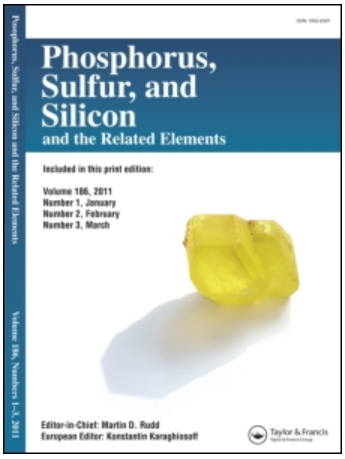

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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS VI[1-5]: Utility of Lawesson's Reagent for Synthesis of Thiaphosphorine, Thioxanthene, and Thiaphosphole Derivatives

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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS VI[1–5]: UTILITY OF LAWESSON'S REAGENT FOR SYNTHESIS OF THIAPHOSPHORINE, THIOXANTHENE, AND THIAPHOSPHOLE DERIVATIVES

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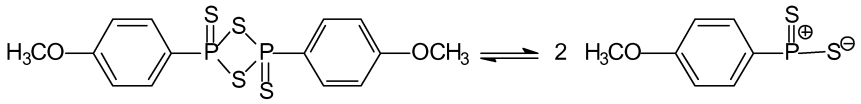
Arylidene malonate derivatives ***2a–c*** *reacted with Lawesson's reagent* ***(1)*** *LR in equimolar ratio to yield the oxathiaphosphorine derivatives* ***3a–c****. The behaviour of LR towards cyclic ketones was also examined and yielded the thioxanthene derivatives* ***5a,b****. On the other hand, arylidene pyrazolone* ***8*** *reacted with LR to give the phosphole* ***10****. Aminobenzenethiophene* ***11*** *reacted with LR under reflux to produce the corresponding thiazaphosphorine* ***12****.*

Keywords: Arylidene; lawesson's reagents; phosphole; thiaphosphorines; xanthene

The reagent 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide **1** (LR; Scheme 1) has been shown to be quite versatile in thionation of different carbonyl compounds,[6] and it is also known that nucleophiles attack **1** at the phosphorus atom.[7,8] In certain cases where the substrate contains two functional groups, phosphorus heterocycles are formed.[9,10]



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SCHEME 1

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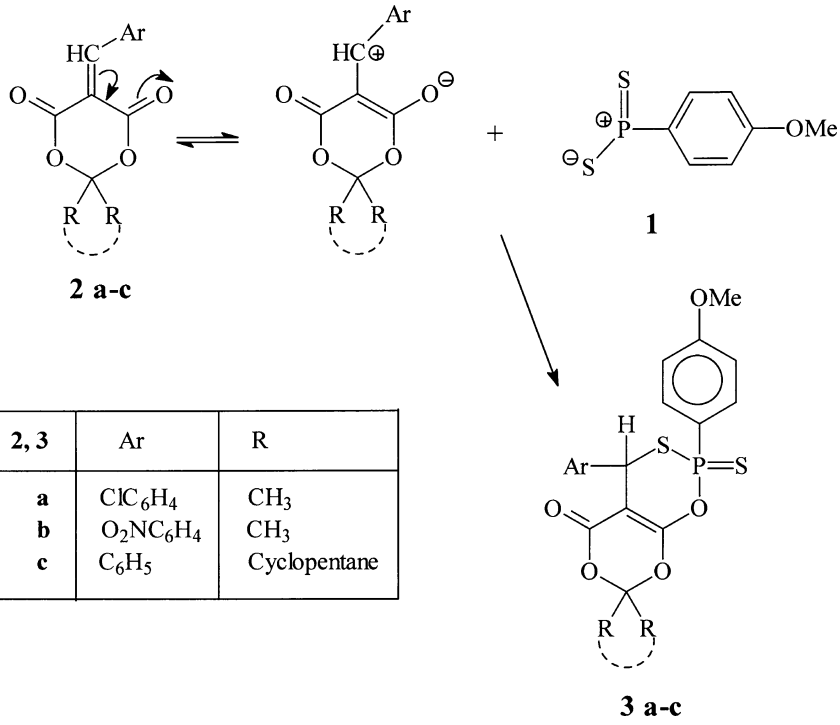
In continuation of our medicinal chemistry program directed towards the development of new procedures for the synthesis of phospholes and phosphorus-related heterocyclic compounds,[1–5] we report an easy facile synthetic methodology for the synthesis of 4H-1,3,2-oxathiaphosphorine derivatives and related heterocyclic compounds.

