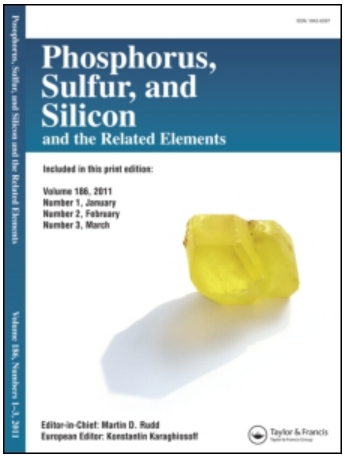

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SYNTHESIS OF 1,3-DIARYL-1,3,2-DIAZAPHOSPHOLIDIN-4-THIONE-2-SULFIDES VIA LAWESSON'S REAGENT

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SYNTHESIS OF 1,3-DIARYL-1,3,2-DIAZAPHOSPHOLIDIN-4-THIONE-2-SULFIDES VIA LAWESSON'S REAGENT

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2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide **(Lawesson's Reagent, LR)**, was treated with N,N'-diaryl glycinamides (**1**) in anhydrous toluene as a solvent at 100 °C to form 1,3-diaryl-1,3,2-ciazaphospholidin-4-thione-2-sulfides (**2**) Compatible analytical and spectroscopic data were obtained for all the new compounds. A mechanism was proposed to explain the formation of compound **2f**. The biological activity of the title products was also tested and some of them showed good herbicidal activity.

Keywords: Lawesson's reagent; N,N'-diaryl glycinamide; 1,3-diaryl-1,3,2-diazaphospholidin-4-thione-2-sulfide cyclization; herbicidal activity

INTRODUCTION

A focus of our research has been the development of new synthetic methodology centered around biologically active phosphorus compounds.[1–7] In previous papers,[2–5] a number of bioactive phosphorus heterocycles were prepared by cyclization reactions of 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide **(Lawesson's Reagent, LR)**, with certain substrates. Recently, we found that N,N'-diaryl glycinamides (**1**)[6] and 1-aryl-1,3,2-diazaphospholidin-4-thione-2-sulfides[7] possess good herbicidal activity. In order to search for better biologically active materi-

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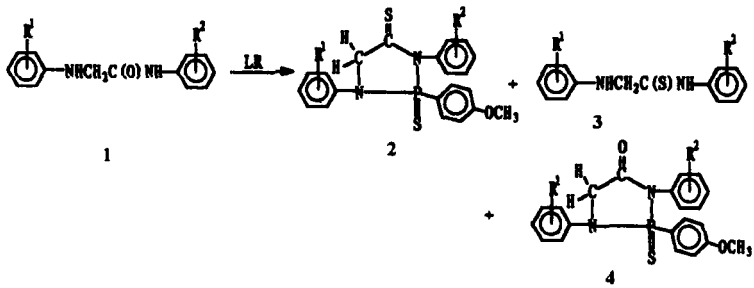
als, cyclization reactions of Lawesson's reagent with N,N'-diaryl glycinamides (**1**) have been investigated and found to give 1,3-diaryl-1,3,2-diazaphospholidin-4-thione-2-sulfides(**2**), which have good herbicidal activity. Our results are reported in this paper.

RESULTS AND DISCUSSION

Lawesson's reagent reacted with N,N'-diaryl glycinamides (**1**) in anhydrous toluene as a solvent using 2:1 molar ratio at 100 °C under dry nitrogen for 12 hrs to yield 1,3-diaryl-1,3,2-diazaphospholidin-4-thione-2-sulfides (**2a-h**), as the main reaction products in significant yields, together with N,N'-diaryl thioglycinamide(**3**), as shown in Scheme 1. When the above reaction was performed using 1 mole of **LR** and one equivalent of 1-phenyl-3-(4'-bromophenyl) glycinamide (**1f**) at different reaction conditions, 1-phenyl-3-(4'-bromophenyl)-1,3,2-diazaphospholidin-4-one-2-sulfides (**4f**) as the main product were obtained in satisfactory yield.



a: R^1,R^2 = H,H; b: R^1,R^2 = H, 4-Me; c: R^1,R^2 = 4-Cl, 4-Me; d: R^1,R^2 = 4-Me, 4-Me ; e: R^1,R^2 = 4-Cl, 4-Cl; f: R^1,R^2 =H, 4-Br; g: R^1,R^2 = 4-Cl,H; h: R^1,R^2 = 4-Me,H

