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Synthesis and Structure of [1,2]Thiaphospholo[4,5-*e*][1,2,4]triazines

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Abstract: The first syntheses of the novel [1,2]thiaphospholo[4,5-*e*][1,2,4]triazine ring system, exemplified by the derivatives **3a-c** have been accomplished by the action of Lawesson's reagent on the 5-arylmethyl-1,2,4-triazin-6-ones **1a-c**, their thiones **2a-c** or the Mannich bases **4-6**. The structure of these new thiaphospholotriazines was established mainly by NMR, and X-ray structural analysis.

Introduction

Much attention has been directed to the chemistry of 1,2,4-triazines and their condensed systems. A large number of derivatives of this class of compound exhibit interesting diverse applications in many fields as medicinal, pharmaceutical, agrochemical, and analytical reagents. Many reviews and monographs covering such applications have been published.[1-3] We recently reported several synthetic routes to the isomeric thieno[2,3-*e*][1,2,4]triazines and thieno[3,2-*e*][1,2,4]triazines which constitute a chemically and biologically interesting class of new ring systems.[4-9] Thus, some of them are shown to exhibit interesting biological activity (high insecticidal, high fungicidal and moderate herbicidal activity).[10]

Results and Discussion

During our recent study of the synthesis of thieno[3,2-*e*][1,2,4]triazines **7a-c** we investigated the action of different thiating agents on 5-arylmethyl-1,2,4-triazin-6(1*H*)-ones **1a-c**, their thiones **2a-c** and their Mannich derivatives **4-6**.[4] Although we found that the action of phosphorus pentasulfide on the Mannich bases **5,6** led directly to the corresponding thieno[3,2-*e*][1,2,4]triazines **7a-c**,[4] the action of Lawesson's reagent (LR) gave new phosphorus-containing compounds for which structures **3a-c** are now assigned.

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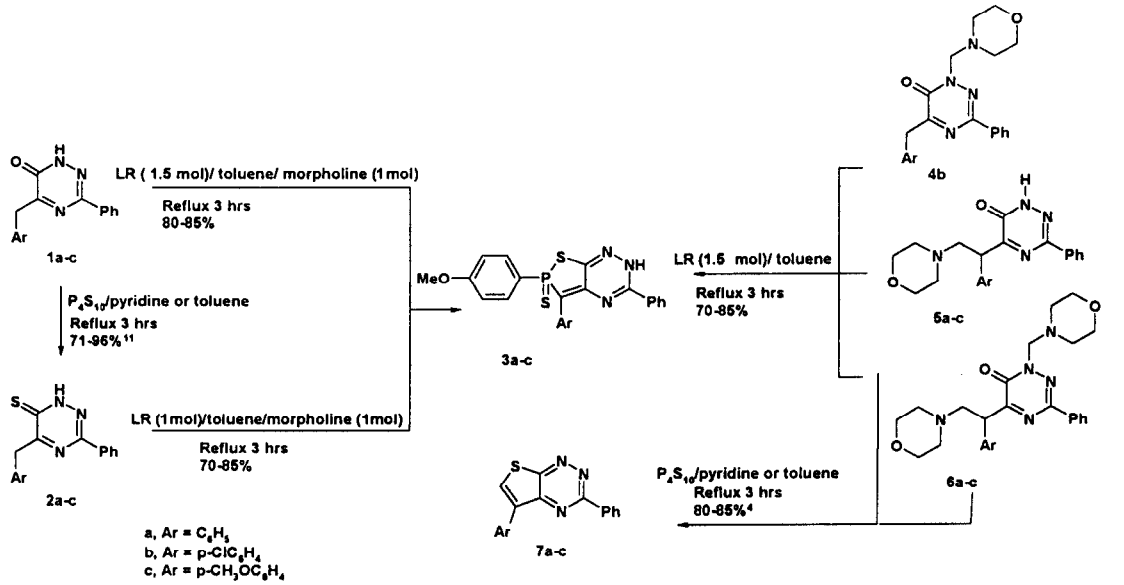
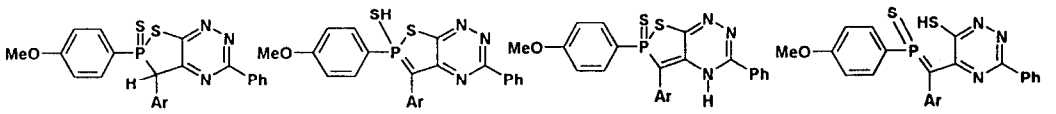
Compound **3c** was also, directly, formed as the sole reaction product in low yield (25%) by the action of LR on the corresponding 1,2,4-triazin-6(1*H*)-one **1c**. The optimum yield (85%) of **3c** was achieved by heating **1c** for 3 hrs in toluene with LR (1.5 mol equivalent) in the presence of morpholine (1.0 mol equivalent). Similar treatment of **1a,b** with LR alone gave the corresponding 6-thioxo derivatives **2a,b** and a trace of the thiaphospholotriazines **3a,b**. However, heating each of **1a,b** with LR (1.5 mol) and morpholine (1.0 mol) in toluene gave good yields of the corresponding thiaphospholotriazines **3a,b**. Additionally, heating each of the 1,2,4-triazine-6(1*H*)-thiones **2a-c** with LR (1 mol) and morpholine (1 mol) gave the corresponding thiaphospholotriazines **3a-c**. The action of phosphorus pentasulfide on **1a-c** has been reported to give good yields of **2a-c**.[11]



