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Reactions of Phosphite Esters and Trisdialkylaminophosphines With 5-Substituted 1,3,4-Thiadiazol Derivatives

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ABSTRACT: *5-{[(1*E*)-(4-methoxyphenyl)methylene] amino}-1,3,4-thiadiazole-2-thiol (***1a***) reacts with trialkyl phosphites (***2a–c***) to give the respective dialkyl phosphonate adducts (***4a–c***). On the other hand, the reactions of trisdialkylaminophosphines (***3a,b***) with* **1a**, *5-{[(1*E*)-(4-phenyl)methylene]amino}-1,3,4-thiadiazole-2-thiol (***1b***) yield the corresponding open dipolar structures* **6a–c**. *In the case of the reaction of triethyl phosphite (***2a***) with* **1b**, *both the dialkyl phosphonate adduct (***7***) and the dipolar product (***8a***) are obtained. Moreover, triisopropyl phosphite (***2c***) reacts with* **1b** *to give both the* S-*alkyl and the* N-*alkyl phosphonate adducts (***9a,b***), respectively. Mechanisms are proposed to explain the formation of the new products, and their structures were confirmed on the basis of elemental analysis and spectral studies.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:594–601, 2001

INTRODUCTION

The antibacterial, fungicidal, and pharmacological characteristics [1–3] inherent in substituted 1,3,4-oxa- and thiadiazole derivatives enhanced the synthesis of new compounds incorporating such important nuclei that may possibly lead to further biological activity. Our continuing interest in organophosphorus syntheses [4–8] led us to investigate the reactivity of 5-{[(1*E*)-(4-methoxyphenyl)methylene]amino}-1,3,4-thiadiazole-2-thiol (**1a**) and 5-{[(1*E*)-(4-phenyl) methylene] amino}-1,3,4-thiadiazole-2-thiol (**1b**) toward trialkyl phosphites (**2a–c**), and trisdialkylaminophosphines (**3a,b**) (Scheme 1).

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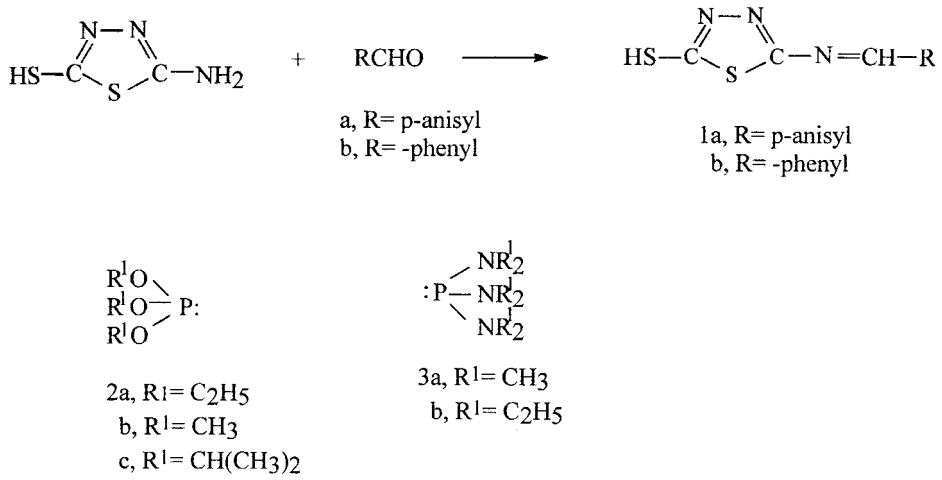
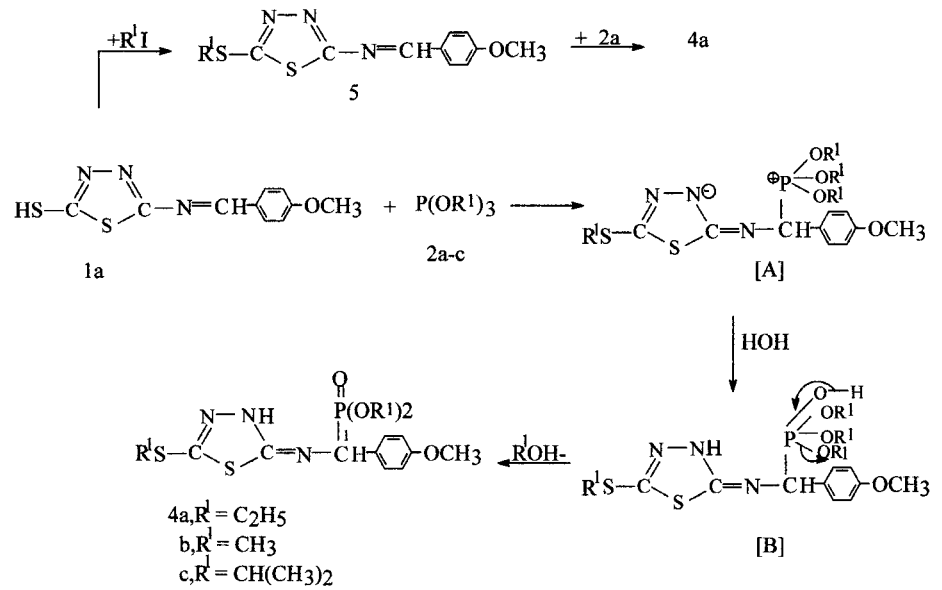
RESULTS AND DISCUSSION

