A FACILE SYNTHESIS OF 1-ALKYL-1,3,2-DIAZAPHOSPHOLIDIN-4-THIONE-2-SULFIDE VIA LAWESSON'S REAGENT

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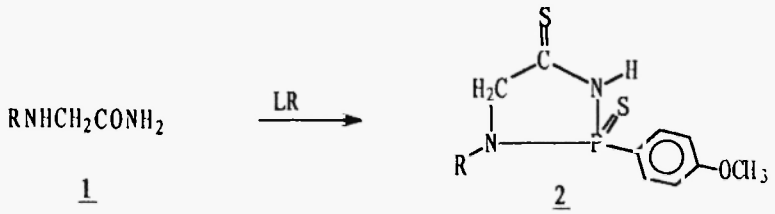
Abstract : 2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide(**Lawesson's Reagent**), was refluxed with 3-alkyl glycinamides **1** in anhydrous toluene to yield 1-alkyl-1,3,2-diazaphospholidin-4-thione-2-sulfides **2** . The structure was confirmed by elementary analysis , NMR, IR, MS. The results of preliminary bioassay indicated that some of the title compounds possess seletive herbicidal activity.

Introduction

In recent years, a focus of our research has been the development of new synthetic methodology centered around biologically active phosphorus heterocycles. Functionlized phosphorus-heterocycles and their dervatives are of great interest as bioactive substances with various properties(1). It was reported that the heterocyclic compounds , which incorporate phosphinothioylene moiety, are of potential interest as herbicides,insecticides,and fungicides(2-6). We became interested in syntheses of phosphorus heterocycles by cyclization reaction of Lawesson's reagent (**LR**), 2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide,with certain substrates, most of them having shown significant selective herbicidal activity(7-10).In order to look for potent herbicides and to extend the use of Lawesson's reagent to other bifunctional substrates, its reaction with 3-alkyl glycinamides has been investigated and found to give new phosphorus heterocycles, 1-alkyl-1,3,2-diazaphospholidin-4-thione-2-sulfides **2** .Our results are reported in this paper.

Results and Discussion

The reaction of the 1-alkyl glycinamides **1** with 0.5 molar equivalents of Lawesson's reagent in dry toulene at reflux temperature under anhydrous nitrogen for 6 hrs led to five-membered rings , 1-alkyl-1,3,2-diazaphospholidin-4-thione-2-sulfides(**2**), in significant yields (Scheme 1).

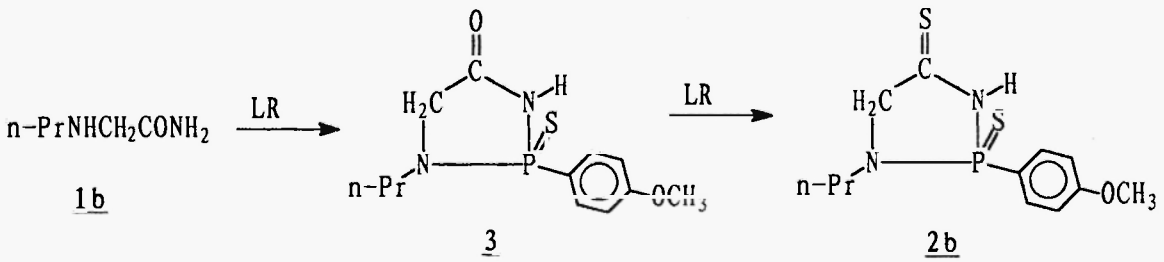


R= Me, n-Pr, n-Bu, t-Bu

Scheme 1

The structure of the title compounds **2** has been comfirmed by analytical results and spectra data IR, NMR, and MS. Compound **2a** (taken as representative example) gave correct elemental analysis, in the IR spectra **2a** showed peaks at 680 cm^{-1} (P=S), 1225 cm^{-1} (C=S), and 3355 cm^{-1} for amino group(N-H) . The ^1H NMR of compound **2a** existed a singlet at 3.80(s,3H,OCH_3), a multiplet at 6.70~8.20 for aromatic protons, a doublet at 8.22 with $^2J_{PH}$ =22.98Hz for mobile hydrogen N-H , which can be exchangeable with D_2O, 4.27(d,2H,*J*=4.2Hz,CH_2C=S), and 1.30(s,3H,CH_3). The EI- MS spectrum showed *m/z* 272(M^+,19).

When the reaction of 1-propyl glycinamide **1b** with lawesson's reagent was carried out in anhydrous toluene at room temperature, the ring-closure product **3** is formed , but the thionation product of **1b** [n-Pr-$NHCH_2C(S)NH_2$] and **2b** were not detected by gas chromatography-mass spectra (GC-MS), as shown in Scheme 2 .As to the formation of **2b** , **1b** undergoes heterocyclization with Lawesson's reagent to **3** which enter into the O,S-interchange reaction with the excess of Lawesson's reagent , yielding **2b** . So, carbonyl group of 3-alkyl glycinamide is thionated after the ring-closure stage.



Scheme 2

The herbicidal activity of compounds **2** was tested . A set amount of each sample was dissolved in acetone to which a drop of an emulsifier was added. Then, the solution was diluted with water until it reached the concentration required. Some herbs such as rape, oats , flax and barnyard grass were subjected to the leaf treatment. Preliminary biological screening tests for rings **2** indicated that some of them possess good selective herbicidal activity against rape.

