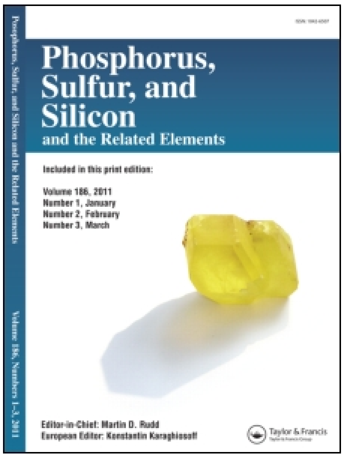

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REACTIONS OF PHOSPHONIUM YLIDES ON THIA- AND OXADIZAOLE DERIVATIVES

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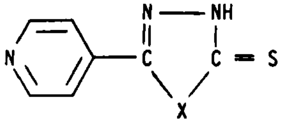
Phosphonium ylides 2(a,b) add to 2-thiono-5-pyridyl 1,3,4-thiadiazole (1a) to give the same ylid-phosphorane adduct 3a. While the same ylides did not affect on 2-thiono-5-pyridyl (1b). On the other hand addition of fluorenylidenetriphenylphosphorane (3c) gave the episulphides (3b) and (3c), respectively. The given structures were based upon analytical, chemical and spectroscopic results.

Key words: 1,3,4-Thiadiazole; 1,3,4-Oxadiazole; phosphonium ylides, Witting reagents.

INTRODUCTION

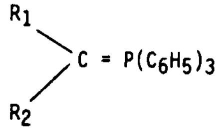
It was reported earlier by Sherman[1] that substituted 1,3,4-oxadiazole and 1,3,4-thiadiazole derivatives were found to have antibacterial properties. 5-Aryl-2-thiono-1,3,4-oxadiazoles are known to have antiphlogestic properties,[2,3] 5-Aryl-2-thiono-1,3,4-thiadiazole, possess depressing effect on the central nervous system and have sedative effect.[4] They also are useful in pharmaceutical industry.[5]

Our continuing interest in the reaction of phosphonium ylides for the production of novel, synthetically useful ylides[6] and new heterocyclic systems[7–12] let us to investigate the reactivity of thia-, and oxadiozole derivatives (1) towards a number of wittig reagents of type (2).



