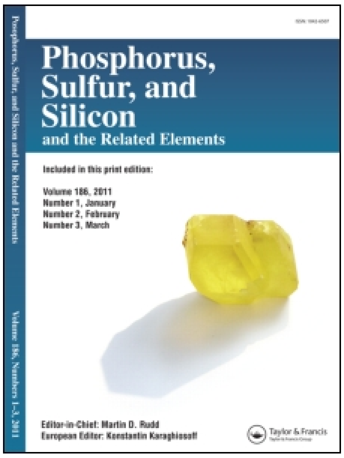

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STUDIES ON ORGANOPHOSPHORUS HETERO-CYCLES PART IV. THE REACTION OF LAWESSON'S REAGENT WITH GLYCINAMIDES, SYNTHESIS AND HERBICIDAL ACTIVITY OF 1,3,2-DIAZAPHOS-PHOLIDIN-4-THIONE-2-SULFIDES

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STUDIES ON ORGANOPHOSPHORUS HETEROCYCLES PART IV. THE REACTION OF LAWESSON'S REAGENT WITH GLYCINAMIDES, SYNTHESIS AND HERBICIDAL ACTIVITY OF 1,3,2-DIAZAPHOSPHOLIDIN-4-THIONE-2-SULFIDES

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2,4-Bis (4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson's Reagent) reacts with glycinamides (**2a–m**) in benzene at 55 ~ 60°C to give 1,3,2-diazaphospholidin-4-thone-2-sulfides (**3a–m**). The structure of the products has been confirmed by elementary analyses, NMR, IR, MS and X-ray diffraction. The result of preliminary bioassay indicates that some of the compounds prepared have high selective herbicidal activity against rape.

Keywords: 1,3,2-Diazaphospholidin-4-thione-2-sulfide; Lawesson's reagent; glycinamide; synthesis; herbicidal activity

INTRODUCTION

2,4-Bis (4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide,[1] commonly known as Lawesson's reagent (LR), is not only a thiating agent for diverse carbonyl compounds,[1–3] but also it undergoes ring-closure reactions with certain substrates containing two functional groups to give phosphorus heterocycles which contain the (4-methoxyphenyl) phosphonothioyliene {4-CH_3O-C_6H_4-P(S)⟨} moiety. These heterocyclic compounds are of potential interest as

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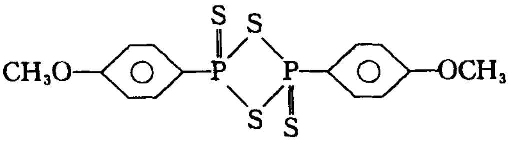


1 (Lawesson's Reagent, LR)

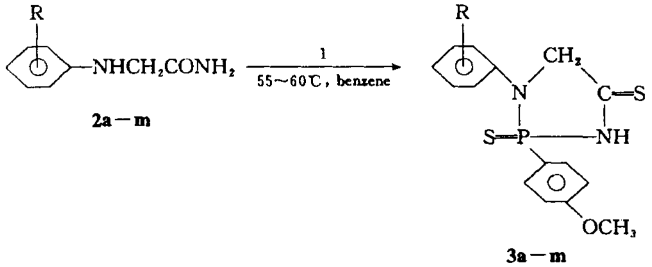
herbicides, insecticides, and fungicides.[4,5] Glycinamides are known as biologically active materials, for example, herbicides,[6] plant-growth regulator.[7] In order to look for potent herbicides and to extend the use of LR to other bifunctional substrates, its reactions with 3-aryl-glycinamides **2a–m** have been investigated and found to give new phosphorus heterocycles which possess high selective herbicidal activity against rape. Our results are reported in this paper.

