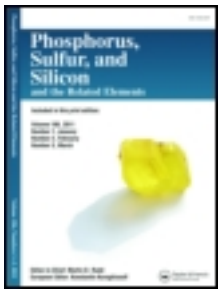

Phosphorus, Sulfur, and Silicon and the Related Elements

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

Thiophosphorylation of Pharmacophoric Phenols, Diols and Triols

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Accepted author version posted online: 01 Nov 2012.

To cite this article: Rafael A. Cherkasov, Ilyas S. Nizamov, Yevgeniy M. Martianov, Lyubov A. Almetkina, Yevgeniy N. Nikitin & Radik R. Shamilov (2012): Thiophosphorylation of Pharmacophoric Phenols, Diols and Triols, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI:10.1080/10426507.2012.740696

To link to this article: http://dx.doi.org/10.1080/10426507.2012.740696

THIOPHOSPHORYLATION OF PHARMACOPHORIC PHENOLS, DIOLS AND TRIOLS

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Keywords: 1,3,2,4-Dithiadiphosphetane-2,4-disulfides; paracetamol; 4-(1*H*-pyrrol-1-yl)phenol; ethambutol; vitamin B_6

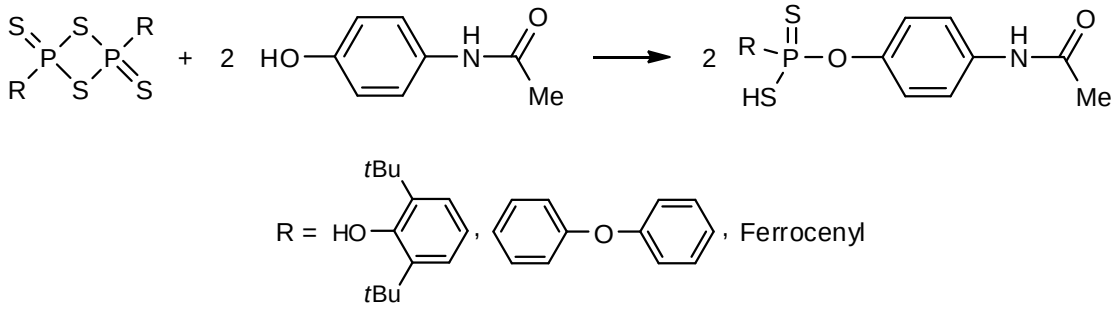
Abstract: Novel organyldithiophosphonic and bis(aryldithiophosphonic) acids were obtained by the reaction of 2,4-diorganyl 1,3,2,4-dithiadiphosphetane-2,4-disulfides with paracetamol, 4-(1*H*-pyrrol-1-yl)phenol, ethambutol dihydrochloride, vitamin B_6 and its acetonide derivatives.

INTRODUCTION

Tetracoordinated organophosphorus thioacids as well as their derivatives are useful to develop convenient methods for preparing new types of drugs and pesticides. Compounds containing stereogenic centers at the phosphorus atom seem to possess appreciable biological activity. To obtain biological active dithiophosphonic and bis(dithiophosphonic) acids we have used substituted phenols, diols and triols bearing pharmacophoric functionalities in the organic framework in the reaction with Lawesson-like reagents.

