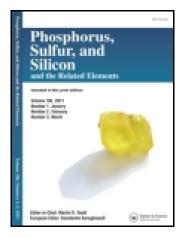
This article was downloaded by: [McMaster University] On: 24 December 2014, At: 05:29 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



# Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/gpss20</u>

# The Synthesis of Phosphonyl Pyrazoles

Hu Chen, Ding-Quan Qian, Guo-Xiang Xu, Yu-Xiu Liu, Xiao-Dong Chen, Xiao-Dong Shi, Ru-Zhen Cao & Lun-Zu Liu

<sup>a</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

<sup>b</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

<sup>c</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

<sup>d</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

<sup>e</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China <sup>f</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

<sup>g</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

<sup>h</sup> National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China Published online: 17 Mar 2008.

To cite this article: Hu Chen , Ding-Quan Qian , Guo-Xiang Xu , Yu-Xiu Liu , Xiao-Dong Chen , Xiao-Dong Shi , Ru-Zhen Cao & Lun-Zu Liu (1999) The Synthesis of Phosphonyl Pyrazoles, Phosphorus, Sulfur, and Silicon and the Related Elements, 144:1, 85-88, DOI: <u>10.1080/10426509908546188</u>

To link to this article: http://dx.doi.org/10.1080/10426509908546188

## PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <u>http://</u><u>www.tandfonline.com/page/terms-and-conditions</u>

## The Synthesis of Phosphonyl Pyrazoles

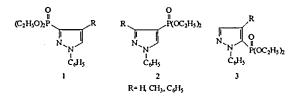
## HU CHEN, DING-QUAN QIAN, GUO-XIANG XU, YU-XIU LIU, XIAO-DONG CHEN, XIAO-DONG SHI, RU-ZHEN CAO and LUN-ZU LIU

### National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P.R.China

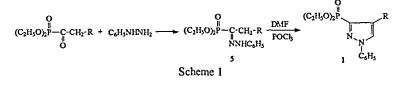
Phosphonyl hydrazones react with DMF/POCl<sub>3</sub> to afford 3-phos-phonyl pyrazoles.Phosphonyl methylene hydrazones react with DMF/POCl<sub>3</sub> to provide 4-phosphonyl pyrazoles. 5-phosphonyl pyrazoles are obtained from the reaction of phosphonyl chlorovinylaldchydes with phenylhydrazine.

Keywords: Phosphonyl pyrazole; Vilsmeier reagent; Hydrazone

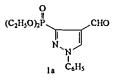
Pyrazoles have recently been exploited as herbicides, acaricides and insecticides, in which many compounds have commercially been produced[1]. To a large degree, the biological activity is attributed to the nature of substituents in pyrazole ring. Furthermore, it is known that the phosphonyl group could 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.



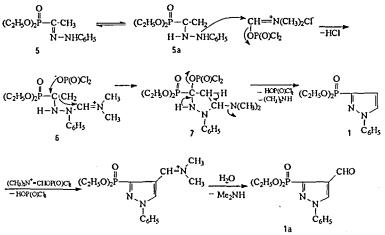
Compounds 1-3 were prepared as representative examples of phosphonyl pyrazoles. The reaction of phosphonyl hydrazones 5 with the Vilsmeier reagent (DMF/POCl<sub>3</sub>) in equimolar ratio affords 1-phenyl-3-diethoxyphosphonyl pyrazoles 1 (Scheme 1).



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



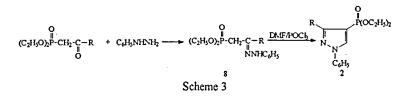
After completion of the reaction , the reaction mixture is directly separated by plate chromatography to give the compound 1 (R = H). If the reaction mixture is hydrolyzed first, the compounds 1, 1a, are isolated respectively by plate chromatography. A more plausible pathway for the above reaction is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



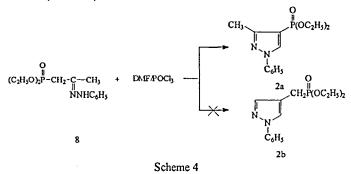
scheme 2

Phosphonyl hydrazone 5 in tautomeric form 5a acts as a nucleophile towards reactive intermediate obtained from DMF/POCl<sub>3</sub> to give 6. Addition of  $^{\circ}OP(O)Cl_2$  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<sub>3</sub> 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<sub>3</sub> (Scheme 3).



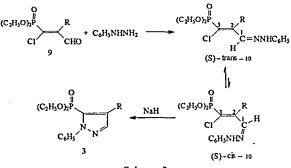
The hydrazones should have two isomers in theory. However, when the phosphonyl hydrazones 5 and the phosphonyl methylene hydrazones 8 were prepared, only one isomer could be detected. This isomeric configuration was not assigned, but it was readily converted to the corresponding pyrazoles in good yield. In the case of the phosphonyl methylene hydrazones 8 (R=CH<sub>3</sub>), 4-diethoxy-phosphonyl pyrazole 2a was obtained instead of 4-diethoxyphosphonyl methyl-ene pyrazole 2b (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-, 5phosphonyl pyrazoles. Other aspects of this process including N-alkylation and R group variants are under investigation.

#### ACKNOWLEDGMENTS

This research has been supported by the National Natural Science Foundation of China. (29672019)

### References

- G. Tomlin, Ed. in *The Pesticide Manual*, 10th Edn. British Crop Protection Pub.Surrey, (1991).
- [2] Ru-Yu Chen and Lun-Zu Liu, Chemistry of Organophosphorus Pesticides, Shanghai Scientific and Technical press. Shanghai, p.69, (1995).
- [3] F. Palacios, D. Aparicio and J. M. de Los Santos, Tetradhedron, 52, 4123, (1996).
- [4] A. Ben Akacha, N. Ayed, B. Baccar and C. Charrier, Phosphorus and Sulfur, 40, 63, (1988).
- [5] A. M. Polozov and A. V. Khotinen, Dokl. Akad. Nauk., 328, 464, (1993).