RESULTS AND DISCUSSION

Synthesis of Heterocycles 3a–m

3-Aryl glycinamides **2a–m** react with LR in benzene at 55 ~ 60°C to give the 1,3,2-diazaphospholidin-4-thione-2-sulfides **3a–m** in moderate yield (Scheme 1). In the reactions of LR with glycinamides, 1 mole of LR is sufficient for the conversion of 1 mole of the substrate to the phosphorus heterocyclic compounds **3a–m**.

The structure of **3b**, taken as representative example, was established by elemental analysis, IR, ^{1}H-NMR, ^{31}P-NMR, MS and X-ray diffraction (Table I). In the ^{1}H NMR, compound **3b** ($CDCl_3$) shows signals at δ = 3.84 (s, 3H, OCH_3, para to the phosphorus atom), 2.17 (s, 3H, CH_3, ortho to the nitrogen



a:R=H; b:R=*o*-Me; c:R=*m*-Me; d:R=*p*-Me; e:R=*o*-Cl; f:R=*p*-Cl; g:R=2,4-2Cl; h:R=*p*-Br; i:R=*o*-Br; j:R=*o*-NO_2; k:R=*m*-NO_2; l:R=*p*-NO_2; m:R=2,4-2NO_2.

SCHEME 1

TABLE I The Physical and Chemical Data of Compounds **3a–m**

			Elemental Analysis/ Found (Cacld.)					
NO	*Yield (%)*	*MP (°C)*	*C (%)*	*H (%)*	*N (%)*	*MS (M^+)*	*IR (cm^{-1})*	*NMR ($CDCl_3$,δ)*
3a	50.74	161 ~ 162	53.87 (53.89)	4.68 (4.49)	8.45 (8.38)	334	3396(N — H) 633(P=S)	8.22 (d, 1H, NH, $^2J_{PH}$ = 25.04Hz), 6.93 ~ 7.83 (m, 9H, Ar — H), 4.80 (d, 2H, CH_2, $^3J_{PH}$=6.8Hz), 3.84 (s, 3H, OCH_3). ^{31}P NMR: 71.57
3b	57.31	149 ~ 150	55.36 (55.17)	4.67 (4.89)	8.23 (8.05)	348	3207(N — H) 637(P=S)	8.48 (d, 1H, NH, $^2J_{PH}$ = 25.04Hz), 6.94 ~ 7.87 (dd, 4H, protons in the anisyl part), 6.87 ~ 7.32 (d, 4H, protons of benzne ring), 4.74 (d, 2H, CH_2, $^3J_{PH}$ = 6Hz), 3.84 (s, 3H, OCH_3), 2.17 (s, 3H, Ph — CH_3). ^{31}P NMR: 74.75
3c	53.24	168 ~ 170	55.29 (55.17)	4.73 (4.89)	8.22 (8.05)	—[a]	—	8.32 (d, 1H, NH, $^2J_{PH}$ = 26.08Hz), 6.77 ~ 7.86 (m, 8H, Ar — H), 4.81 (d, 2H, CH_2, $^3J_{PH}$ = 7.5Hz), 3.84 (s, 3H, OCH_3), 2.24 (s, 3H, $PhCH_3$). ^{31}P NMR: 71.72
3d	56.80	162 ~ 163	55.35 (55.17)	4.78 (4.89)	8.17 (8.05)	—	3283(N — H) 639(P=S)	8.42 (d, 1H, NH, $^2J_{PH}$ = 25.04Hz), 6.88 ~ 7.90 (m, 8H, Ar — H), 4.79 (d, 2H, CH_2, $^3J_{PH}$=8.1Hz), 3.84 (s, 3H, OCH_3), 2.21 (s, 3H, $PhCH_3$). ^{31}P NMR: 71.84