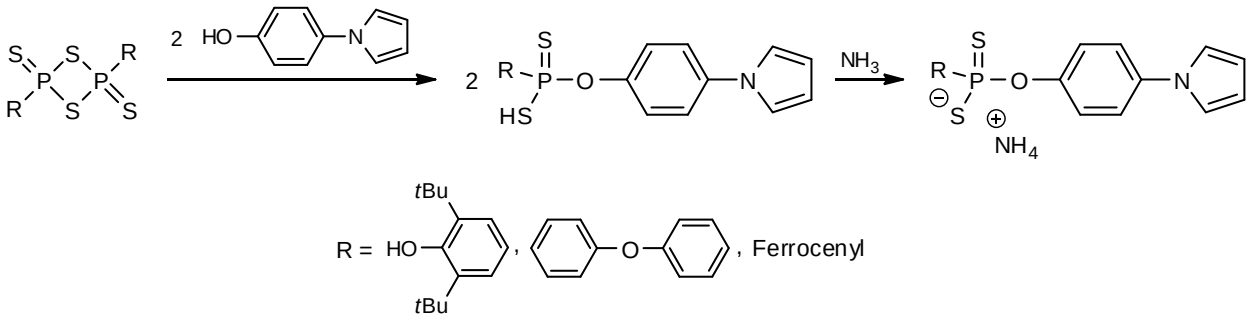
RESULTS AND DISCUSSION

Paracetamol, which is widely used as analgetic and antipyretic agent, reacts with 2,4-diaryl 1,3,2,4-dithiadiphosphetane-2,4-disulfides at 20 – 40 °C during 1-2 h in $C_6H_6/CHCl_3$ suspension with formation of the corresponding aryldithiophosphonic acids. The similar result was obtained in the case of 2,4-diferrocenyl 1,3,2,4-dithiadiphosphetane-2,4-disulfide (Scheme 1). The ^{31}P NMR spectra of the thioacids obtained in benzene solutions show singlets in the range of δ_P = 79 – 89 ppm.



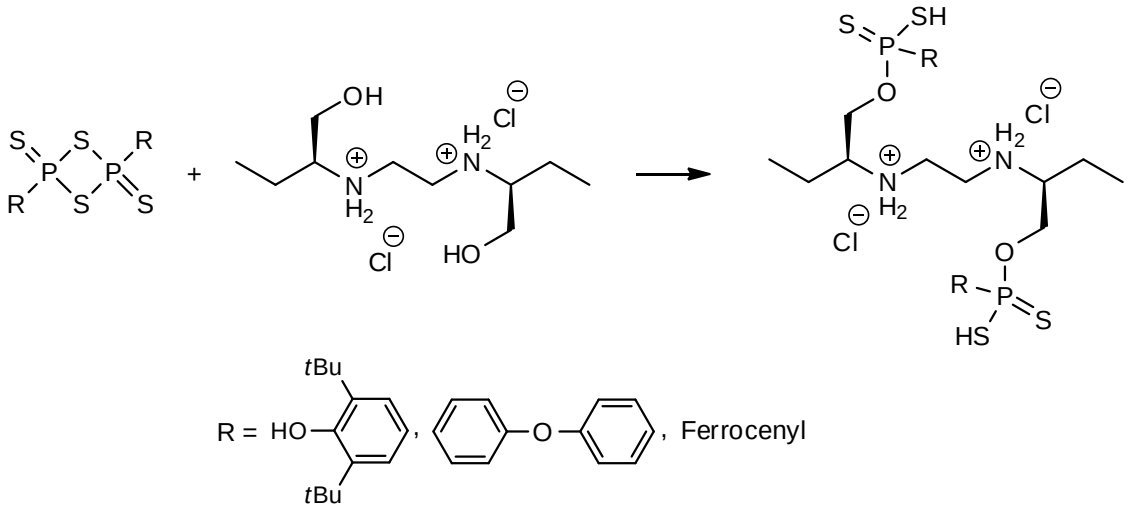
Scheme 1

Thiophosphorylation of 4-(1*H*-pyrrol-1-yl)phenol by 2,4-diorganyl 1,3,2,4-dithiadiphosphetane-2,4-disulfides at 20 °C during 1 h in benzene (Scheme 2) yields new corresponding dithiophosphonic acids (δ_P = 90 ppm). These acids were transformed into the respective ammonium salts (δ_P = 113 ppm).



