Phosphorus, Sulfur, and Silicon and the Related Elements

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SYNTHESIS OF PHOSPHORYLATED PIPERAZINES

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GRAPHICAL ABSTRACT

Abstract Heating 3-methyl-1,2-butadienyl phosphonates with piperazine leads to the formation of 2-piperazinyl-butenyl phosphonates containing the enamine functionality. From the reaction of piperazine with four equivalents of 1,2-butadienyl phosphonate a bis(phosphonate) is obtained, in which the piperazine bridge links two phosphorylbutene fragments.

Keywords Allenes; addition; 3-methyl-buta-1,2-dienyl phosphonates; piperazine; enamines

INTRODUCTION

The interest in the synthesis of polyfunctional organophosphorus compounds, in particular of β-aminoalkyl(alkenyl) phosphonates, originates from numerous possibilities for their practical application. Allenes, due to their unique reactivity, are important and versatile building blocks in the construction of various multifunctional compounds.

RESULTS AND DISCUSSION

Herein, we report the results of our study on the interaction of 3-methylbuta-1,2-dienyl phosphonates with piperazine. Heating of the reactants at 80°C for 1 h in the presence of a sodium alkoxide led to the formation of hygroscopic addition products, which according to their NMR spectra in CDCl3 represent a mixture of tautomeric enamines (Scheme 1). The structure of the products was determined by 1H and 31P NMR spectroscopy as well as by IR spectroscopic studies. Thus, in the 1H NMR spectra of the adduct of diethyl 3-methylbuta-1,2-dienylphosphonate and piperazine (yield 78%, bp 132°C–135°C (0.05 mm), nD20 = 1.4852) a signal at δ = 2.63 ppm (d, 2JPH = 21.9 Hz, 2H, CH2) is observed. It was assigned to the protons of the methylene group linked to the phosphorus atom; that is,
addition of the amino nitrogen atom of piperazine occurred at the β-carbon atom of the butadienyl phosphonate. The signals of the \( (\text{CH}_3)_2\text{C} = \) protons appeared as a two doublets at \( \delta = 1.65 \text{ ppm} \) (d, \( ^3J_{PH} = 4.9 \text{ Hz} \), 3H, CH\(_3\)) and at \( \delta = 1.74 \text{ ppm} \) (d, \( ^5J_{PH} = 6.6 \text{ Hz} \), 3H, CH\(_3\)); this corresponds to the addition of piperazine at 1,2-double bond of the butadienyl phosphonate. Thus, the enamine 1a is present in the reaction mixture. The presence of a signal at \( \delta = 3.93 \text{ ppm} \) (d, \( ^2J_{PH} = 8.7 \text{ Hz} \), 1H, P–CH=) and signals at \( \delta = 1.18 \text{ ppm} \) (d, \( ^3J_{HH} = 7.3 \text{ Hz} \), 6H, CH\(_3\), (CH\(_3\))\(_2\)CH–C) and at \( \delta = 3.70 \text{ ppm} \) (sept., \( ^3J_{HH} = 7.3 \text{ Hz} \), 1H, (CH\(_3\))\(_2\)CH–C) indicates also to the formation of the tautomeric enamine 2a in the mixture.

In the \(^{31}\)P NMR spectrum of the adduct two signals at \( \delta = 27 \text{ ppm} \) (major) and at \( \delta = 24 \text{ ppm} \) (minor) are observed.

\[
\text{(RO)}_2\text{P(O)CH}=\text{C}=\text{C} + \text{HN} \quad \rightleftharpoons \quad \text{HN}\]

\( R = \text{Et (a), iPr (b)} \)

\[ \text{Scheme 1} \]

The interaction of four equivalents of 3-methyl-buta-1,2-dienyl phosphonates with piperazine leads to the formation of bisphosphonates, which consist of two phosphoryl-butenes symmetrically linked to each other by the piperazine bridge. Their \(^1\)H NMR spectra differed from the spectra of the 1:1 adducts by the signal intensity ratio and the absence of the broad singlet at \( \delta = 2.26 \text{ ppm} \) (NH).

It was found that the reaction of 3-methyl-buta-1,2-dienyl phosphonates with 2-aminoethyl piperazine involves the addition of the primary exocyclic amino group to the sp-hybridized carbon atom of the phosphorylallene and leads also to a mixture of tautomeric enamines. The adducts show fungicide activity.