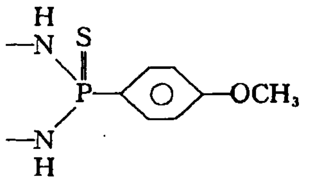
TABLE I *continued*

NO	*Yield (%)*	*MP (°C)*	*Elemental Analysis/ Found (Cacld.)* *C (%)*	*H (%)*	*N (%)*	*MS (M^+)*	*IR (cm^{-1})*	*NMR ($CDCl_3$,δ)*
3e	43.12	154 ~ 155	48.96 (48.85)	3.92 (3.80)	7.73 (7.60)	—	—	8.40 (d, 1H, NH, $^2J_{PH}$ = 23.96HZ), 6.97 ~ 7.88 (m, 8H, Ar — H), 4.68 (d, 2H, CH_2, $^3J_{PH}$ = 7.2Hz), 3.85 (s, 3H, OCH_3). ^{31}P NMR: 71.68
3f	49.80	148 ~ 149	48.64 (48.85)	3.92 (3.80)	7.43 (7.60)	368	3374(N — H) 640(P=S)	8.48 (d, 1H, NH, $^2J_{PH}$ = 25.04Hz), 6.88 ~ 7.88 (m, 8H, Ar — H), 4.74 (d, 2H, CH_2, $^3J_{PH}$ = 7.0Hz), 3.84 (s, 3H, OCH_3). ^{31}P NMR: 71.66
3g	31.43	170 ~ 172	44.34 (44.55)	3.28 (3.32)	6.85 (6.93)	—	—	8.46 (d, 1H, NH, $^2J_{PH}$ = 24.82Hz), 6.93 ~ 7.80 (m, 7H, Ar — H), 4.72 (d, 2H, CH_2, $^3J_{PH}$ = 7.6Hz), 3.85 (s, 3H,OCH_3).
3h	55.38	156 ~ 157	43.57 (43.58)	3.31 (3.39)	6.58 (6.78)	413	3386(N — H) 638(P=S)	8.48 (d, 1H, NH, $^2J_{PH}$ = 22.95Hz), 6.93 ~ 7.89 (m, 8H, Ar — H), 4.61 (d, 2H, CH_2, $^3J_{PH}$ = 7.6Hz), 3.86 (s, 3H, OCH_3). ^{31}P NMR: 71.60
3i	48.36	157 ~ 158	43.41 (43.58)	3.42 (3.39)	6.93 (6.78)	—	—	8.46 (d, 1H, NH, $^2J_{PH}$ = 23.40Hz), 6.95 ~ 7.83 (m, 8H, Ar — H), 4.70 (d, 2H, CH_2, $^3J_{PH}$ = 7.2HZ), 3.84 (s, 3H, OCH_3).

TABLE I *continued*

			Elemental Analysis/ Found (Cacld.)					
NO	*Yield (%)*	*MP (°C)*	*C (%)*	*H (%)*	*N (%)*	*MS (M^+)*	*IR (cm^{-1})*	*NMR ($CDCl_3$, δ)*
3j	40.08	124 ~ 126	47.62 (47.49)	3.54 (3.69)	11.23 (11.08)	379	3342(N — H) 642(P=S)	8.54 (d, 1H, NH, $^2J_{PH}$ = 25.38Hz), 6.98 ~ 7.90 (m, 8H, Ar — H), 4.76 (d, 2H, CH_2, $^3J_{PH}$ = 7.6HZ), 3.89 (s, 3H, OCH_3). ^{31}P NMR: 70.12
3k	35.63	101 ~ 102	47.55 (47.49)	3.56 (3.69)	11.26 (11.08)	—	3360(N — H) 640(P=S)	8.46 (d, 1H, NH, $^2J_{PH}$ = 24.36Hz), 6.92 ~ 7.88 (m, 8H, Ar — H), 4.72 (d, 2H, CH_2, $^3J_{PH}$ = 6.8HZ), 3.85 (s, 3H, OCH_3).
3l	30.78	142 ~ 143	47.38 (47.49)	3.52 (3.69)	11.25 (11.08)	—	3380(N — H) 634(P=S)	8.72 (d, 1H, NH, $^2J_{PH}$ = 25.84Hz), 6.95 ~ 7.92 (m, 8H, Ar — H), 4.77 (d, 2H, CH_2, $^3J_{PH}$ = 7.8HZ), 3.88 (s, 3H, OCH_3).
3m	25.64	160 ~ 161	42.29 (42.45)	3.21 (3.07)	13.08 (13.21)	424	3358(N — H) 644(P=S)	8.64 (d, 1H, NH, $^2J_{PH}$ = 24.38Hz), 6.94 ~ 7.85 (m, 7H, Ar — H), 4.74 (d, 2H, CH_2, $^3J_{PH}$ = 7.4Hz), 3.87 (s, 3H, OCH_3). ^{31}P NMR: 68.94