We have found that the reaction of **1a** (prepared by the reaction of 2-amino-5-mercapto-1,3,4-thiadiazole with 4-methoxybenzaldehyde) with 2 mole equivalents of triethyl phosphite (**2a**) in dry toluene proceeds at reflux temperature to give the dialkyl phosphonate adduct (**4a**) in 86% yield (Scheme 2). Structure elucidation of the diethyl phosphonate adduct (**4a**) is based on the following evidence: (i) Compound **4a** exhibits $\delta = +21.19$ in its ^{31}P NMR spectrum which clearly indicates a phosphonate structure [9,10]. (ii) The IR spectrum of **4a** shows strong absorption bands at 1248 cm^{-1} (P=O), 1023 cm^{-1} (P—O—C_2H_5) [11], and at 3453 cm^{-1} (NH). Moreover, its IR spectrum lacks the thiol (SH) absorption band appearing in the spectrum of (**1a**) at 2800 cm^{-1}. The ^1H and ^{13}C NMR spectra also furnish strong evidence in support of the phosphonate structure **4a** (cf. Experimental). The mass spectrum of **4a** yielded a prominent ion peak for M^+ at *m/z* 417.

Compound **4a** can also be obtained by the reaction of the alkylated product (**5**) (prepared from **1a** and ethyl iodide) with excess triethyl phosphite (**2a**) in boiling toluene (cf. Scheme 2, Experimental).



SCHEME 1



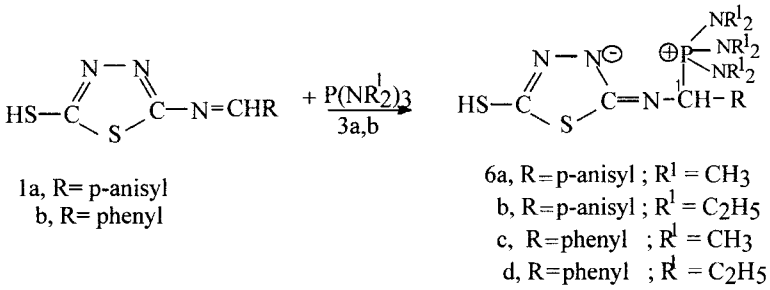
SCHEME 2

When **1a** is allowed to react with trimethyl- and triisopropyl phosphites (**2b,c**), the phosphonate products **4b** and **4c**, respectively are obtained. Compatible analytical and spectral data [IR, ^{1}H, ^{31}P, ^{13}C NMR and MS] have been recorded for the new products (cf. Experimental).

Intermediates (**A**) can be obtained by alkylation [12–15] of **1a** by trialkyl phosphites, followed by addition of the phosphite esters to the active methine carbon of the double bond of **5** to give the open dipolar ions. Addition of water (unavoidable moisture) to each dipolar ion, structure (**A**), produces a transient intermediate (**B**) with pentacovalent phosphorus [16]. The latter collapses to give the respective dialkyl phosphonate products (**4a–c**) (Scheme 2).

The reactions of **1a** with trisdialkylaminophosphines (**3a,b**) were also investigated to determine the mode of addition, as each hexaalkylphosphorustriamide (HAPT) possesses a greater nucleophilicty than the trialkyl phosphites [17,18].

We have found that the reaction of trisdimethylaminophosphine (**3a**) with **1a** proceeds in boiling toluene to give chromatographically the pure adduct **6a** assigned the open dipolar structure based on the following evidence: (i) elemental analyses and a molecular weight determination (MS) for compound **6a** support the molecular formula $C_{16}H_{27}N_6OPS_2$ (ii) The IR spectrum of **6a**, in KBr, exhibits strong absorption bands at 2600 cm^{-1} (SH), 1312 cm^{-1} and at 865 cm^{-1} $P[N(CH_3)_2]_3$. Moreover, its IR spectrum



SCHEME 3

lacks, both the NH and (P=O) absorption bands at 3235 cm^{-1} and 1240 cm^{-1}, respectively. The ^1H NMR spectrum of **6a** reveals signals at $\delta = 2.16$[d, 12H, $J_{HP} = 11.21$ Hz] and 2.67 [d, 6H, $J_{HP} = 11.21$ Hz], corresponding to the 18 hydrogens of the three magnetically unequivalent dimethylamino groups attached to the phosphorus atom of the $P[N(CH_3)_2]_3$ moiety [19].