The key precursor Lawesson's reagent **1** reacted with an equimolar amount of arylidene malonate **2a** in acetonitrile at room temperature to yield 4H-1,3,2-oxathiaphosphorine **3a**. The formation of **3a** is assumed to proceed via a dipolar cycloaddition reaction (Scheme 2).



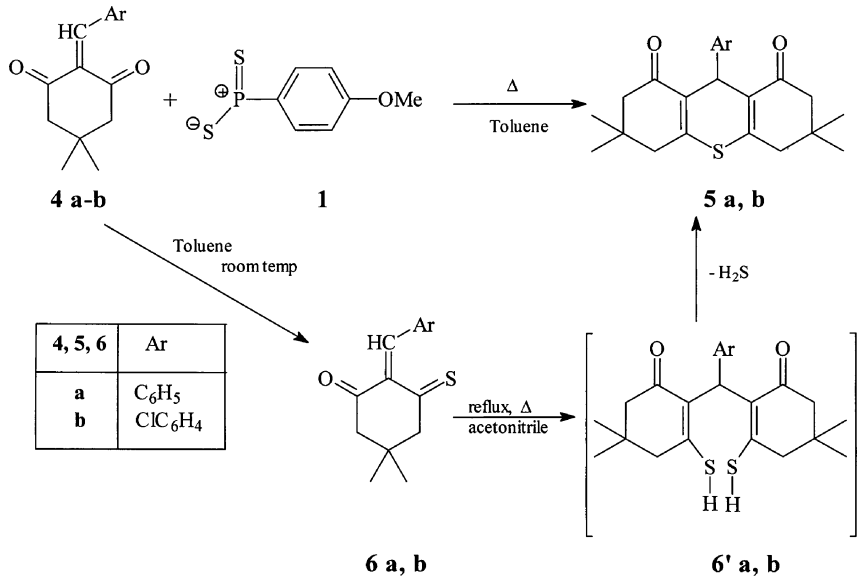
2, 3	Ar	R
a	ClC_6H_4	CH_3
b	$O_2NC_6H_4$	CH_3
c	C_6H_5	Cyclopentane

SCHEME 2

The structure **3a** was confirmed from its analysis and spectroscopic data. The ^{1}H NMR spectrum showed signals at $\delta = 1.60$ and $\delta = 1.75$ for two CH_3 protons (singlets), $\delta = 3.70$ for OCH_3 (singlet), $\delta = 4.10$ ppm for CH proton (singlet), and $\delta = 6.80$–7.70 and $\delta = 7.90$–8.40 for aromatic protons (multiplet). The IR spectrum of compound **3a** revealed two bands at 2960 and 2925 for the CH_3 groups, a band at 1690 cm^{-1} for (C=O) and a band at 1605 for C=C. The mass spectrometry and the

microanalytical data supported the proposed structure. Similarly, the arylidene malonate derivatives **2b,c** reacted with **1** to yield the corresponding phosphorine derivatives **3b,c**. The structure of the products was also confirmed by analysis and spectroscopic data (see the Experimental section below).

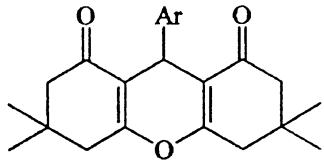
The study was also extended to the behavior of Lawesson's reagent **1** on 2-arylidene-5,5-dimethyl-1,3-cyclohexanedione **4**. We explained before that when the reaction was carried out at room temperature, the thione derivative **6** was formed.[5] This report explains the possibility of formation of 1,8-dioxo-9-aryl-1,2,4,5,7,8-hexahydro-3,3,6,6-tetramethyl thiaxanthene **5a,b** in high yield when the reaction was carried out in toluene under reflux (Scheme 3).



SCHEME 3

The thioxanthene **5** was also obtained by reacting compound **4** with LR at room temperature to give the thione derivative **6**, which dimarized and cyclized by loss of H_2S upon refluxing in toluene. Similarly, xanthene's derivatives **7** (Figure 1) were previously prepared by us[11] and others.[12–16]

The structures of **5a,b** was verified from analytical and spectroscopic evidence. The ^1H NMR spectrum of compound **5a** showed signals at $\delta = 0.90$ and 1.10 ppm for CH_3 (singlets), $\delta = 2.15$ and $\delta = 2.45$ ppm for CH_2 groups (doublets), $\delta = 4.70$ ppm for the CH group (singlet),



7

FIGURE 1

and $\delta = 6.95$–7.35 ppm for aromatic protons (multiplet). The mass spectrometry of **5a,b** showed ion peaks at m/z = 366 $[M]^+$ and 400.5$[M]^+$, respectively, (see Experimental section below).