Structure of Compounds **3a-c**:

Careful investigation of the elemental analysis, mass spectra, ^{31}P, ^{13}C, ^{1}H NMR led to the postulation of structures **3, 8, 9, 10** or **11** to these products. Thus, compounds **3a-c** showed in their mass spectra the parent ion peak. In their ^{31}P NMR they showed a signal around δ = -74 ppm (t, $^{3}J_{HP}$ = 15 Hz). This same coupling constant was similarly observed in the ^{1}H NMR where the *p*-methoxyphenyl-H ortho to the phosphorus showed a coupling constant $^{3}J_{PH}$ = 15 Hz. ^{13}C NMR using APT pulse sequence (Table 1) showed that there is no CH carbon except those of the sp^2 aryl groups, thus excluding structure **8**. Morcover, the presence of an exchangeable proton at δ = 13-13.2 (for **3a,b** in $CDCl_3$) and 9.88 (for **3c** in DMSO-d_6) is in favor of **3, 9, 10** or **11**. The ^{31}P-^{13}C coupling of aryl-CH's, aryl-C's and thiaphosphole-C's is all in accordance with any of the structures **3, 9, 10, 11**.

The structure was finally solved and shown to be **3** by X-ray structural analysis of compound **3c** shown in Figure 1.[21]



8 9 10 11

Table 1: ^{13}C NMR* using APT pulse sequence (VARIAN-GEMINI 200) of compounds 3a-c:

Compd.	sp^2 C's (multiplicity, J_{PC} Hz)	sp^2 CH's/ (multiplicity, J_{PC} Hz)	OCH_3
3a	106.8 (d, 92), 126.8 (d, 93), 130.3 (s), 132.4 (d, 10), 142.4 (d, 23), 151.8 (s), 154.0 (d, 9), 162.2 (d, 3)	114.0 (d, 16), 126.6 (d, 8), 126.9 (s), 127.6 (s), 128.2 (d, 8), 128.6 (s), 131.9 (s), 133.3 (d, 15)	55.0 (s)
3b	104.5 (d, 92), 126.1 (d, 94), 130.4 (s), 131.0 (s), 136.6 (d, 11), 143.0 (d, 23), 152.1 (s), 154.0 (d, 9), 162.4 (d, 3.5)	114.1 (d, 14), 127.1 (s), 127.8 (s), 128.7 (s), 129.7 (d, 8), 132.1 (s), 133.4 (d, 15)	55.2 (s)
3c	107.1 (d, 92), 125.0 (d, 10), 126.1 (d, 92), 131.0 (s), 141.7 (d, 23), 152 (s), 154.5 (d), 158.4 (s), 162.8 (d, 3)	113.7 (s), 114.5 (d, 15), 127.5 (s), 129.2 (s), 130.0 (d, 8), 132.5 (s), 133.9 (d, 15)	55.1 (s) 55.6 (s)

*Compounds 3a,b were measured in $CDCl_3$, 3c in DMSO-d_6.