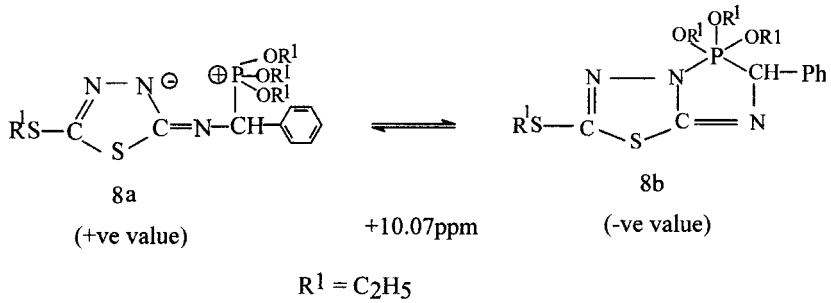
The ^{31}P NMR spectrum of **6a** exhibits a signal at $\delta = +32.03$, a value that falls in the range frequently recorded for the open dipolar structure **6a** [20]. This result rule out the alternative cyclic structure since the latter would predict a negative value for its ^{31}P NMR spectrum. The ^{13}C NMR spectrum of **6a**, $CDCl_3$ shows a doublet at $\delta = 64.78$ with coupling constant $^1J_{CP} = 131.8$ Hz ascribed to the presence of the methine proton attached to the phosphorus CH—P (cf. Experimental). The mass spectrum of **6a** yields a prominent ion peak for M^+ at $m/z = 414$ (Scheme 3).

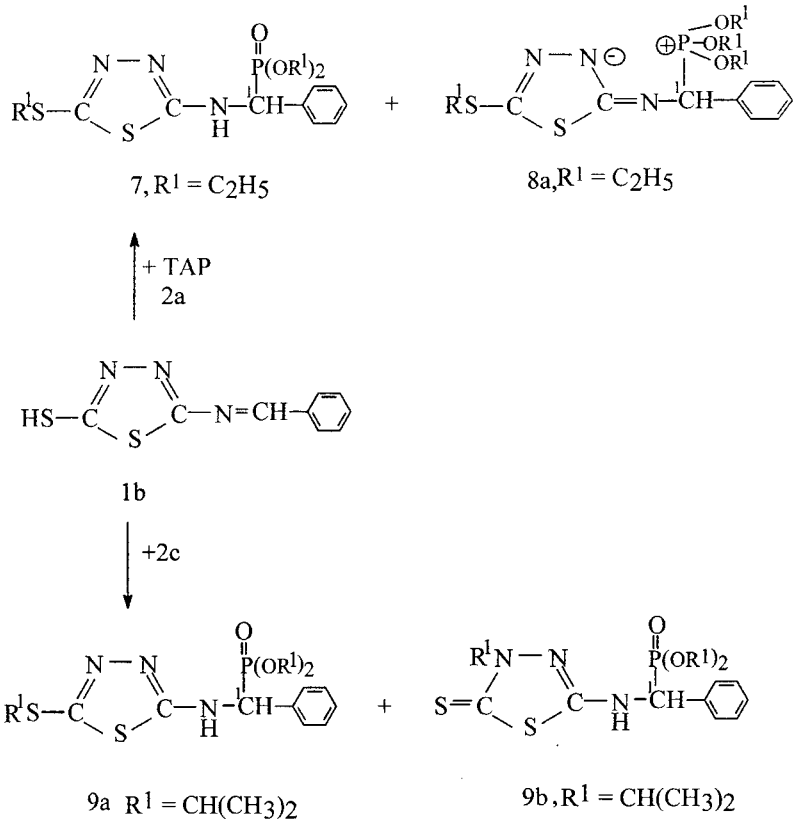
Furthermore, trisdiethylaminophosphine (**3b**) reacts with **1a** without solvent at 105°C to give the open dipolar structure, **6b**. The structure of **6b** is deduced from its analysis, IR, ^1H, ^{31}P, ^{13}C NMR and mass spectral data (cf. Experimental Section).

Also, this study has been extended to include the reaction of 5-{[(1*E*)-(4-phenyl)methylene]amino}-1,3,4-thiadiazole-2-thiol (**1b**) with the same phosphite and trisdialkylaminophosphine reagents **2** and **3** to establish whether it would behave in a similar manner. We have found that the reaction of **1b** with an excess of triethyl phosphite (**2a**), also employed as a solvent, was completed after heating at 130°C for 8 h to give a mixture of two main products **7** and **8a**, which could be separated by column chromatography.

The first product (~52% yield) was assigned structure **7** because its ^{31}P NMR spectrum (in $CDCl_3$) showed a signal at $\delta = +20.76$ that agrees with the dialkyl phosphonate adduct (Scheme 4). Moreover, IR, ^1H, and ^{13}C NMR spectral data support structure **7** (cf. Experimental). The mass spectrum of **7** yielded a prominent ion peak for M^+ at m/z 387.