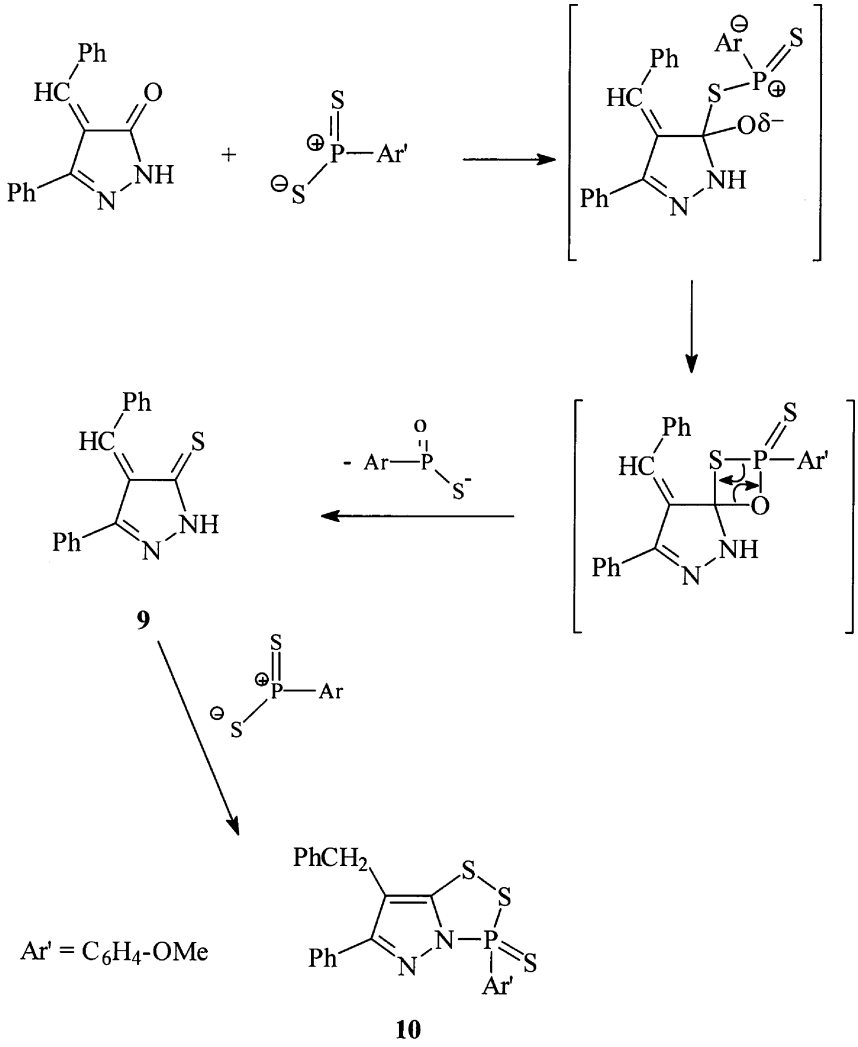
Our study was also extended to the effect of Lawesson's reagent on the arylidene heterocyclic ketones. Arylidene pyrazolone derivative **8** reacted with LR in benzene under reflux for 3 h to form 1,2,5,4 dithiazaphosphole derivative **10** (Scheme 4). It is believed that the phosphole **10** may be formed via the thione **9**, which is initially formed by a betaine mechanism. The interaction of the thione **9**, with another species from LR leads to the formation of the phosphole derivative **10**. Lawesson et al. previously reported similar formation of phosphole derivatives.[9]

The investigation was also concerned with the behavior of aminobenze-thiophene derivative **11** towards LR. When one mole equivalent of compound **11** was allowed to react with one mole equivalent of LR in dry toluene under reflux, 1,3,2 thiazaphosphorine derivative **13** was formed. The reaction was believed to proceed by loss of ethanol to form the phosphorine derivative **12**, which undergoes further thionation with LR to form the final product **13**. The ^{31}P NMR chemical shift for compound 13 was 72.3 ppm which is in complete accordance with shifts recorded for structures incorporated the moiety **14**[8,17] (Scheme 5).

EXPERIMENTAL

All melting points are uncorrected. Solvents used were distilled and dried over sodium sulphate. IR spectra were taken in KBr on a OK9712 IR spectrometer. ^1H NMR were recorded on Varian EM360- 60 MHz spectrometer with dimethylsulfoxide (DMSO) and $CDCl_3$ as solvents and tetramethylsilane (TMS) as internal reference.