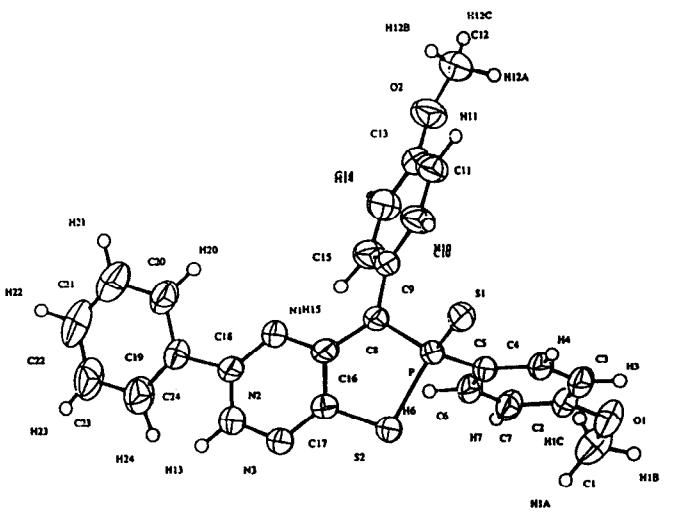
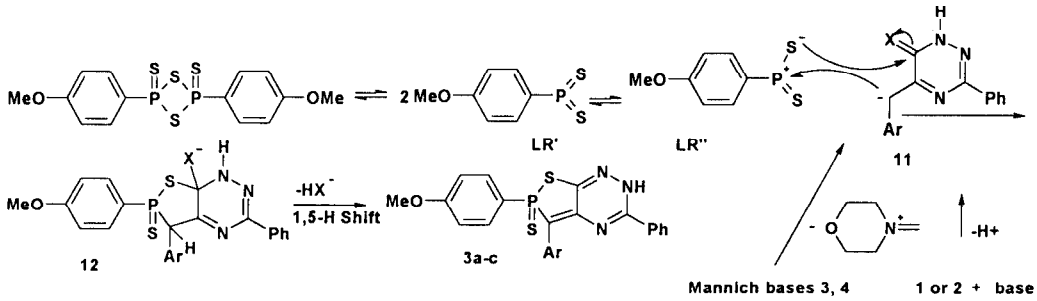


Figure 1: X-ray structure of 3c showing atoms and numbering scheme

The formation of these thiaphospholotriazines presumably proceeds through the action of 1,3,2,4-dithiadiphosphetane-2,4-disulfide (LR), which exist in equilibrium with the monomeric species (LR' and LR'')[12-14], on the triazine anions 11 to give the cycloadducts 12. The latter then via loss of HO^- or HS^- and H-shift yields the products 3 as shown in the following Scheme. The anions 11 are formed by the action of morpholine on the starting triazines 1 or 2 or by decomposition of the Mannich bases 4-6.



Experimental Part

All melting points were uncorrected. ^{1}H NMR and ^{13}C NMR (using VARIAN APT pulse sequence) spectra (δ scale) were recorded with a VARIAN GEMINI-200 spectrometers, ^{31}P NMR spectra (δ scale) were recorded with a JEOL JNM-LA300. Mass spectra were determined with GCMS-QP 1000 EX spectrometers. IR (KBr) were recorded on a Perkin-Elmer 1430 spectrophotometer. Microanalyses wee carried out at the Microanalytical Centre, Cairo University. The starting compounds **1a-c**,[15,16] **2a-c**,[11] **4**,[4] **5**,[4] **6**[4] were prepared as reported.

For X-ray crystallography, compound **3c** was recrystallized as yellow needles from methanol. Preliminary Weissenberg photographs were used to derive approximate cell dimensions, Laue symmetry, possible space groups, and to check crystal quality. A suitable crystal was mounted on a CAD4 automated diffractometer. CAD4 EXPRESS'88 software[17] was used for unit cell determination and refinement, data collection, and data reduction. Accurate cell parameters were determined from 25 reflections ($25 < \theta < 28°$) employing graphite monochromated Cu$K\alpha$ radiation with ω-2θ scans. Intensities of 2896 reflections were measured for $\theta < 70°$.The crystal showed no significant variation in intensities of three check reflections during the course of data collection. Lorentz and polarization corrections were applied but absorption effects were ignored.[21]

The structure was solved using SHELX-86[18] and refined using SHELX-93.[18] Geometrical calculations were made with SHELX-93[19] and the same software was used to prepare publication material and Tables. The program SNPI[20] was used to prepare the structure drawings. Hydrogen atoms were refined in riding mode with isotopic temperature factors. Calculations were performed on PC486 computer.

The chemical formula and ring labeling system is shown in Figure 1. Full X-ray data are separately provided as supplementary materials.[21]

Synthesis of 6*H*-[1,2]thiaphospholo[4,5-*e*][1,2,4]triazine 2-sulfides (3a-c):

General Procedures

(A) From 5-arylmethyl-1,2,4-triazin-6(1*H*)-ones (1a-c):

A solution of each of **1a-c** (2 mmol), Lawesson's reagent (1.3 g, 3 mmol) and morpholine (0.2 g, *ca.* 2 mmol) in anhydrous toluene (20 ml) was heated under reflux for 3 h. After cooling the precipitate was collected and recrystallized from acetic acid or DMF to give yellow crystals of the corresponding **3a-c**.

(B) From 5-arylmethyl-1,2,4-triazine-6(1*H*)-thiones (2a-c):

A solution of each of **2a-c** (2 mmol) and Lawesson's reagent (0.81 g, 3 mmol) and morpholine (0.2 g, *ca.* 2 mmol) in anhydrous toluene (20 ml) was heated under reflux for 3 h. After cooling the precipitate was collected and recrystallized from acetic acid or DMF to give yellow crystals of the corresponding **3a-c**.

