



Reaction of Lawesson's Reagent with Triethylphosphite

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PREVIOUSLY, it has been reported that the reaction of L.R. with Di and Tri alkyl phosphites afforded the thioproducts. Here in, we have reacted Lawesson's reagent (L.R., **1**) with triethylphosphite **2** in refluxing acetonitrile to give three phosphonate derivatives **3**, **4** and **5** respectively. Structures of the later products were confirmed by analytical and spectroscopic evidences.

Keywords: Lawesson's reagent; Triethylphosphite; Phosphonates.

Introduction

Organothio phosphorus compounds are versatile chemicals that can be used as agrochemicals and pesticides (Figure 1) [1-4]. Besides, they represent important categories in therapeutic drugs in human and veterinary medicine [5,6].

Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide, L.R., **1**) is H₂S donor which reduces the gastric damage induced by ethanol, participates in ulcer repair and regulates gastric mucosal blood flow.[7]

L.R. has a significant role in the synthesis of a lot of medicinal important products having sulfur atom in their chemical structures such as Althiomycin, Dehydrogliotoxin, Sporidesmin A, etc... (Figure 2) [8-11].

In addition, Lawesson's reagent (L.R., **1**) is the most used agent for the transformation of a carbonyl group into thiocarbonyl as well as for the synthesis and construction of huge numbers of P- and/ or S-containing heterocyclic compounds. [12-22].

Shabana *et al.* [23] and Zabiroy *et al.* [24] have reported the reaction of dialkyl phosphites with LR (*cf.* Scheme 1).

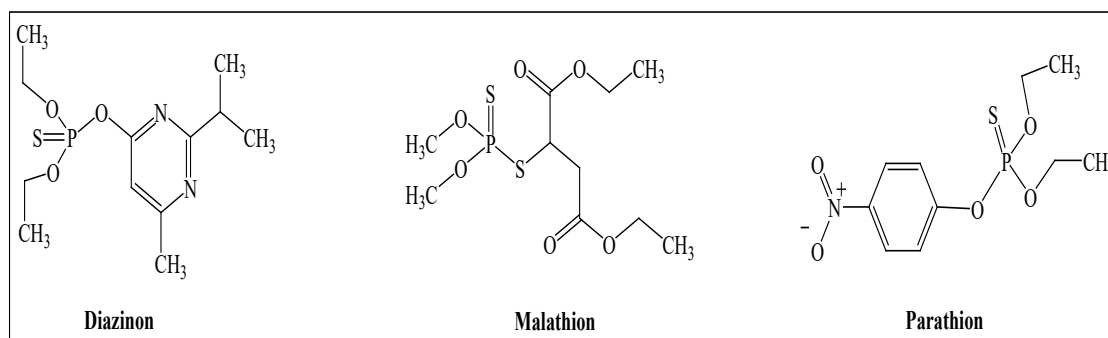


Fig. 1. Some commonly organophosphorus pesticides.

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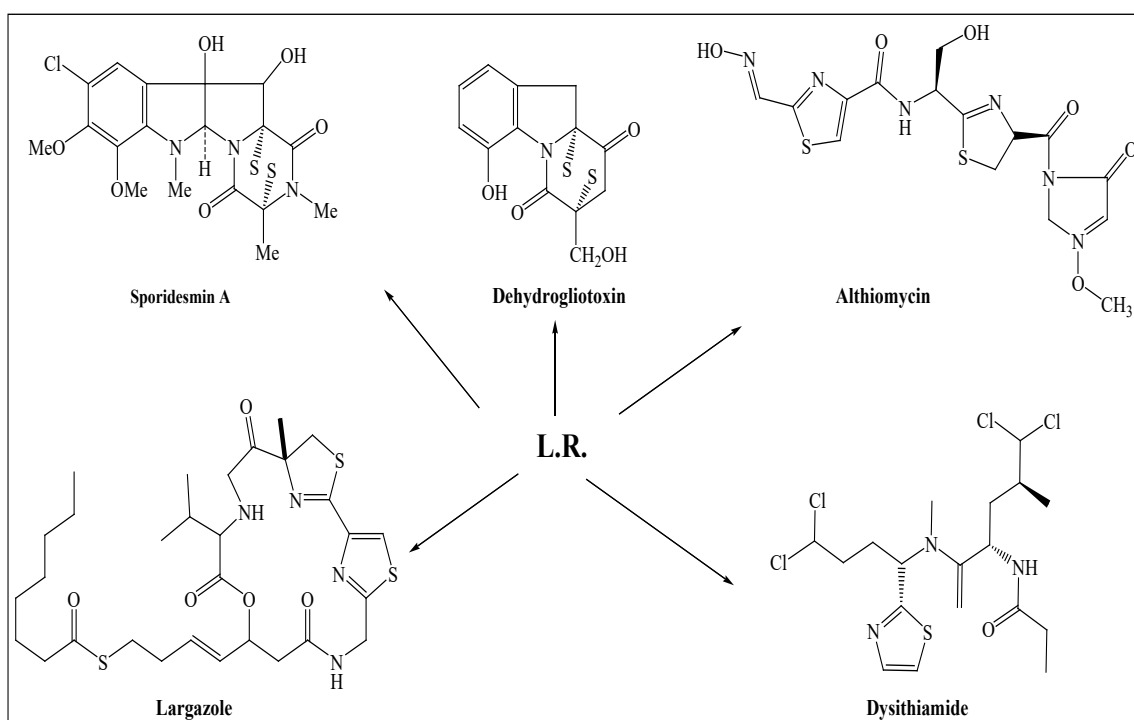
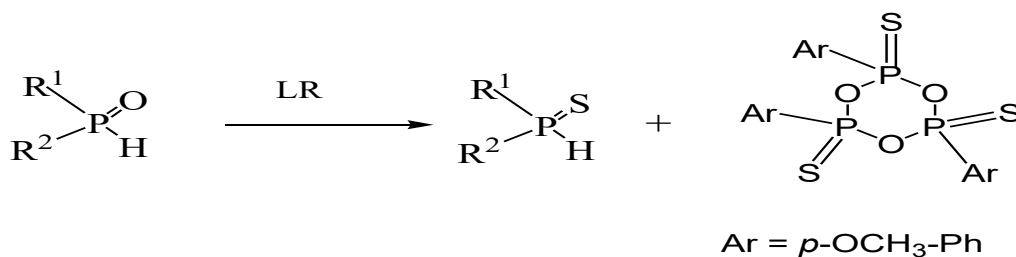


