

Phosphorus, Sulfur, and Silicon and the Related Elements

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THIOPHOSPHORYLATION OF PHARMACOPHORIC PHENOLS, DIOLS AND TRIOLS

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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-(1H-pyrrol-1-yl)phenol, ethambutol dihydrochloride, vitamin B₆ and its acetonide derivatives.

INTRODUCTION

¹ ACCEPTED MANUSCRIPT

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 2,4diaryl 1,3,2,4-dithiadiphosphetane-2,4-disulfides at 20 – 40 °C during 1-2 h in C₆H₆/CHCl₃ 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 ³¹P NMR spectra of the thioacids obtained in benzene solutions show singlets in the range of $\delta_P = 79 - 89$ ppm.



² ACCEPTED MANUSCRIPT

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 ($\delta_P = 90$ ppm). These acids were transformed into the respective ammonium salts ($\delta_P = 113$ ppm).



Scheme 2

The bis(organyldithiophosphonic) acids ($\delta_P = 93 - 97$ 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, C₆H₆/CHCl₃).

³ ACCEPTED MANUSCRIPT



Scheme 3

A tris(aryldithiophosphonic) acid ($\delta_P = 93$ ppm) was isolated from the reaction of vitamin B₆ 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 B₆ react with a 2,4-diaryl 1,3,2,4-dithiadiphosphetane-2,4-disulfide (20 – 30 °C, 1 h, C₆H₆/CHCl₃) to form inner ammonium salts of the corresponding aryldithiophosphonic acids.

⁴ ACCEPTED MANUSCRIPT



Scheme 4

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

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⁵ ACCEPTED MANUSCRIPT