

Facile Synthesis of Five-membered Phosphoroheterocycles Bearing N-P-N and S-P-N Moieties

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Abstract: New reactions of Lawesson reagent (LR) with α -hydroxy (amino)nitriles have been studied. The experimental results showed that the five-membered phosphoroheterocycles **2** and **4** bearing N-P-N or S-P-N moiety could be readily prepared in high yields. Meanwhile, the possible mechanism of the reactions was also discussed.

Keywords: New reactions, Lawesson reagent, nitriles, phosphoroheterocycle, mechanism.

In past decades, Lawesson reagent (LR) has aroused extensive interests of chemists. Various papers on LR's structure, physical and chemical properties appeared in literature¹⁻⁵, application of its unique reactivity in the synthesis of bio-active compounds also attracted much attention^{6,7}. In particular, some potential bio-active phosphorus heterocycles could be novelly prepared by reacting LR with proper functional compound⁸. Peterson reported that the reaction of LR with 3-oxo-propanenitrile derivatives easily afforded high yield of 4H-1, 3, 2-oxazaphosphorin-4-thiones⁹. Testa also found that treatment of LR with 3-amino-propenenitrile derivatives almost led to the formation of phosphorus-containing uracil analogue, 1, 2-dihydro-2-(4-methoxyphenyl)-2-sulfide-1, 3, 2-diazaphosphorin-4-(3H)-thiones¹⁰. Based on literature, it can be concluded that the moieties of N-P-N and S-P-N in phosphoroheterocycles may play important roles in bioactivity¹¹. Therefore, in this context, as a part of our ongoing program, except the study on structure-activity relationship, we are still interested in exploitation of new methodologies, which are able to carry out a rapid synthesis of 5-membered phosphoroheterocycles bearing N-P-N or S-P-N moiety. Herein we represent a new and simple method for the synthesis of 5-membered heterocycles **1**, **3**, 2-diazaphospholidine-4-thione and **1**, **3**, 2-thiazaphospholidine-4-thione by the reaction of LR with α -hydroxy (amino) nitriles (**Scheme 1**).

Experimental

¹H NMR and ³¹P NMR spectra were recorded with a BRUKER AC-P200 spectrometer (CDCl₃ as solvent, TMS as internal, 85% H₃PO₄ as external standard). Melting points were determined with THOMASHOOVER melting point apparatus and the thermometer

Experimental data for the selected compounds 2a and 4a

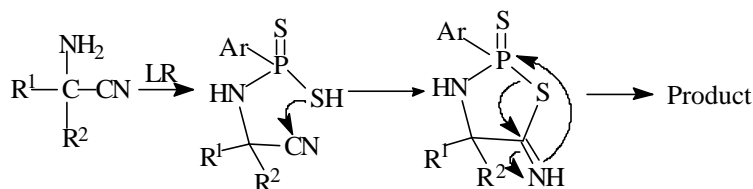
2a: colorless crystal, mp: 143-144°C, yield: 84.6%. ^1H NMR (CDCl_3 , δ ppm): 8.15 (br, 1H, NHC=S), 7.87 (dd, 2H, $^3J_{\text{P-H}}=7.23$ Hz, $^3J_{\text{H-H}}=7.84$ Hz, Ar-H), 6.94 (dd, 2H, $^4J_{\text{P-H}}=3.02$ Hz, $^3J_{\text{H-H}}=7.84$ Hz, Ar-H), 3.85 (s, 3H, OCH_3), 1.72 (s, 3H, CH_3), 1.65 (s, 3H, CH_3); ^{31}P NMR (CDCl_3 , δ ppm): 69.83; FTIR (KBr, cm^{-1}): 3307 ($\nu_{\text{N-H}}$), 1589, 1495, 1457 (ν_{Ar}), 1438, 1260 ($\nu_{\text{C=S}}$), 1102 ($\nu_{\text{Ar-O-C}}$); Elemental analysis for $\text{C}_{11}\text{H}_{15}\text{N}_2\text{OPS}$: Calcd (%) C: 46.15, H: 5.24, N: 9.79; Found (%) C: 45.99, H: 4.89, N: 9.77; EI-MS: M^+ = 286 (68%).

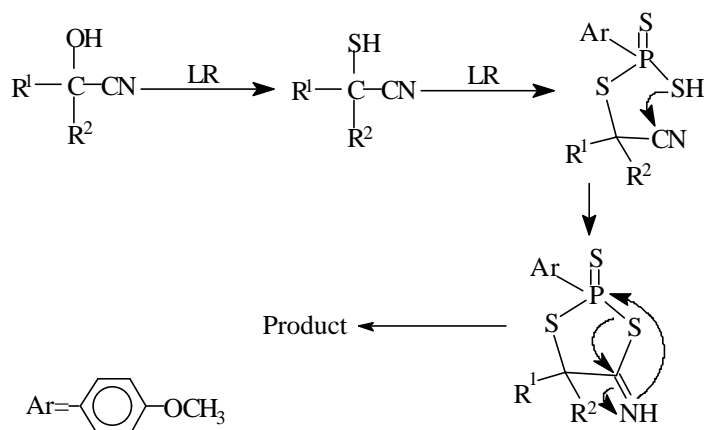
4a: colorless crystal, mp: 124-126°C, yield: 85.30%. ^1H NMR (CDCl_3 , δ ppm): 8.92 (br, 1H, NH), 7.96 (dd, 2H, $^3J_{\text{P-H}}=13.4$ Hz, $^3J_{\text{H-H}}=7.24$ Hz, Ar-H), 7.02 (dd, 2H, $^4J_{\text{P-H}}=3.5$ Hz, $^3J_{\text{H-H}}=7.24$ Hz, Ar-H), 3.86 (s, 3H, OCH_3), 2.01 (s, 3H, CH_3), 1.87 (s, 3H, CH_3); ^{31}P NMR (CDCl_3 , δ ppm): 67.87; FTIR (KBr, cm^{-1}): 3307 ($\nu_{\text{N-H}}$), 1589, 1495, 1457 (ν_{Ar}), 1438, 1260 ($\nu_{\text{C=S}}$), 1102 ($\nu_{\text{Ar-O-C}}$); Elemental analysis for $\text{C}_{11}\text{H}_{14}\text{NOPS}_3$: Calcd (%) C: 43.56, H: 4.62, N: 4.62; Found (%) C: 43.87, H: 4.73, N: 4.52; X-ray data are available if necessary.

Results and Discussion

Reacting LR with α -aminonitriles at high temperature readily afforded 1, 3, 2-diazaphospholidin-4-thiones in 76-89% yields, as shown in **Scheme 1**. The suitable molar ratio of compounds **1** to LR should be 1:0.5, excess of LR would not promote the yields of the target compounds. Based on the investigation by Peterson⁹ and Testa¹⁰, the reaction mechanism for the formation of **2** was demonstrated in **Scheme 2**.

Surprisingly, the treatment of α -hydroxynitriles with equimolar LR almost led to the formation of 1, 3, 2thioazaphospholidin-4-thiones. The possible mechanism was suggested that thionation of hydroxy group of substrate **3** occurred in the first step, and a nucleophilic attack on LR afforded thiophosphoric intermediate, further addition of P-SH to nitrile and rearrangement gave the final product, as shown in **Scheme 3**.

Scheme 2**Scheme 3**



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