THE BEHAVIOUR OF ARYLIDENEMALONONITRILES TOWARDS CERTAIN THIATING PHOSPHORUS REAGENTS

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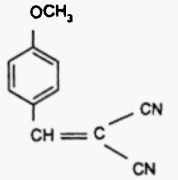
Abstract: The behaviour of arylidenemalononitriles **1, 2 and 3** towards certain thiating phosphorus reagents, namely, phosphorus pentasulfide and Lawesson's reagent **10**, has been outlined. The products obtained depend on the nature of reactants. Analytical and spectroscopic (IR, ^{1}H NMR and MS) data confirmed the structures assigned for the reaction products **4-9, 11** and **13**. The mechanism accounting for the formation of compound **11**, is discussed.

Introduction

Malonitrile derivatives have marked pesticidal (insecticidal, fungicidal, acaricidal and herbicidal) (1) as well as different biological activities(2,3). These compounds have been reported to affect the growth of transplanted tumor in mice(2), and are used generally in antitumor chemotherapy. In view of these observations and in connection with our studies on the reaction of arylidenemalononitrile derivatives with phosphite esters (4,5), we have now investigated the behaviour of 4-Methoxybenzylidenemalononitrile **1**, 3,4-dimethoxybenzylidenemalononitrile **2** and 3,4,5-trimethoxy-benzylidenemalononitrile **3** towards some sulfur and phosphorus nucleophiles.



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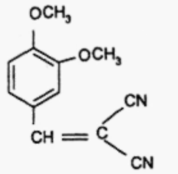

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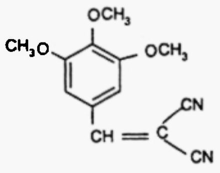

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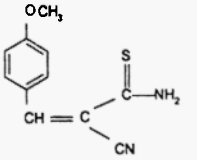
Results and Discussion

It has been found that the reaction of phosphorus pentasulfide with 4-methoxybenzylidenemalonitrile **1** proceeded in dry toluene at the reflux temperature whereby a mixture of two products was produced and could be separated by column chromatography. These were formulated as the thioacrylamide derivative 4 and the bis-thiophosphorylated product 5, respectively due to analytical and spectroscopic evidences.



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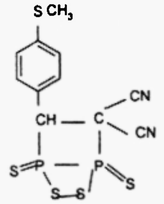

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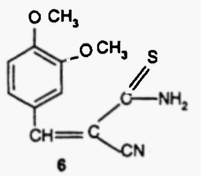
The mass spectrum and microanalyses of compound 5 correspond to $C_{11}H_8N_2P_2S_5$. Its mass spectrum revealed the presence of an ion peak at m/z = 391 [M^++1]. The ^{31}P NMR spectrum of this compound showed a singlet at $\delta = 3.4$ ppm, which is in accordance with the value of compounds bearing similar phosphorus moieties (6). The ^{1}H NMR spectrum of compound 5 showed a singlet at $\delta = 3.91$ ppm due to protons of the SCH_3 group and two doublets each with $J_{HH} = 8$ Hz at $\delta = 7.17$ and $\delta = 8.05$ ppm, for the 4 aromatic protons (AB system). The exocyclic methine proton appeared as a doublet centered at $\delta = 7.4$ ppm due to coupling with phosphorus; $^2J_{HP} = 20$ ppm).

The thioacrylamide 4 was found identical (m.p., mixed m.p. and comparative MS) with that produced from the reaction of nitrile 1 and Lawesson's Reagent (7) (*vide infra)*.

On the other hand, the thioacrylamides **6** and **7** constituted the sole reaction products when 3,4-dimethoxybenzylidenemalononitrile **2** and 3,4,5-trimethoxybenzylidenemalononitrile **3** were respectively allowed to react with phosphorus pentasulfide under the same experimental conditions.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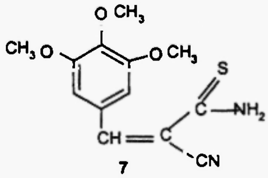
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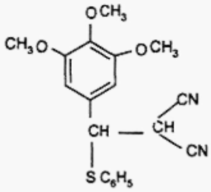
When the nitrile **3** was allowed to react with thiophenol in dry toluene at the reflux temperature, the addition product **8** was produced. However, benzylmercaptan reduced nitrile **3** to compound **9** under the same experimental conditions.

The structure of compounds **6-9** was assigned depending upon analytical and spectroscopic evidences (cf. experimental).