(C) From Mannich bases (4-6):

A solution of each of the appropriate Mannich bases **4-6** (2 mmol) and Lawesson's reagent (1.3 g, 3 mmol) in anhydrous toluene (20 ml) was heated under reflux for 3 h. After cooling the precipitate was collected and recrystallized from acetic acid or DMF to give yellow crystals of the corresponding **3a-c**.

2-*p*-Methoxyphenyl-3,5-diphenyl-6*H*-[1,2]thiaphospholo[4,5-*e*][1,2,4]triazine 2-sulfide (3a).

From **1a** (80%, Method A), **2a** (80%, Method B), **5a, 6a** (65%, Method C), yellow crystals mp. 240 °C. Ms: m/z 447 (M^+, 49%), 309 (100%), 277 (6%), 145 (19%), 121 (11%), 104 (40%); ^{1}H NMR ($CDCl_3$) δ 3.81 (s, 3H, OCH_3), 7.09 (dd, 2H, $^3J_{HH}$ = 9 Hz, $^4J_{PH}$ = 3 Hz), 7.26 (m, 3H), 7.51 (m, 3H), 7.75 (dd, 2H, , 2H, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.4 Hz), 7.84 (d, 2H, $^3J_{HH}$ = 8 Hz), 8.03 (dd, 2H, $^3J_{HH}$ = 8.8 Hz, $^3J_{PH}$ = 15 Hz), 13.22 (s, 1H, NH).

Anal. Calcd. for $C_{23}H_{18}N_3OPS_2$: C 61.73; H 4.05; N 9.39. Found C 62.00; H, 3.80; N 9.24.

3-*p*-Chlorophenyl-2-*p*-methoxyphenyl-5-phenyl-6*H*-[1,2]thiaphospholo[4,5-*e*][1,2,4]triazine 2-sulfide (3b).

From **1b** (80%, Method A), **2b** (80%, Method B), **4b, 5b, 6b** (70%, Method C), yellow crystals mp. 280 °C. IR: 3280, 1599, 1570, 1539, 1500, 1496, 1489, 1467, 1437, 1409, 13044, 1306, 1292, 1259, 1176, 1143, 1099, 1025, 1015, 983, 831, 812, 800, 778, 745, 717, 689, 680, 641 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.81 (s, 3H, OCH_3), 7.1 (dd, 2H, $^3J_{HH}$ = 9 Hz, $^4J_{PH}$ = 2.9 Hz), 7.36 (d, 2H, $^3J_{HH}$ = 8.5 Hz), 7.6 (m, 3H), 7.8 (d, 2H, $^3J_{HH}$ = 9 Hz), 7.95 (dd, 2H, $^3J_{HH}$ = 9 Hz, $^3J_{PH}$ = 15 Hz), 8.04 (d, 2H, $^3J_{HH}$ = 8.4 Hz), 13.0 (s, 1H, NH). ^{31}P ($CDCl_3$) δ -74.5 (t, $^3J_{HP}$ = 15 Hz).

Anal. Calcd. for $C_{23}H_{17}ClN_3OPS_2$: C 57.32; H 3.56; N 8.72. Found C 57.33; H, 3.50; N 8.70.

2,3-Di-*p*-methoxyphenyl-5-phenyl-6*H*-[1,2]thiaphospholo[4,5-*e*][1,2,4]triazine 2-sulfide (3c).

From **1c** (85%, Method A), **2c** (85%, Method B), **5c, 6c** (70%, Method C), yellow crystals mp. 270 °C. Ms: m/z 477 (M^+, 83%), 446 (12%), 338 (100%), 267 (12%), 239 (12%), 175 (10%), 151 (17%), 104 (7%); ^{1}H NMR (DMSO-d_6) δ 3.75, 3.85 (2s, 6H, $2OCH_3$), 6.79 (d, 2H, $^3J_{HH}$ = 9 Hz), 6.97 (dd, 2H, $^3J_{HH}$ = 8.5 Hz, $^4J_{PH}$ = 3 Hz), 7.5 (m, 3H), 7.83 (d, 2H, $^3J_{HH}$ = 8.2 Hz), 7.98 (dd, 2H, $^3J_{HH}$ = 8.5 Hz, $^3J_{PH}$ = 15 Hz), 9.88 (s, 1H, NH). ^{31}P ($CDCl_3$) δ -73.88 (t, $^3J_{HP}$ = 15 Hz).

Anal. Calcd. for $C_{24}H_{20}N_3O_2PS_2$: C 60.36; H 4.22; N 8.80. Found C 60.50; H, 4.20; N 8.80.

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