Fig. 2. Some medicinal important products have been prepared using L.R.



Scheme 1. Reaction of L.R. with Dialkyl phosphites.

Extending our work on the reaction of 2,4-bis-(4-methoxy-phenyl)-1,3,2,4-dithiadiphosphatane-2,4-disulphide (Lawesson's reagent) **1** with different types of substrates [25-29], we have now studied the reaction of reagent **1** with triethyl phosphite (**2**).

Experimental

Melting points were determined on a Gallenkamp melting apparatus and are uncorrected. The IR spectra were recorded in KBr disks, on Jasco Fourier Transform Infrared spectrophotometer Model FR/IR 300 E. The ¹H NMR were measured in CDCl₃ on JOEL JNMEX 270 FT NMR system (NRC) and chemical shifts were recorded in δ ppm relative to TMS. The ³¹P NMR spectra were referenced to external

85% H₃PO₄. The MS were performed at 70 eV on a Finnigan MAT SSQ 7000 spectrometer. The microanalyses were carried out at the microanalytical Center, Cairo University, Egypt.

The microanalyses for the new compounds were in good agreement with (C, H ± 0.1, P ± 0.05, S ± 0.05). Toluene (thiophene-free) was dried with sodium metal and distilled. All solvents were purified and dried. L.R. reagent was freshly prepared [31]. Triethyl phosphite was purchased from Merck. The reaction mixtures were resolved into their individual constituents by column chromatography on silica gel [particle size 0.2-0.5 mm, 37-70 mesh (ASTM) E Merck, Darmstadt] through elution with petroleum ether (60-80°C), cyclohexane and / or methylene chloride in suitable percentage.

Reaction of Triethyl phosphite (2) with L.R. (1)

A mixture of triethyl phosphite (5 mmol, 0.83 g) and L.R. (1) (5 mmol, 1.01 g) in acetonitrile (25 ml) was heated under reflux for 2 h. The reaction mixture was evaporated under reduced pressure. The solid product thus produced, was applied to silica gel column chromatograph using acetone/pet. Ether (60-80°C) as an eluent. The first fraction, O-ethyl-S-ethyl-di(4-methoxyphenyl)-thiophosphonate (3) was produced as colourless crystals, 13.5% yield, m.p. 112°C. Analyses calcd. for $C_{18}H_{24}O_3P_2S_4$ (478.53); C, 45.17; H, 5.05; O, 10.03; P, 12.94; S, 26.80. Found, C, 45.09; H, 4.99; P, 12.99; S, 26.84

Second fraction: diethyl(4-methoxyphenyl) ethylmercaptophosphino-thiothionylphosphonate (4), colorless oil, 25% yield. IR spectrum of product 4 (in KBr) gave an absorption bands at 645 cm^{-1} , 640 cm^{-1} (P=S); 1040 cm^{-1} (P-O-C). The 1H NMR of 4 gave signals at δ 1.3 (m, 3H, SCH_2CH_3); δ 3.1 (m, 4H, SCH_2CH_3 and OCH_2CH_3); δ 3.85 (s, 3H, OCH_3); δ 4.20 (m, 6H, OCH_2CH_3); δ 7.0 (dd, 2H, *m*- to phosphorus); δ 8.0 (dd, 2H, *o*- to phosphorus). Analyses Calcd. for $C_{13}H_{22}O_3P_2S_3$ (384.459), C, 40.62; H, 5.77; P, 16.11; S, 25.02. Found: C, 40.70; H, 5.72; P, 16.14; S, 24.98. ^{31}P NMR: δ 57.66, 80.82 (d, J_{pp} = 189 Hz).