[a]Data were not recorded.



atom), 4.74 (d, 2H, CH_2, split by phosphorus atom $^3J_{PH}$ = 6 Hz), 8.48 (d, 1H, NH, split by phosphorus atom $^2J_{PH}$ = 25.04 Hz), 7.75 ~ 7.87 (dd, 2H, with $^3J_{PH}$ = 14.8Hz and $^3J_{HH}$ = 9Hz, ortho proton to phosphorus), 6.94 ~ 6.99 (dd, 2H, $^3J_{HH}$ = 9Hz and $^4J_{PH}$ = 4Hz, meta proton to phosphorus in the anisole ring), 7.28 ~ 7.32 (d, 2H, $^3J_{HH}$ = 8.8Hz, ortho proton to nitrogen), 6.82 ~ 6.87 (d, 2H, $^3J_{HH}$ = 8.8Hz, meta proton to nitrogen of the ring benzene). Compound **3b** gives ^{31}P NMR chemical shift at δ74.75 which in accordance with other compounds containing the following structure.[8]

Compound **3b** under electron impact gives the molecular ion peak m/z (%): 348 (38.94).

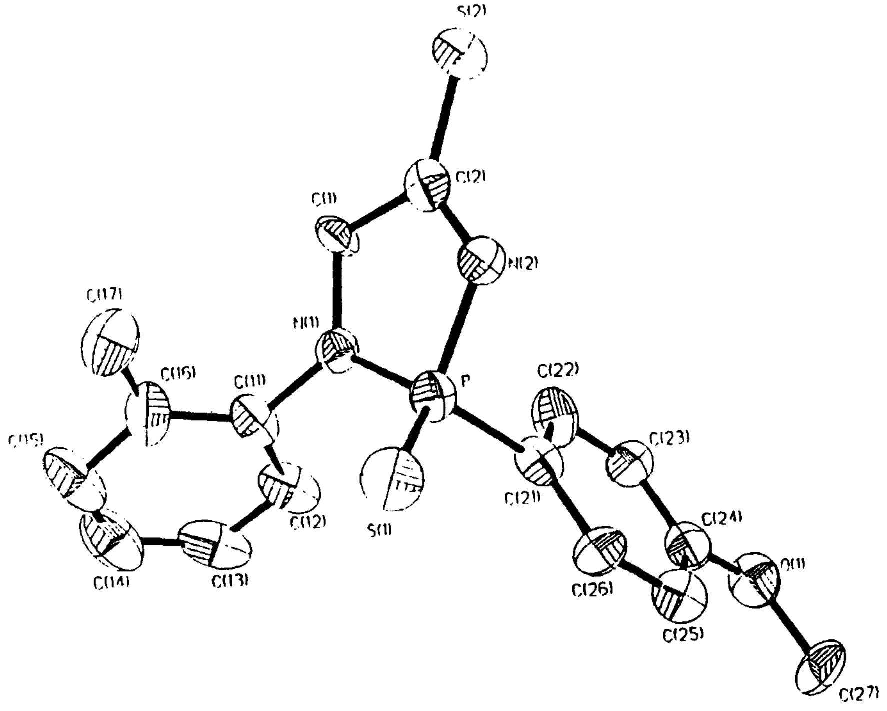
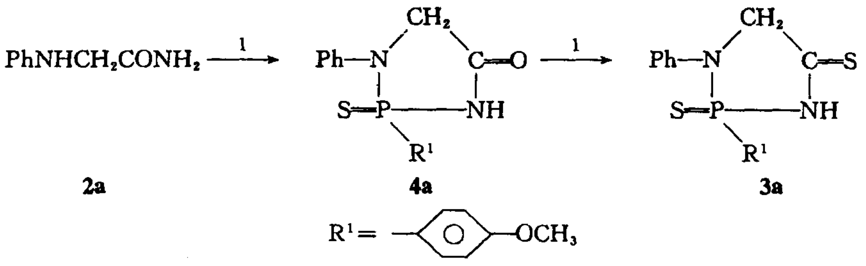


