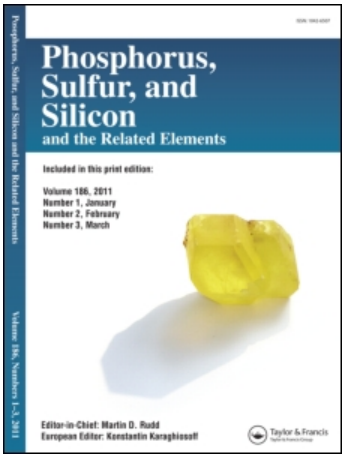

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Liangnian He[a]; Yanping Luo[ab]; Kai Li[a]; Guangfu Yang[a]; Mingwu Ding[a]; Xiaopeng Liu[c]; Tianjie Wu[c]
[a] Institute of Organic Synthesis, Central China Normal University, China [b] College of Plant Protection, South China University of Tropical Agriculture, China [c] Center of Analysis and Testing, Central China Normal University, China

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A FACILE SYNTHESIS OF FUSED PHOSPHORUS-HETEROCYCLE WITH BIOACTIVITY VIA LAWESSON'S REAGENT

Liangnian He,[a] *Yanping Luo,*[a,c] *Kai Li,*[a] *Guangfu Yang,*[a] *Mingwu Ding,*[a] *Xiaopeng Liu,*[b] *and Tianjie Wu*[b]
Institute of Organic Synthesis, Central China Normal University, China;[a] *Center of Analysis and Testing, Central China Normal University, China;*[b] *and College of Plant Protection, South China University of Tropical Agriculture, China*[c]

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A convenient one-pot synthesis of fused phosphorus-heterocycles with biological activity via the cyclization reactions of Lawesson's reagent with bifunctional substrates is reported.

Keywords: Fused phosphorus-heterocycle; herbicidal activity; Lawesson's reagent

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 heterocylic compounds, which incorporate phosphinothioylene moiety, are of potential interest as herbicides, insecticides, and fungicides.[3–7] In the preceding paper,[8–11] we disclosed a methodology for bioactive five-membered and six-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. With this strategy in hand, we have succeeded in the

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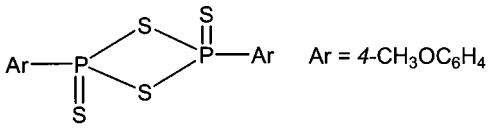
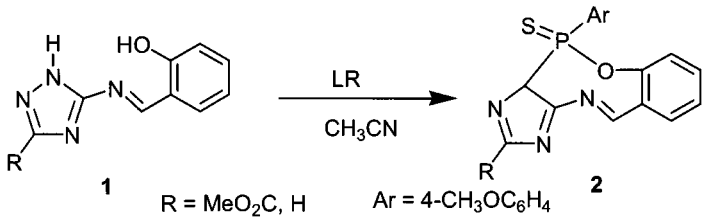
Address correspondence to Liangnian He, Institute for Materials and Chemical Process, National Institute of Advanced Industrial Science and Technology, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8565, Japan. E-mail: helnnan@aist.go.jp

one-pot conversion of bifunctional compounds into the corresponding fused phosphorus-heterocycles employed Lawesson's reagent.



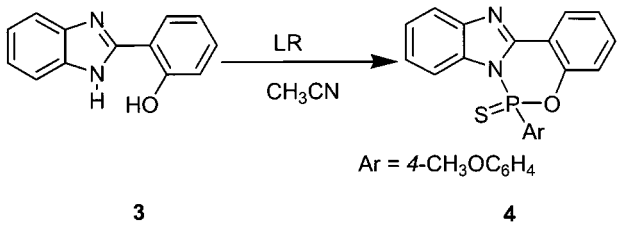
Lawesson's Reagent (LR).

Lawesson's reagent reacted with Schieff bases **1**,[12] which were prepared by condensation of 3-amino-1,2,4-triazole and salicylaldehyde, in anhydrous acetonitrile as a solvent using 2:1 molar ratio at reflux under dry nitrogen for 10 h to afford the fused heterocyles **2** in significant yields, as depicted in Scheme 1.



SCHEME 1

Similarly, 0.5 molar equivalent of Lawesson's reagent was treated with benzimidazole **3**,[13] synthesized from 1,2-phenylenediamine and salicylaldehyde to provide the fused ring **4** (Scheme 2).



SCHEME 2

All of the new fused heterocycles **2** and **4** containing phosphorus were characterized satisfactorily by elemental analyses and spectra, IR, ^{1}H NMR, ^{31}P NMR, and MS, as described in the Experimental section. Particularly noteworthy is the ^{31}P chemical shift of **2a** (R=MeO_2C), which has slightly up-field shift compared with **2b** (R=H), probably due

to the different extent of $d\pi$–$p\pi$ bond[14,15] between phosphorus atom and sulfur atom influenced by substituent through the cyclic conjugation.

Preliminary biological screening tests* for these fused rings **2** and **4** indicated that they possess significant selective herbicidal activity against rape. In conclusion, the cyclization of Lawesson's reagent with bifunctional substrates provides a facile route leading to fused phosphorus heterocycles with biological activity.

EXPERIMENTAL

Melting points were determined with a model X_4 apparatus and were uncorrected. ^{1}H NMR 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. 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. Lawesson's reagent was prepared in a yield of 75% according to published procedure.[16]

General Procedure for the Cyclization Reaction of Lawesson's Reagent with Bifunctional Substrates. Synthesis of the Fused Phosphorus-Heterocycles 2 and 4

A three-necked flask equipped a dropping funnel, stirrer, drying $CaCl_2$ tube, and nitrogen gas inlet was charged with anhydrous acetonitrile (10 ml) and Lawesson's reagent (1 mmol). Then a mixture of substrates (**1** or **3**, 1 mmol) and anhydrous CH_3CN (10 ml) 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 h 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 (b.p. 40–60°C)-dry ethyl ether as eluent yielded the corresponding heterocycles **2** or **4**. 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.

*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.

2a (R=MeO_2C) yield 35%, brown solid, m.p. 169–170°C; δ_H (DMSO-d_6) 2.46 (s, 3H, CH_3O_2C), 3.94 (s, 3H, CH_3O), 6.88–8.22 (m, 9H, Ar—H and CH=N). δ_p (DMSO-d_6) 68.46. *m/z* (EI-MS) 414 (M^+, 14.45%). Anal. Calcd. For $C_{18}H_{15}N_4O_4PS$: C, 52.17; H, 3.62; N, 13.52. Found: C, 52.34; H, 3.59; N, 13.68.

2b (R=H) yield 33%, colorless crystal, m.p. 198–200°C; δ_H (DMSO-d_6) 3.83 (s, 3H, CH_3O), 7.05–8.08 (m, 10H, Ar—H and CH=N). δ_p (DMSO-d_6) 70.85. *m/z* (EI-MS) 356 (M^+, 20.49%). Anal. Calcd. For $C_{16}H_{13}N_4O_2PS$: C, 53.93; H, 3.65; N, 15.73. Found: C, 53.56; H, 3.57; N, 15.52.

4 yield 42.2%, white powder, m.p. 128–130°C; δ_H (DMSO-d_6) 3.85 (s, 3H, CH_3O), 7.00–8.15 (m, 12H, Ar—H). δ_p (DMSO-d_6) 78.32. *m/z* (EI-MS) 378 (M^+, 90.58%). Anals. Calcd. For $C_{20}H_{15}N_2O_2PS$: C, 63.49; H, 4.00; N, 7.41. Found: C, 63.81; H, 3.93; N, 7.18.

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