Third fraction: O,S-diethyl(4-methoxyphenyl) phosphonodithioate (5), colorless oil, 20% yield. IR spectrum of product 5 (in KBr) gave absorption bands at 630 cm^{-1} (P=S); 1035 cm^{-1} (P-O-C).

The 1H NMR of 5 gave signals at δ 1.1 and δ 1.25 ppm (2t, OCH_2CH_3 , SCH_2CH_3); δ 3.85 (s, 3H, OCH_3); δ 4.1 (m, OCH_2 and SCH_2); δ 6.85 (dd, 2H, *m*- to phosphorus); δ 7.85 (dd, 2H, *o*- to phosphorus). ^{31}P NMR: δ 67.04 ppm. Analyses Calcd. for $C_{11}H_{17}O_2PS_2$ (276.359), C, 47.81; H, 6.20; P, 11.21; S, 23.20. Found: C, 47.90; H, 6.27; P, 11.18; S, 23.15.

Results and Discussion

We have found that when reagent 1 is allowed to react with triethyl phosphite 2 in refluxing acetonitrile in a molar ratio (1:1), three phosphonate products could be obtained, O-ethyl-S-ethyl-di(4-methoxyphenyl)-thiophosphonate (3), diethyl(4-

methoxyphenyl) ethylmercaptophosphino-thiothionylphosphonate (4) and O,S-diethyl(4-methoxyphenyl)- phosphonodithioate (5) respectively and did not afford the thione phosphonate 6 [30] (Scheme 2). The structures of the three products 3, 4 and 5 have been confirmed by spectroscopic evidences (IR, 1H NMR, MS and ^{31}P NMR) and elementary microanalyses. Taking product 3 as an example, (a) The IR spectrum of 3 (in KBr) gives an absorption band at 451 cm^{-1} (P-S-C), 639 cm^{-1} (P=S) and 1036 cm^{-1} (P-O-C). (b) Elemental analyses and molecular weight determination of product 3 corresponded to $C_{18}H_{24}O_3P_2S_4$. (c) The 1H NMR spectrum of 3 shows signals at δ 1.35 and 1.45 as two triplets for the six protons [$-SCH_2CH_3$ and $-OCH_2CH_3$]; multiplet at δ 3.05 integrating as two protons (SCH_2CH_3) two singlets at δ 3.75 and 3.85 for 6 protons ($2-C_6H_4-OCH_3$), multiplet at δ 4.4 for 2H ($-OCH_2CH_3$), δ 6.6 (4H, dd) J_{PH} 3; J_{HH} 9- meta - protons, δ 7.6 (4H, dd) J_{PH} 15; J_{HH} 9-ortho-protons.

(d) The mass spectrum of 3 gave rise to a molecular ion peak at 478 (*cf.* Scheme 3). The fragmentation pattern is consistent with the proposed structure 3. It gave fragments at 417 (478- SC_2H_5 , 70%), 247 (417- C_7H_7OPS , 2.9%), 187(247- (OC_2H_5 + CH_3), 93%) and 155 (187-S, 24%).