The second product (35% yield) was assigned an open dipolar structure with quadruply connected phosphorus **8a** [21]. The spectral properties of this adduct differed from those of compound **7**. The ^{31}P NMR signal of this adduct appeared at 10.07 ppm. This value strongly suggests an equilibrium between the open dipolar structure **8a** [having quadrubly connected phosphorus] and the cyclic diazaphosphacyclopentene (**8b**) [having quintuply connected phosphorus]. The ^{31}P NMR signal should be an average value of both structures. The observed value suggests that the dipolar form greatly predominates over the diazaphosphacyclopentene structure which should have a negative value. The presence of one signal in its ^{31}P NMR spectrum indicates that the equilibrium between the two forms is established rapidly relative to the time scale of the NMR phenomenon. A similar finding has been reported for the coexistance in solutions of a similar structure containing quadruply-connected phosphorus and the corresponding valence tautomer containing quintuply- connected phosphorus [22].





SCHEME 4

The main features of the IR spectrum of **8a** (in KBr, expressed in cm^{-1}) were the presence of absorption bands, at 1050 P(O)C, while no absorption can be detected for both the SH (2600 cm^{-1}) and the NH (3400 cm^{-1}) groups.

Moreover, the structure of compound **8a** was established by ^{1}H NMR and mass spectral data (cf. Experimental). Worthy to mention is that addition of excess water to compound **8a** resulted in the formation of the corresponding dialkyl phosphonate adduct (**7**) (mixed m.p., comparative IR,1H NMR spectra).

On the other hand,when **1b** (prepared from 2-amino-5-mercapto-1,3,4-thiadiazole and benzaldehyde) was allowed to react with excess triisopropyl phosphite (**2c**) without solvent, two main products **9a** and **9b** were obtained which could be separated by column chromatography. The two compounds **9a** and **9b** were assigned the *S*-alkyl-(**9a**) and the *N*-alkyl-(**9b**) phosphonate adducts based on elemental analyses and spectroscopic evidences (IR, ^{1}H, ^{31}P,^{13}C NMR, and MS) (cf. Scheme 4, Experimental).

Next, the reaction of **1b** with trisdialkylaminophosphines (**3a,b**) was also investigated. We have found that the reaction of trisdimethylamino- and diethylaminophosphines (**3a,b**) with **1b** proceeds in the absence of a solvent at 90°C and 105°C, respectively, to give chromatographically pure adducts formulated as **6c** and **6d**, respectively (Scheme 3). Structure elucidations for compounds **6c** and **6d** were attested by analytical and spectral data (IR, ^{1}H, ^{31}P, ^{13}C NMR and MS) (cf. Experimental).

From the aforementioned results, it is evident that the reaction of trialkyl phosphites (**2a–c**) and trisdialkylaminophosphines (**3a–b**) with **1a** and **1b** depends on the substituent at the benzylidene group as well as the reaction temperature used. Also, it is noted that **1b** behaves toward triethyl phosphite (**2a**) in a manner not quite similar to that described for the reaction of **1a** with this phosphite, yielding the dialkyl phosphonate adducts (**4a–c**) predominately or exclusively. Moreover, it has been found that the reaction of **1b** with triethyl phosphite (**2a**) proceeds without solvent to give both the dialkyl phosphonate adduct (**7**) and the open dipolar structure (**8a**). On the other hand,when trisdialkylaminophosphines react with **1a** and **1b**, only one type of products is obtained because of the fact that the reagents (**3a–b**) has no or very low

potential of alkylation. This disparity in the behaviour of **1a** on the one hand and **1b** on the other hand may be dependent upon the stability of the dipolar ion structure. These findings supplement the wide aspects for utilization of trialkyl phosphites and trisdialkylaminophosphines as addition reagents.

EXPERIMENTAL

All melting points are uncorrected. Toluene and petroleum ether (br 60–80°C) were dried over sodium. Trialkyl phosphites and trisdialkylaminophosphines were prepared according to established procedures and were purified by fractional distillation [23–25]. The IR spectra were measured in KBr pellets with a Perkin-Elmer Infracord Spectrophotometer Model 157 (Grating). The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Varian Spectrophotometer at 270 and 67.5 MHz, respectively, using TMS as an internal references. The ^{31}P NMR spectra were recorded in $CDCl_3$ (vs. H_3PO_4 as an external standard) with a JNM-PS- 100Fa Spectrometer. The mass spectra were run at 70 eV with a Kratos MS equipment and/or a Varian MAT 311 A Spectrometer.

*Diethyl(4-methoxyphenyl){[(2*E*)-5-(ethylthio)-1,3,4-thiadiazol-2(3H)-ylidene]amino}methylphosphonate (**4a**)*