FIGURE 1 The molecular structure of **3b**



SCHEME 2

The IR spectra of compound **3b** shows normal stretching absorption bands, indicating the existence of the N-H (3207 cm^{-1}) and P=S (637 cm^{-1}) groups.

Figure 1 is the molecular structure of compound **3b** showing the atomic numbering scheme. There is a five-membered phosphorus heterocycles containing a phosphorus, two nitrogen atoms and two carbon atoms in the molecular. The result of X-ray diffraction analysis indicates the coplanar structure of the five-membered phosphorus heterocycle and the existence of the $d\pi$–$p\pi$ bond between P and N(1) atom.

When the reaction of **2a** with LR is conducted in benzene at room temperature, the ringclosure product **4a** is formed, but the thionation product of **2a** [$PhNHCH_2C(S)NH_2$] and **3a** are not detected by GC-MS (Scheme 2). As to the formation of **3a**, **2a** undergoes heterocyclization with LR to **4a** which enter into the O,S-interchange reaction with the excess of LR, yielding **3a**. So, carbonyl group of glycinamide is thionated after the ringclosure stage.

Herbicidal Activity for Compounds 3

The herbicidal activity of compounds **3** 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. Rape and barnyard grass were subjected to the leaf treatment. Prliminary bioassay indicates that some of compounds **3** display good selective herbicidal activity at 1.5 kg/ha. The results are given in Table II.

In conclusion, the reaction of LR with 3-aryl glycinamide affords novel route to the synthesis of biologically active 1,3,2-diazaphospholidin-4-thione-2-sulfide.

TABLE II Herbicidal Activity of Compounds **3** [inhibition(%)] at 1.5 kg/ha

Compd	*inhibition (%)*		*Compd*	*inhibition (%)*	
	Rape	*Barnyard-grass*		*Rape*	*Barnyard-grass*
3a	73.7	26.5	3h	7.5	4.1
3b	50.0	36.5	3i	76.3	17.7
3c	33.7	3.0	3j	82.8	0
3d	47.3	20.0	3k	50.1	6.8
3e	14.0	11.8	3l	68.7	0
3f	95.2	0	3m	86.8	11.4
3g	90.7	9.5			

EXPERIMENTAL

Elemental analysis was performed with a CHN CORDERD MT-3 elementary analyzer. Mass spectra were recorded with a VG-7070E spectrometer and HP 5988 GC-MS instrument. ^1H NMR spectra were recorded with varian XL-200 spectrometer and BRUKER AC-P200. TMS was used as an internal standard for ^1H NMR and 85% H_3PO_4 was used as an external standard for ^{31}P NMR. The IR spectra were measured by using a SHIMADZU-435 instrument. Melting points were determined with a model YANACO MP-500 apparatus and were uncorrected. Column chromatography was performed on silica gel II ($10 \sim 40\mu$, Hai Yang Chemical Factory of Qingdao).