In conclusion, the cyclization reaction of Lawesson's reagent with 3-alkyl glycinamides provides a facile route leading to biologically active phosphorus heterocycles. 1-alkyl-1,3,2-diazaphospholidin-4-thione-2-sulfides **2**, in significant yields.

Experimental

Elemental analysis was performed with a CHN PE-2400 elementary analyzer. Mass spectra were recorded with a ZAB-HF-3F spectrometer. ^{1}H NMR spectra were recorded with Varian XL-200 spectrometer. TMS was used as an internal standard for ^{1}H NMR. The IR spectra were measured by using SHIMADZU-408 instrument. Melting points were determined with a model X_4 apparatus and were uncorrected. Column chromatography was performed on silica gel II (10-40μ, Hai Yang Chemical Factory of Qingdo). Lawesson's reagent was prepared as described in Ref. 11. Compounds **1** were synthesized according to Ref.12.

General Procedure for the reaction of Lawesson's reagent with 3-alkyl glycinamide **1**, Synthesis of 1-alkyl-1',3,2-diazaphospholidin-4-thione-2-sulfide **2**.

1 Mmole of Lawesson's reagent was treated with 3-alkyl glycinaimde(**1**) in 15 mL of anhydrous toluene under dry nitrogen with stirring at reflux temperature for 6h until no more of the starting material could be detected by TLC. Evaporation of the solvent under reduced pressure and purification of the products on silica gel column using petroleum ether/dry ethyl ether mixtures as eluent (starting from 10% up to 20%) to give **2**.

2a m.p. 50-51℃; yield 30%; Anal. Calcd. for $C_{10}H_{13}N_2OPS_2$; C, 44.12; H 4.78; N,10.29. Found : C 44.32; H 4.49; N 10.03. ^{1}H NMR δ($CDCl_3$): 8.22(s, 1H, NH, exchangeable with D_2O,J= 22.98Hz), 6.71-8.20 (m, 4H, aromatic protons, Ar-H), 4.72(d, 2H, CH_2C=S,J_{PH} = 4.2 Hz), 3.80(s, 3H, OCH_3),1.30(m, 3H,CH_3).IR υ(KBr, cm^{-1}): 680(P=S), 1225(C=S),3355(N-H). EI-MS (int. rel). *m/z* = 272(M^+;19),189(13),170(21),59(14),43(100).

2b m.p. 40-51℃; yield 25%; Anal. Calcd. for $C_{12}H_{17}N_2OPS_2$; C, 48.00; H 5.67; N,9.33. Found : C 48.35; H 5.49; N 9.65. ^{1}H NMR δ($CDCl_3$): 8.32(s, 1H, NH, exchangeable with D_2O,J= 25.04Hz), 7.08-7.85 (m, 4H, aromatic protons, Ar-H), 4.25(d, 2H, CH_2C=S,J_{PH} = 4.4 Hz), 3.85(s, 3H, OCH_3),3.35(m,2H,NCH_2),1.15-1.27(m, 2H,CH_2), 0.85 (t,3H, J=3.6Hz, CH_3). IR υ(KBr, cm^{-1}): 689(P=S), 12305(C=S),3360(N-H). EI-MS (int. rel). *m/z* = 300(M^+;35), 170(17), 130(2),108(31),71(9),63(100),59(22).

2c m.p. 33-34℃; yield 20%; Anal. Calcd. for $C_{13}H_{19}N_2OPS_2$; C, 49.68; H 6.05; N,8.92. Found : C 49.87; H 6.25; N 8.67. ^{1}H NMR δ($CDCl_3$): 8.70(s, 1H, NH, exchangeable with D_2O,J= 22.40Hz), 6.97-7.91 (m, 4H, aromatic protons, Ar-H), 4.31(d, 2H, CH_2C=S,J_{PH} = 5.8 Hz), 3.88(s, 3H, OCH_3),2.86(m,2H,NCH_2),1.96(m, 2H,CH_2),1.24(m, 2H,CH_2), 0.85 (t,3H, J=3.6Hz, CH_3). IR υ(KBr, cm^{-1}): 690(P=S), 1225(C=S),3350(N-H). EI-MS (int. rel). *m/z* = 314(M^+;68), 170(34), 85(10),72(88),63(100),57(66).

2d m.p. 31-32℃; yield 15%; Anal. Calcd. for $C_{13}H_{19}N_2OPS_2$; C, 49.68; H 6.05; N,8.92. Found : C 49.79; H 6.31; N 8.72. ^{1}H NMR δ($CDCl_3$): 8.36(s, 1H, NH, exchangeable with D_2O,J= 23.60Hz), 6.80-8.10 (m, 4H, aromatic protons, Ar-H), 4.36(d, 2H, CH_2C=S,J_{PH} = 7.2 Hz), 3.86(s, 3H, OCH_3),1.33(s, 9H,3×CH_3). IR υ(KBr, cm^{-1}): 685(P=S), 1230(C=S),3396(N-H). EI-MS (int. rel). *m/z* = 314(M^+;40), 299(91),257(3),226(31),170(14), 85(28),69(22),57(100).

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