Triethyl phosphite (**2a**) (0.33 g; 2 mmol) was added dropwise to a solution of **1a** (0.25 g; 1 mmol) in dry toluene (20 ml), and the reaction mixture was refluxed for 6 h. The reaction mixture was concentrated and gave a precipitate by addition of acetone. The precipitate was filtered off and recrystallized from diethyl ether to give colourless crystals **4a**, yield 86%, m.p. 112°C. Anal. calcd. for $C_{16}H_{24}N_3O_4PS_2$ (417.4): C, 46.03; H, 5.79; N, 10.06; P, 7.41; S, 15.36. Found: C, 46.01; H, 5.75; N, 10.03; P, 7.40; S, 15.33%. MS, *m/z* (%) = 417 (25) [M^+], 280 (100) [$M^+ - (O)P(OEt)_2$]. IR: ν = 3453 (NH), 1248 (P=O), 1023 cm^{-1} (P–OEt). ^{1}H NMR: δ = 4.15 [q, 4H, $(O)P(OEt)_2$], 1.32 [t, 6H, $(O)P(OEt)_2$], 3.05 (q, 2H, SEt), 1.01 (t, 3H, SEt), 3.75 (s, 3H, OMe), 5.40 (d, $^{2}J_{HP}$ = 25.1 Hz, 1H, 1-H), 6.85, 7.45 (2d, 4H, Ar), 8.50 (bd, 1H, NH, exchangeable with D_2O). ^{13}C NMR: δ = 53.0 (d, $^{1}J_{CP}$ = 157.0 Hz, C-1), 63.3 [d, J_{CP} = 7.3 Hz, $(O)P(OEt)_2$], 55.0 (s, OMe), 28.7 (SEt), 15.9 [d, $^{3}J_{CP}$ = 5.8 Hz, $(O)P(OEt)_2$], 14.6 (s, SEt), 167.3, 113.7, 126.6, 129.2 (C_6H_4), 168.1, 159.3 (C–S–C). ^{31}P NMR: δ = +21.19.

*Action of Ethyl Iodide on 5-{[(1E)-(4-Methoxyphenyl)methylene]amino}-1,3,4-thiadiazole-2-thiol (**1a**)*

Compound **1a**, (0.25 g; 0.001 mol) was dissolved in 30 ml of dry acetone, and anhydrous potassium carbonate (1.50 g) was added followed by the addition of 1 ml of ethyl iodide. The reaction mixture was refluxed for 3 h on the water bath and then evaporated under reduced pressure. The residue was subjected to silica gel column chromatography, using the eluent ethyl acetate/petroleum ether (5:95) to give **5** as yellow crystals, m.p. 113°C, yield 76%. Anal. calcd. for $C_{12}H_{13}N_3OS_2$ (279.8): C, 51.58; H, 4.69; N, 15.04; S, 22.95%. Found: C, 51.56; H, 4.65; N, 15.03; S, 22.93. MS, *m/z* (%): 279 (100) [M^+]. ^{1}H NMR: δ = 1.45 (t, 3H, SEt), 3.31 (q, 2H, SEt), 3.87 (s, 3H, OMe), 6.96, 7.92 (2d, 4H, Ar), 8.71 (s, 1H, N=CH).

*Reaction of Triethyl Phosphite (**2a**) With **5***

Triethyl phosphite (**2a**) (0.33 g; 0.002 mol) was added dropwise to a solution of **5** (0.27 g; 0.001 mol) in dry toluene (20 ml) and the reaction mixture was refluxed for 10 h. The reaction mixture was concentrated and the precipitate was produced by addition of petroleum ether, giving adduct **4a** as colourless crystals (recrystallization from benzene) (m.p., mixed m.p. 112°C, comparative IR and ^{1}H NMR spectra).

*Dimethyl(4-methoxyphenyl){[(2*E*)-5-(methylthio)-1,3,4-thiadiazol-2(3H)-ylidene]amino}methylphosphonate (**4b**)*

A mixture of **1a** (0.25 g; 0.001 mol), trimethyl phosphite (0.24 g, 0.002 mol) **2b**, and dry toluene (30 ml) was refluxed until no more of the starting material could be detected (TLC, 6 h). The reaction mixture was concentrated and washed several times by petroleum ether. The solid product was recrystallized from benzene to give colourless crystals **4b**, m.p. 162°C, yield 85%. Anal. calcd. for $C_{13}H_{18}N_3O_4PS_2$ (375.4): C, 41.59; H, 4.83; N, 11.20; P, 8.25; S, 17.08. Found: C, 41.57; H, 4.81; N, 11.18; P, 8.25; S, 17.10%. MS, *m/z* (%): 375 (50) [M^+], 266 (100) [$M^+ - (O)P(OMe)_2$]. IR: ν 3250 (NH), 1230 (P=O), 1056 cm^{-1} (P–OMe). ^{1}H NMR: δ = 3.82, 3.49 [2d, J_{HP} = 11.54 Hz, 6H, $P(OMe)_2$], 3.78 (s, 3H, OMe), 2.61 (s, SMe), 5.39 (d, J_{HP} = 25.0 Hz, 1H, 1-H), 7.49, 6.89 (2d, 4H, Ar), 8.23 (bs, 1H, NH exchangeable with D_2O). ^{13}C NMR: δ = 54.2 (d, $^{1}J_{CP}$ = 157.0 Hz, C-1), 53.8 [d, J_{CP} = 6.98 Hz, $P(OMe)_2$], 16.4 (s, SMe), 55.2 (s, OMe), 169.9, 159.6 (s, –C–S–C–), 167.8, 129.5, 126.4, 114.1 (C_6H_4). ^{31}P NMR: δ = +23.77.