1a, X = S

b, X = 0



$$\begin{matrix} R_1 \\ & \rangle C = P(C_6H_5)_3 \\ R_2 \end{matrix}$$

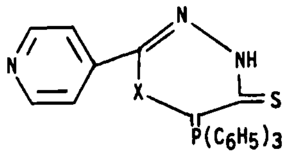
2a, R_1 = H; R_2 = $COOCH_3$

b, R_1 = H; R_2 = $COOC_2H_5$

c, R_1 + R_2 = fluorenyl

RESULTS AND DISCUSSION

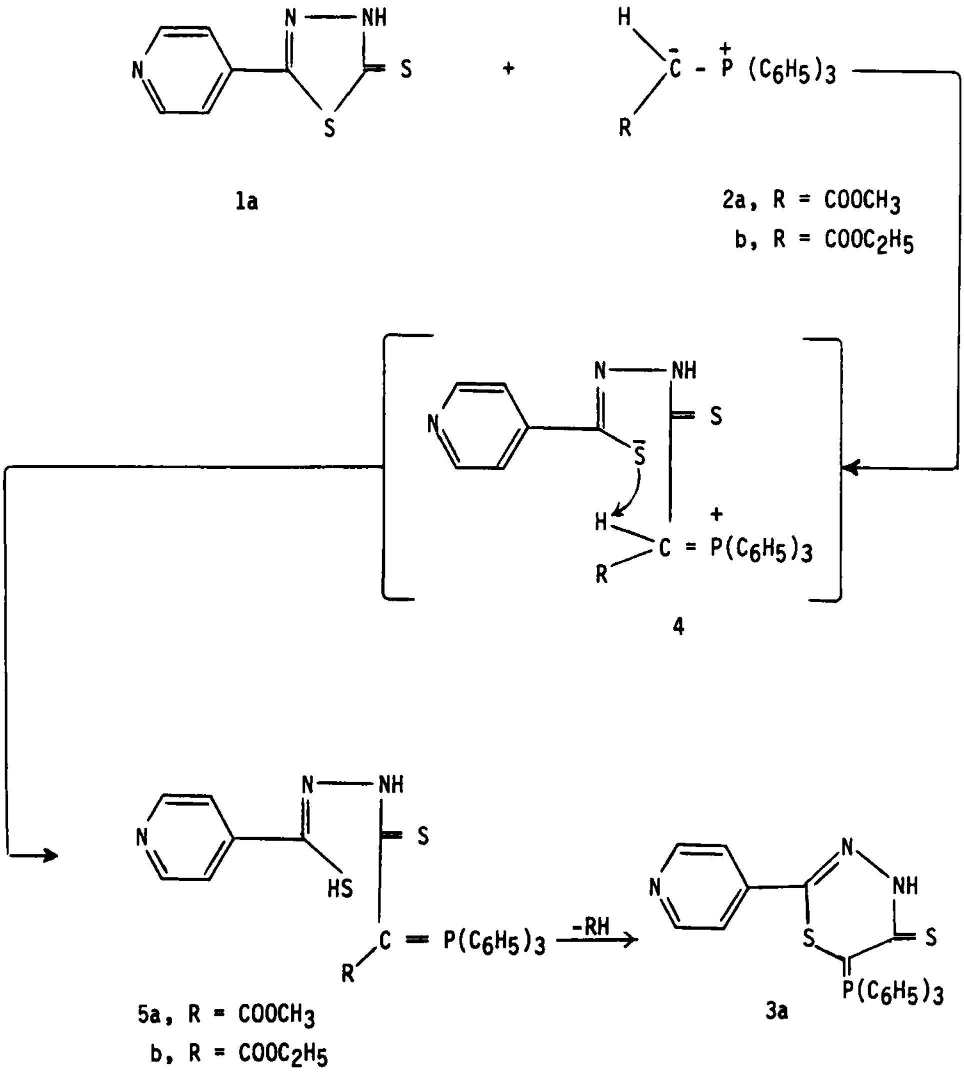
We have found that 2-thiono-5-pyridyl-1,3,4-thiadiazole 1a reacts with carbomethoxymethylenetriphenylphosphorane 2a, in boiling toluene, to give a yellow crystalline compound formulated as 3a. Triphenylphosphine sulphide (TPPS) was neither isolated nor identified in the reaction medium by (TLC). Compound 3a is chromatographically pure and possesses sharp melting point.



3a, X = S

Structure 3a was confirmed by elemental analysis and molecular weight determination (MS) for 3a corresponds to $C_{26}H_{20}N_3S_2P$. Adduct 3a possesses ylid-phosphorane structure since it exhibits a positive shift in its ^{31}P NMR spectrum.

Moreover, the IR spectrum of adduct 3a, (in kBr), reveals the presence of strong



Scheme (A)

bands at 1680 cm^{-1} characteristic for the $>C=P$ group absorption[13] and at 1490 cm^{-1} for the P—C (phenyl) absorption.[14] Compound 3a showed further bands at 1640 cm^{-1} (C=N) and at 1260 cm^{-1} characteristic for the C=S group absorption.[15] The —NH absorption band appeared at 3060 cm^{-1} ascribed to the formation of strong-intramolecular hydrogen bonding.[16] The ^1H NMR spectrum of compound 3a located the 15 aromatic protons as a multiplet at $\delta = 7.4-7.9$ ppm whereas the 4 protons of the pyridyl ring appeared as a multiplet at $\delta 8.8-9$ ppm. The NH proton gave a broad singlet (exchangable with D_2O) at $\delta = 11.1$ ppm. The mass spectrum (MS) of adduct 3a confirms the structure given as it shows M^+ as the base peak at 465 (1%), ($M^+—C_{18}H_{15}P$) 207 (70%).

