-carbon double bond of 6 affords 7. This step is facilitated due to ease in formation of five-membered ring. Activated complex 7 is then converted by base-induced elimination reaction to phosphonyl pyrazole 1. The compound 1 reacts with another mole of DMF/$POCl_3$ to yield 1a according to known formylation pathway.

1-Phenyl-4-diethoxyphosphonyl pyrazoles 2 are obtained by reaction of phosphonyl methylene hydrazones 8 with DMF/$POCl_3$ (Scheme 3).



Scheme 3

The hydrazones should have two isomers in theory. However, when the phosphonyl hydrazones 5 and the phosphonyl methylene hydrazones 8 were prepared, only one isomer could be detected. This isomeric configuration was not assigned, but it was readily converted to the corresponding pyrazoles in good yield. In the case of the phosphonyl methylene hydrazones 8 (R=CH_3), 4-diethoxyphosphonyl pyrazole 2a was obtained instead of 4-diethoxyphosphonyl methyl-ene pyrazole 2b (Scheme 4).

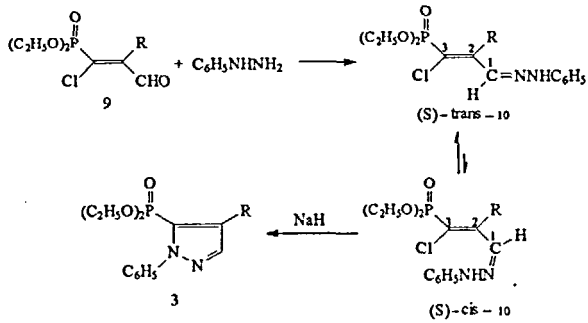


Scheme 4

This may be rationalized that, because of the effect of the phosphonyl group, the electrophilic substitution of the methylene group by the Vilsmeier reagent took place more readily than that of methyl group.

1-Phenyl-5-diethoxyphosphonyl pyrazoles 3 were readily prepared by the action of 9 and phenylhydrazine in presence of sodium hydride(Scheme 5). Hydrazone 10

(R=H) could be separated in absence of sodium hydride. (S)-Trans conformation of 10 is more stable than (S)-cis conformation at room temperature, but in presence of sodium hydride, (S)-trans 10 can be cyclized to give 3 via (S)-cis 10 because of low rotational energy between C_1 and C_2 of 10.



Scheme 5

In summary, we have developed a convenient method for preparing 3-, 4-, 5-phosphonyl pyrazoles. Other aspects of this process including N-alkylation and R group variants are under investigation.

ACKNOWLEDGMENTS

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