*Diisopropyl(4-methoxyphenyl){[(2E)-5-(methylthio)-1,3,4- thiadiazol-2(3H)-ylidene] amino}methylphosphonate (**4c**)*

A mixture of **1a** (0.25 g; 0.001 mol) and 2 ml of triisopropyl phosphite (**2c**) was heated in an oil bath at 130°C for 3 h. The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography; the eluent was acetone/petroleum ether (20:80); **4c** was obtained as colorless crystals, yield 80%, m.p. 126°C. Anal. calcd. $C_{19}H_{30}N_3O_4PS_2$ (459.5): C, 49.65; H 6.58; N, 9.14; P, 6.73; S, 13.95. Found: C, 49.62; H, 6.57; N, 9.11; P, 6.72; S, 13.93%. MS, *m/z* (%): 459 (25) [M^+], 294 (100) [$M^+ - (O)P(O{-}iPr)_2$]. IR: $\nu = 3234$ (NH), 1228 (P=O), 990 [$P(OiPr)_2$], 1608 cm^{-1} (C=C, Ar). ^1H NMR: $\delta = 4.70$, 4.35 (m, 2H, two-*i*Pr), 1.25 {m, 12H, $(O)P[O{-}iPr)_2]_2$}, 3.50 (m, 1H, S—*i*Pr), 0.85 (d, 6H, S-iPr), 3.75 (s, 3H, O—Me), 5.30 (d, $J_{HP} = 27$ Hz, ^1H, 1-H), 6.75, 7.43 (2d, 4H, Ar), 8.22 (bs, ^1H, NH exchangeable with D_2O). ^{13}C NMR: $\delta = 24.22$ [d, $^3J_{CP} = 3.4$ Hz, $P(O{-}iPr)_2$], 23.2 (s, S—*i*Pr), 72.7 [d, $^2J_{CP} = 7.48$ Hz, $P(O{-}iPr)_2$], 56.6 (d, $^1J_{CP} = 177.03$ Hz, C-1), 40.3 (s, S—*i*Pr), 54.28 (s, OMe), 169.2, 129.8, 127.0, 113.8 (C_6H_4), 169.9, 159.6 (s, —C—S—C—). ^{31}P NMR: $\delta = +19.42$.

*Reaction of **1a** With Trisdimethylaminophosphine (**3a**)*

A mixture of **1a** (0.25 g; 0.001 mol), trisdimethylaminophosphine (**3a**) (0.32 g; 0.002 mol), and dry toluene (30 ml) was refluxed for 8 h. The reaction mixture was evaporated under reduced pressure and then applied to silica gel column chromatography using the eluent, acetone/petrolum ether (20:80, v:v) to give **6a** as colourless crystals, m.p. 85°C, yield 60%. Anal. calcd. for $C_{16}H_{27}N_6OPS_2$ (414.5): C, 46.35; H, 6.56; N, 20.27; P, 7.47; S, 15.46. Found: C, 46.31; H, 6.52; N, 20.24; P, 7.45; S, 15.44%. MS, *m/z* (%):414 (9) [M^+], 164 (100) {$P[N(Me)_2]_3$,}. IR: $\nu = 2600$ (SH), 1312, 865 cm^{-1} P $[N(Me)_2]_3$. ^1H NMR: $\delta = 2.67$, 2.16 {2d, $J_{HP} = 11.21$ Hz, 18H, $P[N(Me)_2]_3$}, 3.77 (d, $J_{HP} = 17.81$ Hz, 1H, C-1), 3.75 (s, 3H, OMe), 6.79, 7.33 (2d, 4H, Ar), 10.82 (s, 1H, SH, exchangeable with D_2O). ^{13}C NMR: $\delta = 64.7$ (d, $J_{CP} = 131.8$ Hz, C-1), 35.9, 42.5 {2d, $J_{CP} = 6.2$ Hz, $P[N(Me)_2]_3$}, 54.8 (s, OMe), 158.8, 132.1, 127.8, 112.8 (C_6H_4). ^{31}P NMR: $\delta = +32.03$.

*Reaction of **1a** With Trisdiethylaminophosphine (**3b**)*

A suspension of **1a** (0.25, 0.001 mol), 1 ml of tris(diethylamino)phosphine (**3b**) was heated in an oil bath at 105°C for 3 h. The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography using ethyl acetate/petroluem ether (60:40, v:v) as eluent. Adduct **6b** was obtained as pale yellow crystals (recrystallized from cyclohexane), yield 60%, m.p. 65°C. Anal. calcd. for $C_{22}H_{39}N_6OPS_2$ (498.6): C, 52.98; H, 7.88; N, 16.85; P, 6.21; S, 12.85. Found: C, 52.95; H, 7.86; N, 16.81; P, 6.19; S, 12.83%. MS, *m/z* (%)′: 498 (90) [M^+]. IR: $\nu =$ 2580 (SH), 1310, 854 cm^{-1} $P[N(Et)_2]_3$. ^1H NMR: $\delta = 3.35$, 2.95 {m, 12H, $P[N(Et)_2]_3$}, 1.42, 1.06 {2t, 18H, $P[N(Et)_2]_3$}, 3.98 (s, 3H, OMe), 3.88 (d, 1H, J_{HP} = 16.0 Hz, 1-H), 7.49–7.32 (m, 4H, Ar), 10.71 (s, 1H, SH, exchangeable with D_2O).