SCHEME 1

Efforts had been devoted to optimize the yields of the title compounds **2**. Table I shows that compounds **2h** and **2f** are the main reaction products when using 1.5 mole of **LR** to one mole of **1f-h**, and increase in yields when using 2:1 molar ratio. 1-Phenyl-3-(4'-bromophenyl) thioglycinamide (**3f**) was formed as the main product only when using 1:1 moles of the

reactants (LR:**1f**) in dry toluene as a solvent at 100°C, while using 1:1 moles of the reactants at different reaction conditions, such as, anhydrous toluene at 50–60 °C for 24 hrs, or in dry acetonitrile at 70 °C for 19 hrs, or in chloroform at room temperature for 72 hrs, 1-phenyl-3-(4'-bromophenyl)-1,3,2-diazaphospholidin-4-one-2-sulfide (**4f**) was formed The thioacetamide, as the side product, was obtained only when the reaction was carried out in anhydrous acetonitrile as a solvent.

TABLE I Experimental, Reaction Conditions and the Products of the Reaction of Lawesson's Reagent with **1**

Starting Materials	*Molar Ratio*	*Solvent*	*Reaction Time (h)*	*Reaction Temp.(°C)*	*Reaction Products, Yield(%)**
LR+1h	1.5:1	$PhCH_3$	12	100	**2h**(20)+3h(5)
LR+1a	1:1	$PhCH_3$	2	110	**3a**(30)
LR+1f	1.5:1	$PhCH_3$	12	100	**2f**(18)+**3f**(7)
LR+1f	2:1	$PhCH_3$	12	100	**2f**(23)+**3f**(2)
LR+1f	1:1	$PhCH_3$	12	100	**2f**(5)+**3f**(21)
LR+1f	1:1	$PhCH_3$	24	50–60	**4f**(25)
LR+1f	1:1	CH_3CN	19	70	**4f**(50)+$CH_3C(S)NH_2$
LR+1f	1:1	$CHCl_3$	72	25	**4f**(30)

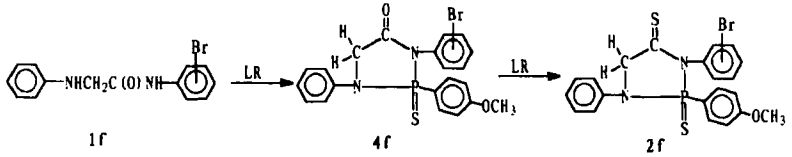
*. Yields were determined after separation on silicon gel column.

The structure of new compounds was confirmed by analytical results and spectral data (IR, NMR and MS). Compound **2b** (taken as representative example) gave correct elemental analysis, in the IR spectrum of **2b** showed peaks at 690 cm^{-1}(P=S) and 1230 cm^{-1} (C=S). The ^1H NMR of compound **2b** (DMSO-d_6) exhibited two singlets at δ =3.77(OCH_3) and δ =2.49 ($PhCH_3$), a doublet at δ =4.65 for methylene (CH_2) in the ring with a couping contant $^3J_{PH}$ = 7.2 Hz, and a multiplet at a range of δ = 6.75–8.10 for aromatic protons (13H). Compound **2b** gave ^{31}P NMR chemical shift at δ = 78.80. Compound **2b** under electron impact gave the molecular ion peak m z 424(M^+, 32). The base peak corresponded to a fragment at m/z 105. The physical data and the spectral data of new compounds **2, 3f** and **4f** are tabulated in Table II.

	C(%)	H(%)	N(%)			
164-165	61.67(61.46)	4.38(4.63)	6.95(6.83)	424(M^+,15); 136(18); 106(100)	687 1240	6.71–7.82(m, 14H,Ar-H), 4.35(d,2H,J=7.2Hz, CH 3.86(s,3H,OCH_3),
172-173	62.03(62.26)	4.75(4.95)	6.91(6.60)	424(M^+,32); 171(22); 119(18); 105(100)	690 1230	6.75–8.10(m, 13H,Ar-H), 4.65(d,2H,J=7.24Hz, C 3.77(s,3H,OCH_3), 2.49(s,3H,$PhCH_3$). ^{31}P NMR:
148-149	57.69(57.58)	4.08(4.36)	6.25(6.11)	458(M^+,24)	675 1230	6.85–7.97(m, 12H,Ar-H), 4.61(d,2H,J=7.2Hz, CH 3.89(s,3H,OCH_3), 2.32(s,3H,$PhCH_3$). ^{31}P NMR:8
112-113	63.29(63.01)	5.13(5.25)	6.45(6.39)	438(M^+,20); 171(35); 105(100)	690 1236	6.73–7.92(m, 12H,Ar-H), 5.13(d,2H,J=5.4Hz, CH 3.80(s,3H,OCH_3), 2.28(s,3H,$PhCH_3$), 2.16(s,3H,P 6.89–7.90(m, 12H,Ar-H),
156 -157	52.34(52.61)	3.37(3.55)	5.72(5.85)	478(M^+,52); 295(28); 139(35); 127(100)	695 1250	6.89–7.90(m, 12H,Ar-H), 5.37(d,2H,J=5.8Hz,CH 3.86(s,3H,OCH_3). ^{31}P NMR : 73.16
118-119	51.71(51.53)	3.46(3.68)	5.58(5.73)	488(M^+,31); 171(20); 105(100)	680 1235	6.75–7.98(m, 13H,Ar-H), 5.23(d,2H,J=7.2Hz. CH 3.89(s,3H,OCH_3)
135-136	56.74(56.69)	4.29(4.05)	6.48(6.30)	444(M^+,15); 111(25); 63(100)	690 1245	6.65–7.71(m, 13H,Ar-H), 4.58(d,2H,J=6.8Hz, CH 3.78(s,3H,OCH_3)