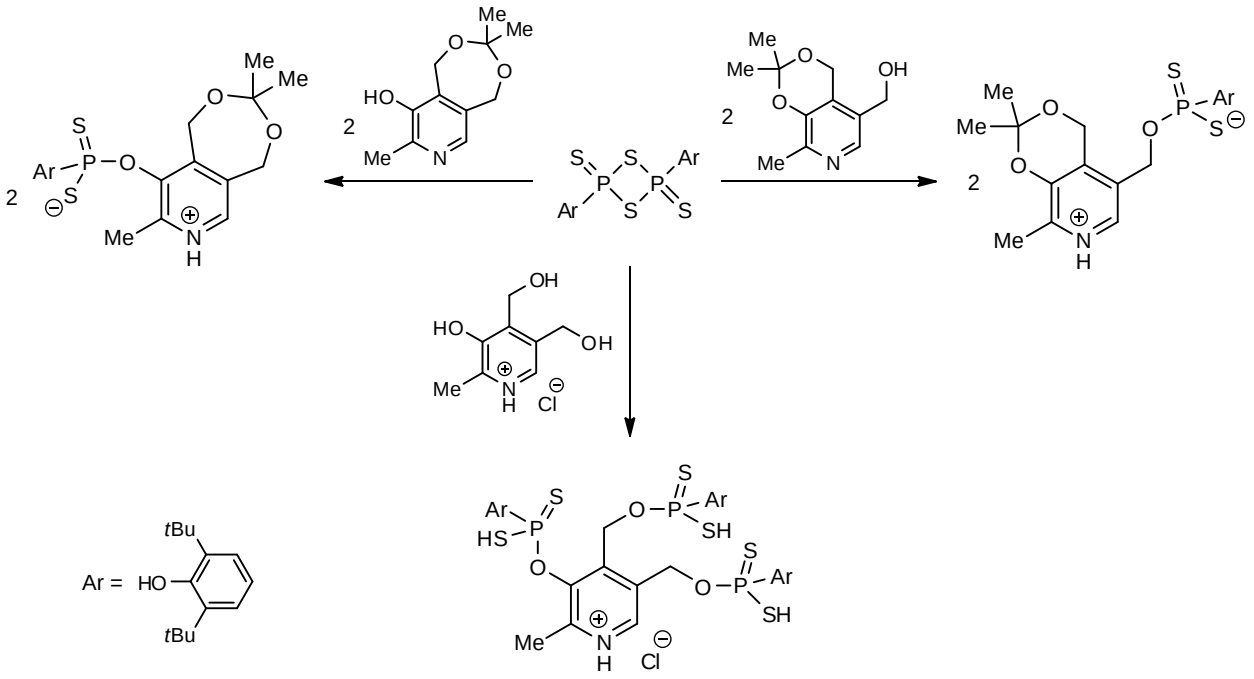
Scheme 2

The bis(organyldithiophosphonic) acids (δ_P = 93 – 97 ppm) were prepared by the reaction of 2,4-diorganyl 1,3,2,4-dithiadiphosphetane-2,4-disulfides with ethambutol dihydrochloride (Scheme 3) usually used as an antimicrobacterial agent (20 °C, 12 h, $C_6H_6/CHCl_3$).



Scheme 3

A tris(aryldithiophosphonic) acid (δ_P = 93 ppm) was isolated from the reaction of vitamin B_6 hydrochloride with an 2,4-diaryl 1,3,2,4-dithiadiphosphetane-2,4-disulfide at 80 °C during 2 h in benzene. Two acetonide derivatives of vitamin B_6 react with a 2,4-diaryl 1,3,2,4-dithiadiphosphetane-2,4-disulfide (20 – 30 °C, 1 h, $C_6H_6/CHCl_3$) to form inner ammonium salts of the corresponding aryldithiophosphonic acids.



Scheme 4

The organyldithiophosphonic and bis(aryldithiophosphonic) acids prepared possess appreciable antimicrobial activity.

ACKNOWLEDGEMENT

The study was performed with financial support of the Russian Foundation for Basic Researches (Grant No. 11-03-00264-a).