*Reaction of 4-[5-[(Benzylidene)amino}-1,3,4 thiadiazol-2-yl]thiol (**1b**) With **2a***

A mixture of **1b** (0.22 g; 0.001 mol) and 1 ml of triethyl phosphite (**2a**) was heated for 8 h at 130°C (bath temperature). The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography to give two adducts **7** and **8a**, respectively.

*Diethyl{[5-(ethylthio)-1,3,4-thiodiazol-2-yl]amino}(phenyl)methylphosphonate (**7**)*

Eluent acetone/petroleum ether (20:80, v:v) as colourless crystals, m.p. 132°C, yield (52%). Anal. calcd. $C_{15}H_{22}N_3O_3PS_2$ (387.4): C, 46.49; H, 5.72; N, 10.85; P, 7.99; S, 16.55. Found: C, 46.46; H, 5.70; N, 10.83; P, 7.97; S, 16.54%. MS, *m/z* (%): 387 (30) [M^+], 250 (100) [$M^+ - (O)P(OEt)_2$]. IR: $\nu =$ 3400 (NH), 1245 (P=O), 1028 cm^{-1} (P—OEt). ^1H NMR: $\delta = 4.28$ [q, 4H, $(O)P(OEt)_2$], 1.31 [t, 6H, $(O)P(OEt)_2$], 3.07 (q, 2H, SEt), 1.06 (t, 3H, SEt), 5.38 (dd, $^2J_{HP} = 22.1$ Hz, $J_{HH} = 10.5$ Hz, 1H, 1-H^2), 7.53–7.15 (m, 5H, Ar), 7.88 (dd, $J_{HH} = 10.5$ Hz, 1H, NH,). ^{13}C NMR: $\delta =$ 55.7 (d, $^1J_{CP} =$ 155.0 Hz, C-1), 63.6 [d, $J_{CP} = 7.1$ Hz, $(O)P(OEt)_2$], 55.0 (s, O—Me), 28.7 (s, SEt), 16.3 [d, $^3J_{CP} = 6.1$ Hz, $(O)P(OEt)_2$], 14.7 (s, SEt), 128.3, 134.8, 127.2, 129.2 (C_6H_5), 168.3, 158.1 (C—S—C).^{31}P NMR: $\delta = +20.76$.

*Compound **8a***

Eluent acetone/petroleum ether (15:85, v:v) as colourless crystals m.p. 40°C, yield 35%. Anal. calcd. for $C_{17}H_{26}N_3O_3PS_2$ (415.5): C,; 49.14, H; 6.31; N, 10.11; P 7.45; S, 5.43. Found: C, 49.12; H, 6.33; N, 10.13; P, 7.42; S, 15.40%. MS, *m/z* (%): 415 (90) [M^+]. IR: $\nu =$ 1050 cm^{-1} (POEt). ^1H NMR: $\delta = 0.85$ (t, 3H, SEt), 1.20, 1.15 [t, 9H, $P(OEt)_3$], 2.83 (q, 2H, SEt), 4.10, 4.04 [m, 6H, $P(OEt)_3$], 4.23 (d, $^2J_{HP} =$ 23.4 Hz, 1H, 1-H), 7.49–7.09 (m, 5H, Ar). ^{31}P NMR: $\delta = +10.07$.

Reaction **1b** *With Triisopropyl phosphite (***2c***)*

A suspension of **1b** (0.22 g; 0.001 mol), 1 ml triisopropyl phosphite (**2c**) was heated in oil bath at 135°C for 3 h. The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography, to give **9a** and **9b** respectively.

*Diisopropyl{[5-(isopropylthio)-1,3,4-thiadiazol-2-yl]amino}(phenyl)methylphosphonate (***9a***)*