Chemical shifts are expressed as δ units (ppm). The mass spectra were recorded on Kratos (75 eV) MS equipment. Microanalysis was carried out in the Analytical Data Unit at National Research Centre.



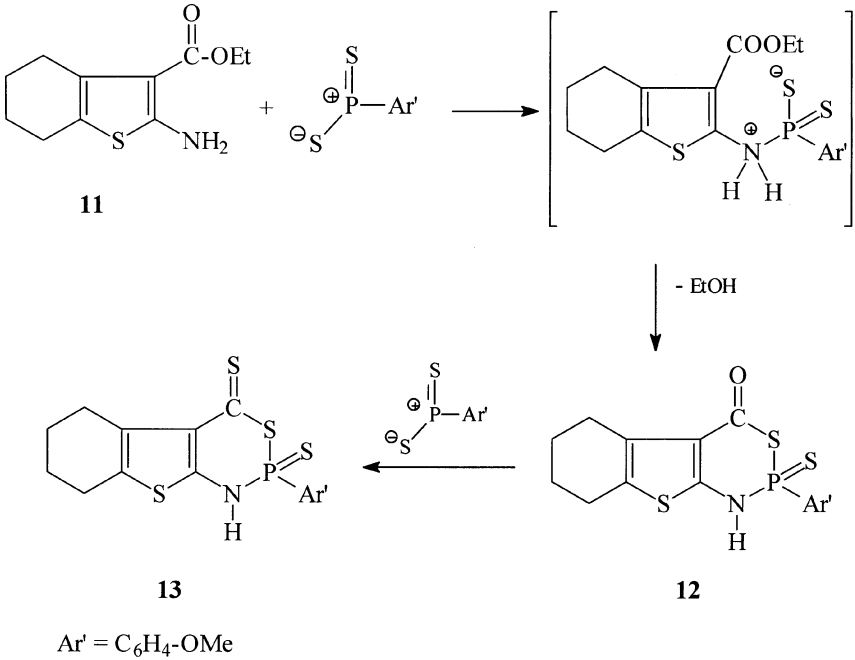
10

SCHEME 4

4H-1,3,2-Oxathiaphosphorine Derivatives (3a–c)

To a suspension of each of **2a–c** (0.01 mole) in dry acetonitrile (30 ml), **1** (0.01 mole) was added. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated under vacuum and the residue was triturated with benzene.

3a: white crystals, m.p. 189–190°C, recrystallized from benezene, yield 2.66 g (57%). IR: ν = 2960, 2925 ($2CH_3$), 1690 (CO), 1605 (C=C).



SCHEME 5

^{1}H NMR (DMSO): $\delta = 1.60$ (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 4.10 (s, 1H, CH), 6.80–7.70 (m, 4H, aromatic protons) and 7.95–8.45 ppm (m, 4H, aromatic protons). MS: m/z = 468.5 (M^+). Anal. Calc. for $C_{20}H_{18}O_5S_2ClP$ (468.5): C, 51.22; H, 3.84; S, 13.66; Cl, 7.57; P, 6.61. Found: C; 51.20; H: 3.81; S: 13.65; Cl: 7.58; P: 6.60.

3b: yellow crystals, m.p. 234°C, recrystallized from methanol, yield 2.87 g (60%). IR: $\nu = 2965$, 2930 ($2CH_3$), 1680 (C=O), 1604 (C=C). ^{1}H NMR (DMSO): $\delta = 1.35$ (s, 3H, CH_3), 1.65 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 4.20 (s, 1H, CH), 6.67–7.60 (m, 4H, aromatic protons), and 7.75–8.15 ppm (m, 4H, aromatic protons). MS: m/z = 479 (M^+). Anal. Calc. for $C_{20}H_{18}NO_7S_2P$ (479): C, 50.10; H, 3.75; N, 2.92; S, 13.36; P, 6.47. Found: C, 50.00; H, 3.75; N, 2.90, S, 13.33; P, 6.45.

3c: white crystals, m.p. 233°C, recrystallized from benzene, yield 2.99 g (65%). IR: $\nu = 1675$ (C=O), 1602 (C=C). ^{1}H NMR (DMSO): $\delta = 0.90$–1.31(m, 8H, $4CH_2$), 3.68 (s, 3H, OCH_3), 4.25 (s, 1H, CH), 6.69–7.63 (m, 4H, aromatic protons), and 7.78–8.18 ppm (m, 5H, aromatic protons). MS: m/z = 460 (M^+). Anal. Calc. for $C_{22}H_{21}O_5S_2P$ (460): C, 57.39; H, 5.83; S, 13.91; P, 6.73. Found: C, 57.36; H, 5.81; S, 13.50; P, 6.74.