M.P.	Elmental Analysis Found(Cacld.)			MS m/z (%)	IR (cm^{-1})	NMR δ (DMSO-d_6)
	C(%)	H(%)	N(%)			
160-161	62.47(62.26)	4.78(4.95)	6.75(6.60)	424(M^+,25); 275(11); 119(100); 91(92)	679 1240	6.65–7.85(m, 13H,Ar-H), 5.03(d,2H,J=8.2Hz, CH 3.87(s,3H,OCH_3), 2.26(s,3H,$PhCH_3$)
120-121				320(M^+,72); 136(18); 106(100)	3355 1245	9.82(s, 1H,NH), 6.65–7.71(m,8H,Ar-H), 4.33(s,2H,CH_2), 2.31(s,3H,$PhCH_3$)
191-192	53.49(53.28)	3.64(3.81)	5.76(5.92)	472(M^+,19); 304(12); 106(100)	1700 685	6.74–7.68(m,13H,Ar-H), 5.12(d,2H,J=7.2Hz, CH 3.80(s,3H,OCH_3). ^{31}P NMR:18.10

When the reaction of **1f** with LR was conducted in toluene at 50–60°C, the ring-closure product **4f** was formed, but the thionation product (**3f**) and the title compound **2f** were not detected by GC-MS (Scheme 2). However, When **4f** was treated with the excess of LR at 100°C, **2f** was obtained. As to the formation of **2f**, **1f** underwent the cyclization with LR to **4f**, which enter into the O,S-interchange reaction with the excess of LR, yielding **2f**. If the reaction was carried on other conditions, as are listed in Table I, the main products were obtained together with the thionated compound of reactant **1f**. In order to understand more about the mechanism of the reaction, we have done the above reaction using GC-MS technique under the same condition and found that the isolated yields for products **2f** and **4f** are much less than the yields detected by GC-MS.



SCHEME 2

The biological activity of the title products **2** was also tested and some of them showed good herbicidal activity against rape at 100ppm.

EXPERIMENTAL

Melting points were uncorrected, ^{1}H NMR spectra and ^{31}P NMR spectra were recorded on a Varian XL-200 MHz spectrometer. TMS was used as an internal standard for NMR, and 85%H_3PO_4 was used as an external standard for the ^{31}P NMR. Mass spectra were measured on a HP 5988A spectrometer. The IR spectra were measured by using a SHIMADZU-408 instrument. Elemental analysis was performed with a PE-2400 elementary analyzer. Column chromatography was performed on silica gel II (10–40 μ, Hai Yang Chemical Factory of Qingdao). All solvents and materials were reagent grade and purified as required. Compounds **1** were synthesized according to Ref.[6,8,9] Lawesson's reagent was prepared as described in Ref.[10]

General procedure for the reaction of Lawesson's reagent with N,N'-diaryl glycinamide 1. Synthesis of 1,3-diaryl-1,3,2-diazaphospholidin-4-thione-2-sulfide 2

2 Mmole of Lawesson's reagent was treated with 1 molar equvalent of N,N'-diaryl glycinamide (**1**) in 15 mL of anhydrous toluene under dry nitrogen with stirring at 100°C for 12h 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 30%) to give **2**.

The same as above process except using 1:1 molar ratio of reactants (LR:**1f**) was made in dry acetonitrile at 70°C to form **4f**, and thioacetamide. Compound **3f** from LR and **1f** (1:1)was prepared at 110°C as described for **2**. The physical spectral data for the title compounds **2** and **4f** are listed in Table II.

Acknowledgements

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