A CONVENIENT SYNTHESIS OF DERIVATIVES OF 1,3,2-DIOXAPHOSPHOCANE-2-SULFIDE WITH BIOACITIVITY VIA LAWESSON'S REAGENT

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Abstract: Lawesson's reagent, 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disufide, reacted with the substituted 1,5-bisphenol **1** to afford derivatives of 1,3,2-dioxaphosphocane-2-sulfide **2**, which were found to possess selective herbicidal activity against rape.

Introduction

Within the rapid development of the chemistry of phosphorus-heterocycles, functionlized phosphorus-heterocycles and their derivatives have received considerable attention since they are of great interests as bioactive substances with various properties(1,2). It was reported that the heterocyclic compounds, which incorporate phosphinothioylene moiety, are of potential interest as herbicides, insecticides, and fungicides(3-7). In the preceding paper(8), we disclosed a methodology

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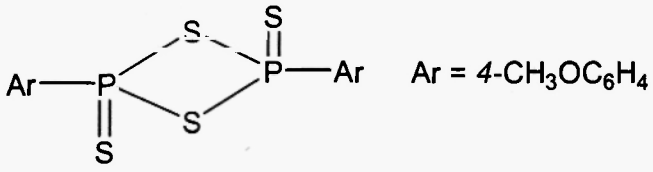
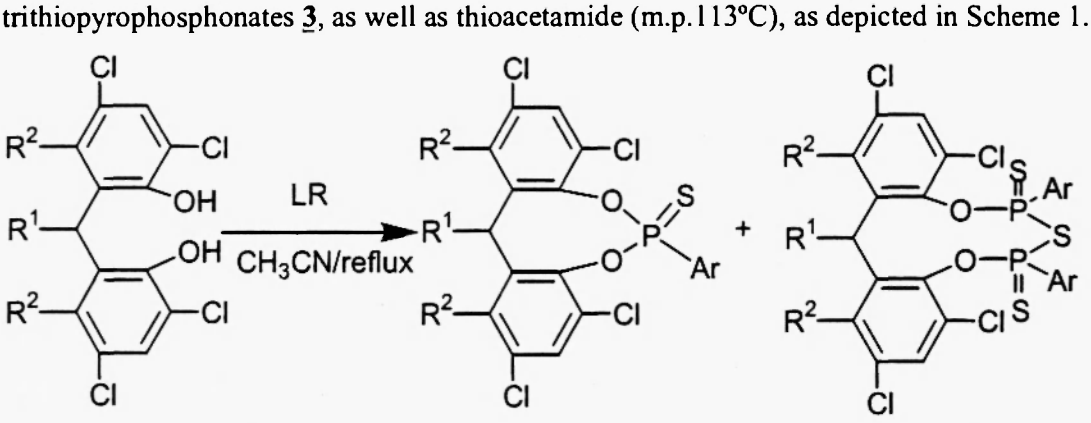
for bioactive 5-membered and 6-membered phosphorus- heterocycles via cyclization reactions of 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disufide (Lawesson's reagent, LR) with bifunctional compounds, as well as its addition toward unsaturated substrates. This cyclization reaction of Lawesson's reagent is readily applicable to other bifunctional compounds to form different kinds of phosphorus-heterocycles. Derivatives of 1,3,2-dioxaphosphecane were tested as germicides for prevention and treatment of plant frost mycosis(9). We report here synthesis of derivatives of 1,3,2-dioxaphosphocane-2-sulfide via cyclization of Lawesson's reagent with one kind of aromatic dihydroxy compound, namely, 1,5-bisphenols **1**.



Lawesson's Reagent (LR)

Results and Discussion

0.6 Molar equivalents of Lawesson's reagent reacted with one mole of the corresponding 1,5-bisphenols **1** (10), which were prepared by condensation of substituted phenols with aldehydes in the presence of concentrated sulfuric acid, in anhydrous acetonitrile as a solvent at reflux under dry nitrogen for 10-12 hrs to afford the phosphorus-heterocyles **2** in significant yields and cyclic trithiopyrophosphonates **3**, as well as thioacetamide (m.p.113°C), as depicted in Scheme 1.



1 **2a-c** **3d**

Ar = 4-$CH_3OC_6H_4$

2a: R^1, R^2 = H, Cl; **2b**: R^1, R^2 = *p*-ClC_6H_4, H; **2c**: R^1, R^2 = o-ClC_6H_4, H; **3d**: R^1, R^2 = *p*-$NO_2C_6H_4$, H.

Scheme 1

The structure of the title compounds has been confirmed by analytical results and spectral data IR NMR, and MS. Compound **2a** (taken as representative example) gave correct elemental analysis, in the IR spectra **2a** showed peaks at 750 cm^{-1}, 1020 cm^{-1} (P-O-C), and 1590 cm^{-1}, 1500 cm^{-1}, 1425 cm^{-1} for aromatic ring. The ^1H NMR existed a singlet at 3.90(s, 3H, CH_3O), two kinds of multiplet at 6.50(m, 2H, CH_2), 7.02-8.02(m, 6H, aromatic protons, Ar-H). The ^{31}P NMR ($CDCl_3$) showed a singlet peak: δ_P 83.6. The EI-MS spectra showed *m/z* (%): 572(M^+, 20).

