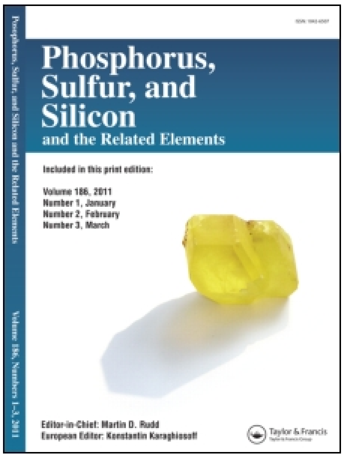
This article was downloaded by:
On: *28 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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

To cite this Article Chen, Hu , Qian, Ding-Quan , Xu, Guo-Xiang , Liu, Yu-Xiu , Chen, Xiao-Dong , Shi, Xiao-Dong , Cao, Ru-Zhen and Liu, Lun-Zu(1999) 'The Synthesis of Phosphonyl Pyrazoles', Phosphorus, Sulfur, and Silicon and the Related Elements, 144: 1, 85 — 88

To link to this Article: DOI: 10.1080/10426509908546188

URL: http://dx.doi.org/10.1080/10426509908546188

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Phosphorus, Sulfur and Silicon, 1999, Vol. 144-146, pp. 85-88
Reprints available directly from the publisher
Photocopying permitted by license only

Published by license under the
Gordon and Breach Science Publishers imprint.
Printed in Malaysia

The Synthesis of Phosphonyl Pyrazoles

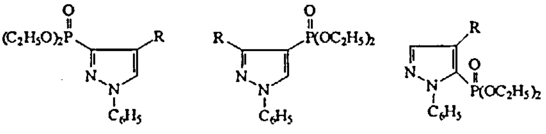
HU CHEN, DING-QUAN QIAN, GUO-XIANG XU, YU-XIU LIU, XIAO-DONG CHEN, XIAO-DONG SHI, RU-ZHEN CAO and LUN-ZU LIU

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

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

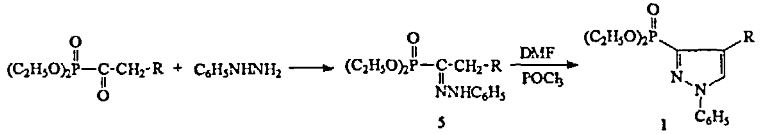
Keywords: Phosphonyl pyrazole; Vilsmeier reagent; Hydrazone

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.



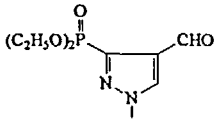
R= H, CH_3, C_6H_5

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).



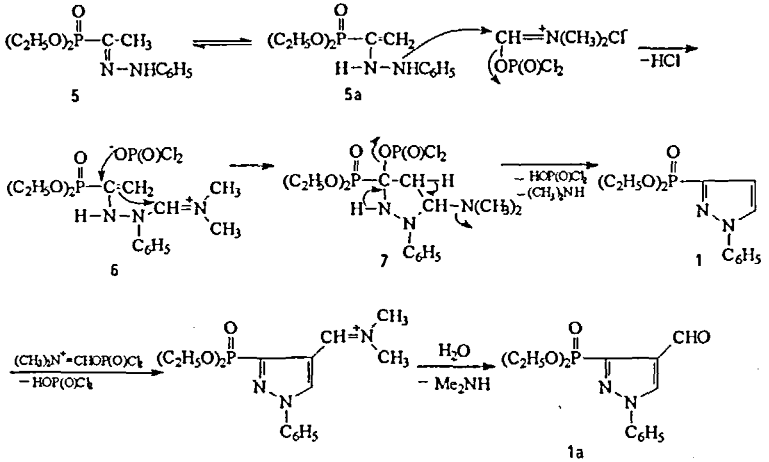
Scheme 1

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



1a

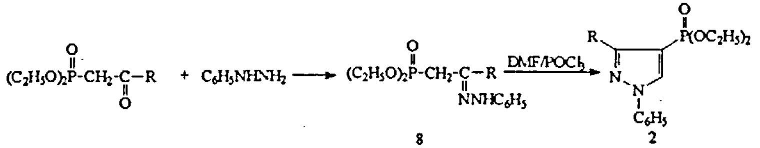
After completion of the reaction , the reaction mixture is directly separated by plate chromatography to give the compound 1 (R = H). If the reaction mixture is hydrolyzed first, the compounds 1, 1a, are isolated respectively by plate chromatography. A more plausible pathway for the above reaction is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



scheme 2

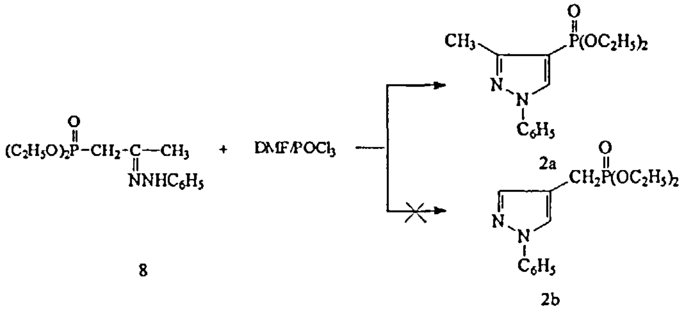
Phosphonyl hydrazone 5 in tautomeric form 5a acts as a nucleophile towards reactive intermediate obtained from DMF/$POCl_3$ to give 6. Addition of $^-OP(O)Cl_2$ to carbon-carbon double bond of 6 affords 7. This step is facilitated due to ease in formation of five-membered ring. Activated complex 7 is 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).

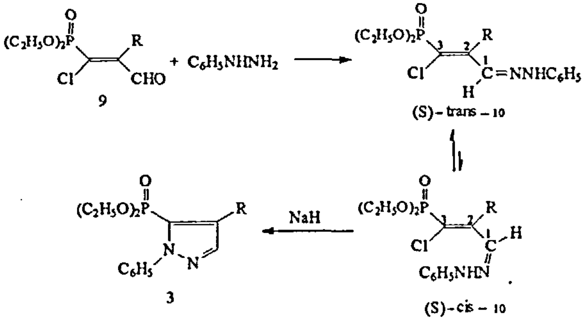


Scheme 4

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

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

References

[1] 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).