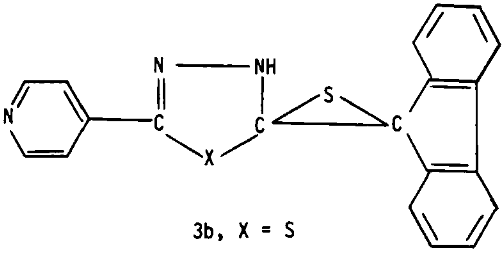
The reaction of 2-thiono-5-pyridyl-1,3,4-thiadiazole 1a with carboethoxymethylenetriphenylphosphorane 2b was next investigated. In boiling toluene, the reaction of Ia with ylide 2b was almost complete after 48 h. The yellow crystalline compound thus formed was proved to be identical with 3a (TLC, mp, mixed mp, comparison of IR and NMR spectra).

A possible explanation for the course of the reaction of ylides 2a,b with 1a is illustrated in Scheme A.

Attempts were made to study the chemical reactivity of 2-thiono-5-pyridyl-1,3,4-oxadiazole (1b) towards Wittig reagents (2a,b) in toluene, but under all conditions the starting oxadiazole (1b) was separated practically unchanged (mixed mp).

It was also interest to examine the behaviour of thia-, and oxadiazole (1a,b) towards fluorenylidenetriphenylphosphorane (FTP, 2c), the reaction proceeded in refluxing toluene yielding colourless products, assigned the structures 3b and 3c, respectively. Triphenylphosphine was also isolated in both reactions.

Compound 3b, taken as an example, is a colourless crystalline substance, gave elemental and mass spectroscopic analysis confirming $C_{20}H_{19}N_3S_2$.



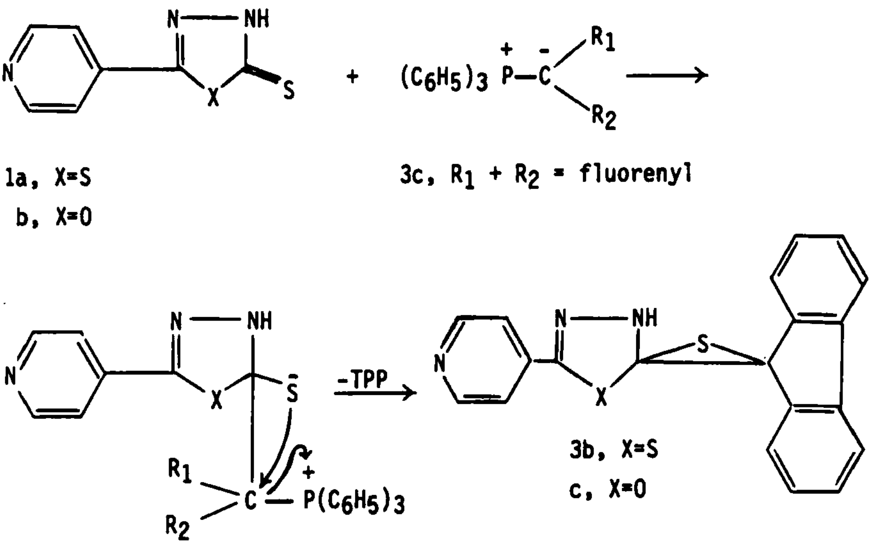
3b, X = S
c, X = O

Its IR spectrum, in kBr, lacks the absorption band at 1225 cm^{-1} recorded for the C=S is the starting thiadiazole 1a. The spectrum of 3b showed a free NH absorption band at 3200 cm^{-1}.

Moreover, the mass spectrum (MS) of adduct 3b offers another evidence for the structure affording M^+ as the base peak at 359, ($M^+—S$) 327, ($M^+—C_{13}H_8$) 164 and ($M^+—C_7H_5N_3S_2$) 163.

Formation of adducts 3b and c can be explained (Scheme B) in terms of initial attack by the carbanion centre in the Wittig reagent 2c on the thiocarbonyl carbon of the starting compounds 1a,b followed by splitting off triphenylphosphine to give the corresponding episulphides 3b,c, respectively. This is in agreement with the finding of Krapcho et al.[17] who reported episulphide formation from reaction of 2-thiono-adamantans with methylenetriphenylphosphorane.

The significance of this finding is not only the demonstration of a novel route for the production of ylid-phosphorane (cf. Scheme A) but also the new synthesis of episulphides of the type 3b and c via phosphonium ylides.