1,8-Dixo-9-aryl-1,2,4,5,7,8-hexahydro3,3,6,6,-tetramethyl thiaxanthene (5a,b)

To a solution of each of **4a,b** (0.01 mole) in toluene (25 ml), LR (0.05 mole) was added. The reaction mixture was refluxed for 3 h. The solvent was evaporated under vacuum, the remaining residue was treated with petroleum: ether 40 : 60. The solid product formed was collected by filtration.

5a: yellow crystals, m.p. 185°C, recrystallized from benzene, yield 2.74 g (75%). IR: $\nu = 1655$ (C=O), 1605 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 0.95$ (s, 6H, $2CH_3$), 1.10 (s, 6H, $2CH_3$), 2.15 (s, 2H, CH_2), 2.20 (s, 2H, CH_2), 2.45 (dd, 4H, $2CH_2$), 4.71 (s,1H, CH), 6.95–7.35 (m, 5H, aromatic protons); MS: m/z = 366 (M^+). Anal. Calc. for $C_{23}H_{26}O_2S$ (366): C, 75.40; H, 7.10; S, 8.74. Found: C, 75.38; H, 7.00; S, 8.71.

5b: yellow crystals, m.p. 234°C, recrystallized from methanol, yield 3.12 g (78%). IR: $\nu = 1660$ (C=O), 1604 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 0.95$ (s, 6H, $2CH_3$), 1.05 (s, 6H, $2CH_3$), 2.20 (d, 2H, CH_2), 2.28 (d, 2H, CH_2), 2.52 (dd, 4H, $2CH_2$), 4.47(s, 1H, CH), 6.80–7.28 (m, 4H, aromatic protons). MS: m/z = 400.5 (M^+). Anal. Calc. for $C_{23}H_{25}O_2SCl$ (400.5): C, 68.91; H, 6.24; S, 7.99; Cl, 8.86. Found: C, 68.88; H, 6.23; Cl, 8.83; S, 7.95.

Reaction of Arylidene Pyrazolone with Lawesson's Reagent

A solution of **8** (0.01 mol) and LR (0.01 mol) in dioxane (20 ml) was heated under reflux for 5 h. The solvent was evaporated under vacuum. The remaining residue was treated with benzene. The solid product formed was collected by filteration.

11: yellow crystals, m.p. 212°C, recrystallized from benzene, yield 1.51 g (54%). IR: $\nu = 2920$ (CH_3), 1512 (C=C) cm^{-1}. ^1H NMR (DMSO): $\delta = 3.72$ (s, 3H, CH_3), 5.07 (s, 2H, CH_2), 6.90–7.08 (m, 4H, aromatic protons), 7.11–7.22 (m, 5H, aromatic protons), 7.24–7.59 (m, 5H, aromatic protons). MS: m/z = 466 (M^+). Anal. Calc. for $C_{23}H_{19}N_2S_3OP$ (466): C, 59.22; H, 4.07; N, 6.00; S, 20.60; P, 6.65. Found: C, 59.20; H, 4.05; N, 6.02; S, 20.64; P, 6.63.

Reaction of Aminobenzethiophene with LR

A solution of **11** (0.01 mol) and LR (0.01 mol) in toluene (30 ml) was refluxed for 8 h. The reaction was followed up by TLC. After complete reaction, the solvent was evaporated under vacuum and the remaining residue was treated with n-hexane and left overnight. The solid product formed was collected by filtration.

13: yellow crystals, m.p. 70°C, recrystallized from methanol, yield 2.77 g (70%). IR: $\nu = 3440$ (NH), 2923 (CH_3), 1519 (C=C) cm^{-1}. ^1H NMR (DMSO): $\delta = 0.90$ (m, 2H, CH_2), 1.24 (m, 2H, CH_2), 3.77 (s, 3H, OCH_3), 4.05 (m, 2H, CH_2), 4.23 (m, 2H, CH_2), 6.99 (d, 2H, aromatic protons), 7.71 (d, 2H, aromatic protons). MS: m/z = 397 (M^+). Anal. Calc. for $C_{16}H_{16}NOPS_4$ (397): C, 48.36; H, 4.03; N, 3.52; P, 7.80; S, 32.24. Found: C, 48.33; H, 4.00; N, 3.52; P, 7.60; S, 32.22.

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