Very interestingly, distribution of products **2** and **3** depends on the substituted groups (R^1 and R^2). Generally, derivative of 1,3,2-dioxaphosphocane-2-sulfide **2** was obtained as main product and cyclic trithiopyrophosphonates **3** as minor product (less than 3%). However, in the case of R^1 and R^2 contain *p*-$NO_2C_6H_4$, **3d** was separated as main product and **2d** as minor product (less than 5%).

Preliminary biological screening tests (11) for these rings **2** and **3** indicated that products **2** have significant selective herbicidal activity against rape. In conclusion, the cyclization of Lawesson's reagent with aromatic dihydroxy compounds provides a facile route leading to phosphorus heterocycles with biological activity.

Experimental

Melting points were determined with a model X_4 apparatus and were uncorrected. ^1H NMR spectra and ^{31}P NMR spectra were recorded on a Varian XL-200 MHz spectrometer. Mass spectra were measured on a HP 5988A spectrometer. Elemental analysis was measured with a PE-2400 elementary analyzer. The IR spectra were measured by using a shimdzu-408 instrument. Column chromatography was performed on silica gel II (10-40μ, Hai Yang Chemical Factory of Qingdao). All solvents and materials were reagent grade and purified as required. Lawesson's reagent was prepared in a yield of 75% according to published procedure (12).

General Procedure the cyclization reaction of Lawesson's reagent with 1,5-bisphenol ***1****. Synthesis of the phosphorus-heterocycles* ***2*** —A three-necked flask equipped a dropping funnel, stirrer, drying $CaCl_2$ tube and nitrogen gas inlet was charged with anhydrous acetonitrile (10ml) and Lawesson's reagent (0.6mmol). Then a mixture of substrates **1** (1mmol)and anhydrous CH_3CN (10ml) was added dropwise to the solution at room temperature. When the addition was complete, the reaction mixture was heated and refluxed under dry nitrogen with stirring for 10-12h until no more of the starting materials could be detected by TLC. Evaporation of the solvent followed by column chromatography on silica gel using light petroleum ether (bp 40-60 °C)-dry ethyl ether as eluent yielded the

corresponding heterocycles **2a-c** or **3d**, together with thioactamide. Yields were determined after separation on silicon gel column. The structures of new compounds were confirmed by correct elemental analysis and spectral results. Spectral data for products are given below.

2a colorless crystal; mp 188-189°C; yield 32%; ^{1}H NMR δ_H($CDCl_3$): 3.90(s, 3H, CH_3O), 6.50(m, 2H, CH_2), 7.02-8.02(m, 6H, aromatic protons, Ar-H). ^{31}P NMR δ_P($CDCl_3$): 83.6. IR ν (KBr, cm^{-1}): 750 (P=S), 1020(P-O-C), 1180, 1200(C-O-C), 1590, 1500, 1425 (aromatic ring). EI-MS (int.rel) *m/z*(%): 572(M^+, 20), 539(64), 403(100), 367(14), 171(198), 63(30).

2b white crystal; mp 214-216°C; yield 33%; ^{1}H NMR δ_H ($CDCl_3$): 3.85(s, 3H, CH_3O), 6.80(s, 2H, CH), 6.95-7.71(m, 12H, aromatic protons, Ar-H). ^{31}P NMR δ_P ($CDCl_3$): 85.8. IR ν (KBr, cm^{-1}): 740 (P=S), 1030(P-O-C), 1190, 1210(C-O-C), 1590, 1510, 1455 (aromatic ring). EI-MS (int.rel) *m/z*(%): 614(M^+, 44), 583(100), 445(43), 139(29), 63(22).

2c white crystal; mp 143-145°C; yield 29%; ^{1}H NMR δ_H ($CDCl_3$): 3.95(s, 3H, CH_3O), 6.45(s, 1H, CH), 6.85-7.49(m, 12H, aromatic protons, Ar-H). ^{31}P NMR δ_P ($CDCl_3$): 84.3. IR ν (KBr, cm^{-1}): 690 (P=S), 1020(P-O-C), 1105, 1255(C-O-C), 1590, 1500, 1400 (aromatic ring). EI-MS (int.rel) *m/z*(%): 614(M^+, 4), 581(14), 448(30), 413(25), 139(100), 63(35).

3d yellow powder; mp 216-218°C; yield 37%; ^{1}H NMR δ_H ($CDCl_3$): 3.94(s, 6H, CH_3O), 6.82(s, 1H, CH), 6.95-8.32(m, 16H, aromatic protons, Ar-H). ^{31}P NMR δ_P ($CDCl_3$): 84.4 and 77.0. IR ν (KBr, cm^{-1}): 710 (P=S), 1025(P-O-C), 1105, 1255(C-O-C), 1590, 1510, 1440 (aromatic ring). EI-MS (int.rel) *m/z*(%): 827(M^+, 2), 778(54), 628(43), 610(100), 440(29), 139(43), 63(41).

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(11) A set of 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.

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