Scheme (B)

EXPERIMENTAL

All mp's were uncorrected. The toluene used was dried over Na. Carbomethoxymethylene,[18] carboethoxymethylene[21] and fluorenylidenetriphenylphosphorane[19] were prepared according to established procedures. The IR spectra were measured in kBr, on Perkin-Elmer Infracord Spectrometer Model 157 G (Grating). The ^{1}H-NMR spectra were taken in $CDCl_3$ or DMSO-d_6 at MHz on Bruker 90 Instrument and the ^{31}P NMR spectra were measured in $CDCl_3$ (vs H_3PO_4 as external standard) on Varian CFT 20, 32 MHz spectrometer. The mass spectra were run at 70 eV on kratos MS 50 equipment and/or Varian MAT 711 specrometer.

The reaction of 2-thiono-2-pyridyl-1,3,4-thiadiazole (1a) with carbomethoxymethylenetriphenylphosphorane (2a). A mixture of thiadiazole 1a (0.19 g, 0.001 mole) and ylide 2a (0.33 g, 0.001 mole) in dry toluene (30 ml) was refluxed for 10 hr. The material that precipitated after cooling was filtered off, washed with toluene (2 ml) and recrystallized from chloroform ether to give 3a as yellow crystals in 80% yield, m.p. 190°C. Anal. Calcd. for $C_{26}H_{20}N_3S_2P$ (469.44) C, 66.52; H, 4.26; N, 8.95; S, 13.64; p, 6.61. Found: C, 66.6; H, 4.3; N, 8.8; S, 13.7; P, 6.65% ^{31}P NMR (in $CDCl_3$, vs 85% H_3PO_4): + 29.53 ppm.

Similarly, the reaction of thiadiazole 1a with carboethoxymethylenetriphenylphosphorane (2b) in boiling toluene for 12 hr, afforded yellow crystals proved to be 3a in 90% yield (mixed m.p. and comparative IR, ^{1}H NMR and mass spectra). In both reactions the corresponding ester (methyl- or ethyl formate) was detected using TLC.

The reaction of 2-thiono-5-pyridyl-1,3,4-oxadiazole (1b) with ylides 1a or 1b. Compound (1b) (0.18 g, 0.001 mole) was refluxed with ylides 2a or 2b (0.001 mole) in dry toluene for 24 hrs. The reaction mixture was left to cool at room temperature, orange substance was precipitated, filtered and crystallized from ethyl alcohol to give yellow-orange crystals in 100% yield, m.p. 250° proved to be the starting material 1b (mixed m.p. and comparative IR spectra).

The reaction of 2-thiono-5-pyridyl-1,3,4-thiadiazole (1a) with FTP (2c). Compound (1a) (0.19 g, 0.001 mol) was refluxed with ylide 2c (0.42 g, 0.001 mol) in dry toluene for 16 hrs. The reaction mixture was left to cool at room temperature, pale violet substance was precipitated, filtered and crystallized using chloroform (charcoal) to give 3b as colourless crystals in 85% yield, m.p. 209°C, Anal. Calcd. for $C_{20}H_{13}N_3S_2$ (359) C, 55.71; H, 3.62; N, 11.67; S, 17.83. Found: C, 55.67; H, 3.64; N, 11.68; S, 17.9%. IR: bands at 3200 cm^{-1} (NH), 1645 cm^{-1} (C=N).

Similarly, the reaction of oxadiazole 1b with fluorenylidentriphenylphosphorane (2c) afforded (3c). The colourless crystals of 3c were obtained (80%) from chloroform (charcoal). m.p. 255°C. Anal. Calcd. for $C_{20}H_{13}N_3SO$ (343,00) C, 69.97; H, 3.79; N, 12.24; S, 9.33; 0, 4.66. Found: C, 69.85; H, 3.83; N, 12.3; S, 9.45%. IR: bands at 3220 cm^{-1} (NH), 1645 cm^{-1} (C=N). Mass spectrum (MS) for 3c, M^+ (343), (M^+—S) (311), (M^+—$C_{13}H_8$) 147. In both reactions, triphenylphosphine was isolated from the filteration (m.p. and mixed m.p.).

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