A single crystal of **3b** was cultured from the mixture of petroleum ether and dry ethyl ether. The reflections in the range of $4^\circ < 2\theta < 46^\circ$ were collected on an ENRAF-NONIUS CAD_4 X-ray diffractometer with M_oK_α radiation ($\lambda = 0.071073nm$). All calculations were performed on a PDP 11/44 computer using the SDP-PLUS program system. The crystal is monoclinic with space group $P2_1/n$,a = 9.459(2)Å, b = 7.954(5) Å, c = 23.039(8)Å, β = 96.30(2)°, V = 1739(2)$Å^3$, Z = 4, Mr = 348, F(000) = 728, $\mu(M_oK_\alpha) = 0.386mm^{-1}$, Dx = 1.331$Mg/m^3$. The final R factor is 0.044 and Rw is 0.047 for 1002 observed reflections [$I \geq 3\sigma(I)$].

2a–i and **2**j–m were synthesized according to Ref.[7] and Ref.[9], respectively. Lawesson's reagent was prepared as described in Ref.[10].

General procedure for the reaction of LR with 3-aryl glycinamide, preparation of 1,3,2-diazaphospholidin-4-thione-2-sulfides (3a–m)

A solution of 0.01 mole of the starting compound and 0.01 mole of Lawesson's reagent in 10ml dry benzene were stirred with a magnetic mixer at 55 ~ 60°C until no more of the starting material could be detected (TLC). The solvent was evaporated under reduced pressure and the residue purified on a silica gel col-

TABLE III Atomic Coordinates and Thermal Parameters of 3**b**

Atom	*x*	*y*	*z*	*Beq*($Å^2$)
P	0.9514(2)	0.0334(3)	0.1401(1)	3.60(5)
S(1)	1.0581(3)	0.2230(3)	0.1215(1)	5.30(6)
N(1)	1.0297(6)	−0.1233(8)	0.1765(3)	3.4(1)
C(1)	0.9738(8)	−0.165(1)	0.2303(4)	3.7(2)
C(2)	0.8586(7)	−0.044(1)	0.2386(4)	3.9(2)
N(2)	0.8435(6)	0.0622(7)	0.1942(3)	3.5(1)
S(2)	0.7657(2)	−0.0468(3)	0.2946(1)	4.41(5)
C(11)	1.1507(8)	−0.208(1)	0.1586(4)	4.2(2)
C(12)	1.1326(9)	−0.324(1)	0.1135(4)	5.2(2)
C(13)	1.243(1)	−0.412(1)	0.0972(5)	7.3(3)
C(14)	1.3757(9)	−0.377(1)	0.1252(5)	6.9(3)
C(15)	1.3982(8)	−0.267(1)	0.1690(5)	6.2(3)
C(16)	1.284(1)	−0.177(1)	0.1869(4)	5.5(2)
C(17)	1.3082(9)	−0.054(1)	0.2315(5)	6.5(3)
C(21)	0.8338(8)	−0.044(1)	0.0811(3)	3.6(2)
C(22)	0.7643(9)	−0.196(1)	0.0865(4)	4.8(2)
C(23)	0.6757(9)	−0.255(1)	0.0415(4)	5.1(2)
C(24)	0.6496(8)	−0.168(1)	−0.0092(4)	4.4(2)
C(25)	0.7172(9)	−0.017(1)	−0.0161(4)	4.8(2)
C(26)	0.8107(8)	0.041(1)	0.0299(4)	4.5(2)
O(1)	0.5568(6)	−0.240(8)	−0.0509(3)	5.8(2)
C(27)	0.527(1)	−0.157(1)	−0.1039(4)	6.9(3)

Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $Beq = (4/3) * [a^2 * \beta(1,1) + b^2 * \beta(2,2) + c^2 * \beta(3,3) + ab(\cos\Gamma) * \beta(1,2) + ac(\cos\beta) * \beta(1,3) + bc(\cos\alpha) * \beta(2,3)]$

umn using petroleum ether/dry ethyl ether mixtures as eluent. The physical and chemical data are summarized in Table I.

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