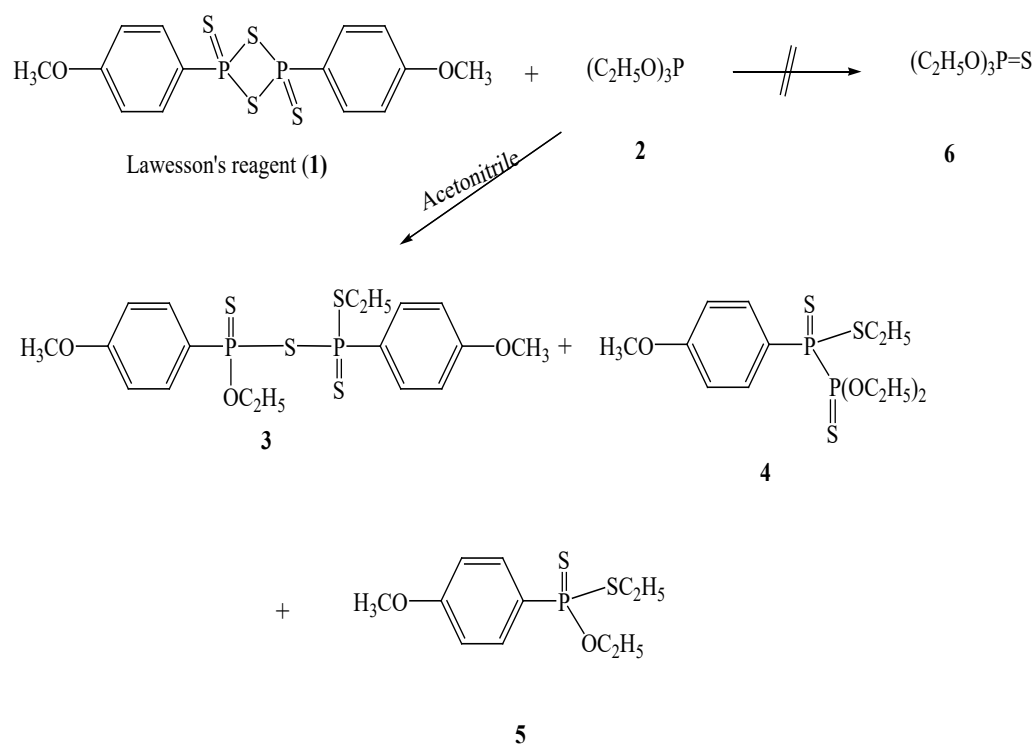
(e) The ^{31}P NMR of compound 3 gave two phosphorus chemical shifts at 90.8 and 74.6 ppm corresponding to the two phosphorus atoms.

Products 4 and 5 are established from their correct spectroscopic data and microanalyses (*cf.* experimental).

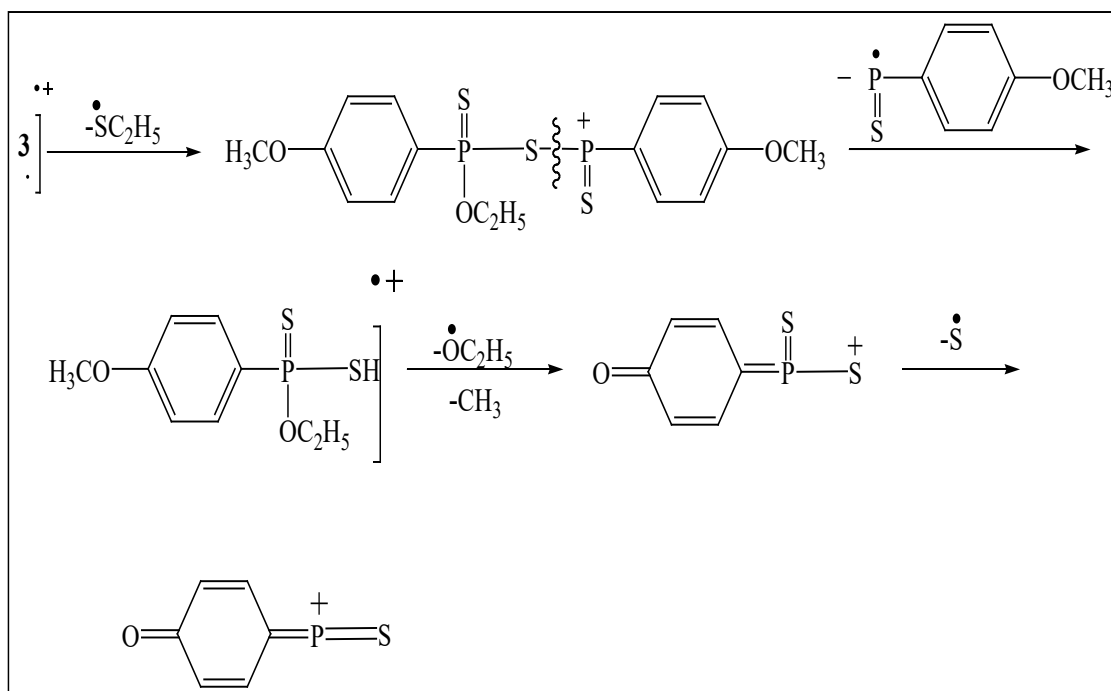
Conclusion

From the present investigation we have found that the reaction of Lawesson's reagent with triethylphosphite leads to the formation of three phosphonate derivatives, instead of the thianalogue as observed from our previous work from reaction of reagent 1 with dialkyl phosphites. Moreover, the present study affords a new phosphonates derivatives of expected interesting biological evaluation as phosphorus insecticides.

Formation of compounds 3,4 and 5 lends an additional support for the activity of trialkylphosphites as strong alkylating agents [32].



Scheme 2. Reaction of L.R. with Trialkyl phosphites.



Scheme 3. Fragmentation pattern of compound 3.

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