Eluent ethyl acetate/petroleum ether (40:60, v:v), colourless crystals m.p. 145°C, yield 65%. Anal. calcd. for $C_{18}H_{28}N_3O_3PS_2$ (429.5): C, 50.33; H, 6.57; N 9.78; P, 7.21; S, 14.92. Found: C, 50.30; H, 6.54; N, 9.77; P, 7.20; S, 14.91%. MS, *m/z* (%): 429 (18) [M^+], 353 (30) ($M^+ - S{-}iPr$), 264 (100) [$M^+ - (O)P(O{-}iPr)_2$,]. IR: ν = 3350 (NH), 1225 (P=O), 995 [$P(O{-}iPr)_2$], 1600 cm^{-1} (C=C, Ar). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 4.74, 4.35 (m, 2H, two-*i*Pr), 1.26 [m, 12H, $(O)P(O{-}iPr)_2$], 3.50 (m, 1H, S–*i*Pr), 0.78 (d, 6H, S–*i*Pr), 5.36 (dd, J_{HP} = 22.4 Hz, J_{HH} = 9.3 Hz, 1H, 1-H), 7.53–7.24 (m, 5H, Ar), 8.12 (dd, J_{HH} = 9.3 Hz, 1H, NH). ^{13}C NMR (65 MHz, $CDCl_3$): δ = 23.8 [d, $^3J_{CP}$ = 4.9 Hz, $P(O{-}iPr)_2$], 23.2 (s, S–*i*Pr), 72.7 [d, $^2J_{CP}$ = 7.30 Hz, $P(O{-}iPr)_2$], 57.5 (d, $^1J_{CP}$ = 156.2 Hz, C-1), 40.3 (s, S–*i*Pr), 135.2, 128.6, 128.3, 127.8 (C_6H_5).

*Diisopropyl[(4-isopropyl-5-thioxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)amino] (phenyl) methylphosphonate (***9b***)*

Eluent ethyl acetate/petroleum ether (30:70, v:v), colourless crystals m.p. 163°C, yield 30%. $C_{18}H_{28}N_3O_3PS_2$ (429.5): Anal. calcd. C, 50.33; H, 6.57; N, 9.78; P, 7.21; S, 14.92. Found: C, 50.30; H, 6.54; N, 9.77; P, 7.20; S, 14.91. MS, *m/z* (%): 429 (18) [M^+], 387 (30) [$M^+ - (iPr)$], 264 (100){$M^+ - (O)P[(O{-}iPr)_2$]. IR : ν = 3350 (NH), 1225 (P=O), 995 [$P(O{-}iPr)_2$], 1200 (C=S), 1600 cm^{-1} (C=C, Ar). ^{1}H NMR: δ = 5.19, 4.74 (m, 2H, two-*i*Pr), 1.26 [m, 12H, $(O)P(OiPr)_2$], 4.31 [m, 1H, N–*i*Pr], 0.73 [d, 6H, N–*i*Pr], 5.15 (dd, J_{HP} = 22.4 Hz, J_{HH} = 9.3 Hz, 1H, C-1), 7.53–7.24 (m, 5H, Ar), 8.12 (d, J_{HH} = 9.3 Hz, 1H, NH). ^{31}P NMR: δ = 19.81.

Reaction of 4-[5-[(Benzylidene)amino}-1,3,4thiadiazol-2-yl]thiol **1b** *With Trisdimethylaminophosphine (***3a***)*

A mixture of **1b** (0.22 g; 0.001 mol) and 1 ml of **3a** was heated in oil bath at 90°C for 4 h. The reaction mixture was evaporated under reduced pressure and the residue subjected to silica gel column chromatography; eluent was acetone/petroleum ether (20:80); to give **6c** as pale yellow crystals, yield 65%, m.p. 126°C. Anal. calcd. for $C_{15}H_{25}N_6PS_2$ (384.5): C, 46.85; H, 6.55; N, 21.85; P, 8.05; S,16.67. Found: C, 46.83; H, 6.51; N, 21.82; P, 8.02; S, 16.63%. MS, *m/z* (%)′: 384 (92) [M^+]. IR: ν = 2560 (SH), 865 cm^{-1} $P[N(Me)_2]_3$. ^{1}H NMR: δ = 2.20, 2.64 {2d, 18H, J_{HP} = 10.2 Hz, $P[N(Me)_2]_3$}, 3.88 (d, J_{HP} = 18.57 Hz, 1H, 1-H), 7.49–7.26 (m, 5H, Ar), 10.87 (s, 1H, SH, exchangeable with D_2O). ^{13}C NMR: δ = 65.2 (d, J_{CP} = 130.6 Hz, C-1), 42.7, 37.7 {2d, J_{CP} = 8.6 Hz, $P[N(Me)_2]_3$}. ^{31}P NMR: δ = +30.7.

Similarly trisdiethylaminophosphine **3b** reacts with **1b**, using eluent acetone/petroleum ether (15:85, v:v) to give **6d** as colorless crystals, yield 55%, m.p. 86°C. Anal. calcd. for $C_{21}H_{37}N_6PS_2$ (468.6): C, 53.81; H, 7.95; N, 17.93; P, 6.60; S, 13.68. Found: C, 53.80; H 7.92; N, 17.90; P, 6.57; S, 13.64%. MS, *m/z* (%): 468 (95) [M^+]. IR: ν = 2520 (SH), 1210, 840 cm^{-1} $P[N(Et)_2]_3$. ^{1}H NMR: δ = 3.18, 2.95 {2m, 18H, $P[N(Et)_2]_3$, 1.14, 1.02 {2t, 18H, $P[N(Et)_2]_3$}, 4.06 (d, J_{HP} = 16.0 Hz, 1H, 1-H), 7.49–7.25 (m, 5H, Ar),10.73 (s, 1H, SH, exchangeable with D_2O). ^{31}P NMR: δ = +31.51.

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