Next, the reaction of 2,4-bis-(4-methoxyphenyl)-1,3,2,4-dithiaphosphetane-2,4-disulfide (Lawesson's reagent) **10**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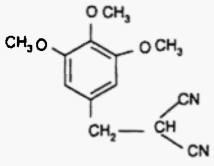
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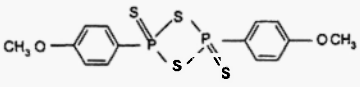
with nitrile **1** was found to proceed in dry toluene at reflux temperature whereby two products were obtained and identified as the thioacrylamide **4** and the thiophosphorylated product **11** due to the following evidences: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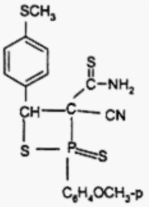
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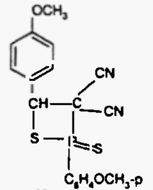
1) The mass spectrum and microanalyses of compound **11** corresponded to $C_{18}H_{18}N_2POS_4$. 2). Its mass spectrum showed an ion peak at m/z = 436 [M^{+}+1]. 3) Its ^{1}H NMR spectrum revealed the presence of signals at $\delta = 4.21$ and 4.24 ppm (OCH_3 and SCH_3, respectively), a signal at $\delta = 7.15$ ppm (methine proton), multiplet centered at $\delta = 7.63$ ppm (aromatic protons, 8H). A signal at $\delta = 8.25$ ppm, exchangeable by the addition of D_2O (NH_2 protons). The thioacrylamide **4** was found identical with the same compound obtained from the reaction of nitrile **1** and Lawesson's reagent (7). However, under the prevailing experimental condition, it was not possible to obtain the previously reported (7) addition product **12** from this reaction.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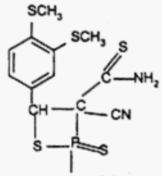
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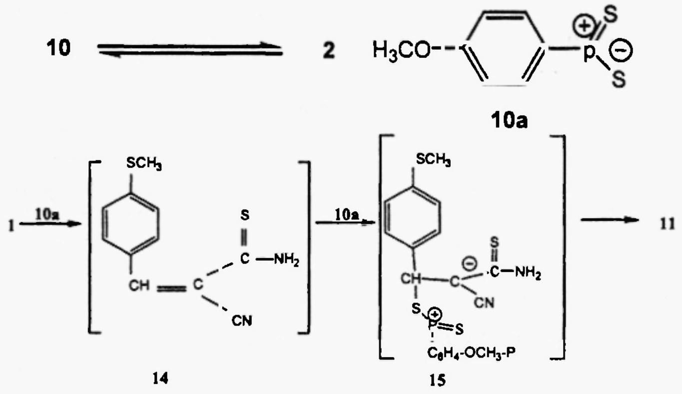
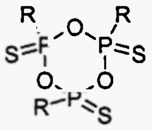
Nitrile **2** reacted with Lawesson's reagent **10** under the same experimental conditions to give exclusively the thiophosphorylated product **13** (55% yield) confirmed by analytical and spectroscopic data (cf. experimental) With another product identical in all respects with amide **6** (30% yield) (mp., mixed mp., comparative IR and MS) (*vide supra*). Moreover, the thioacrylamide **7** constituted the sole reaction product of nitrile **3** and Lawesson's reagent **10**.

Formation of compound **11**, for example, is best explained in terms of the intial thiation of nitrile **1** with the monomeric species **10a** (existing in equilibrium with lawesson's reagent **10** at elevated temperature (8) to give intermediate **14**, followed by addition of another species **10a** to form the phosphonium **15**, which afforded the final product **11**.



A colourless crystalline compound was isolated in reactions of nitriles **1**, **2** and **3** with **10**, and proved to be trimer **16** (mixed m.p., comparative IR and mass apectra) (9-11).



16, R = $C_6H_4OCH_3$-p

Experimental

Melting points were determined on a Gallenkamp apparatus and are uncorrected . The IR spectra were recorded in KBr disks, on a Jasco Fourier Transform Infrared Spectrophotometer Model FT/IR-3000E. The ^{1}H NMR were recorded on Joel JNM-EX 270 FTNMR system (NRC) and chemical shifts are recorded in δ ppm relative to TMS. The MS were performed at 70 eV on a Finnigan MAT SSQ 7000 spectrometer. The microanalyses were carried out at the microanalytical Centre, Cairo University, Egypt. The microanalyses for the new compounds were in a good agreement with (C, H ± 0.1, N ± 0.05, P ± 0.05,S ±0.05). Toluene (thiophene-free) was dried with sodium metal and distilled. All solvents were purified and dried. The arylidenemalononitriles **1**, **2**, and **3** were prepared by established procedures (12-13). LS reagent was freshly prepared (14,15). Phosphorus pentasulfide and thiols were purchased from E.Merk. The reaction mixtures were resolved into their individual constituents by column chromatography on silica gel G [particle size 0.2-0.5 mm, 37-70 mesh (ASTM)E.Merk, Darmstadt] through elution with petroleum-ether (60-80°C), methylene chloride and/or ethyl acetate in a suitable percentage.

Reaction of Nitrile Compound 1 with Phosphorus Pentasulfide.

A mixture of and the nitrile **1** (5 mmol) and phosphorus pentasulfide (5 mmol) in dry toluene (25 ml) was heated under reflux until no more of the starting material could be detected (TLC) for 10 h. The reaction mixture was evaporated on silica gel under reduced pressure. The solid product was applied to silica gel coloumn using ethyl acetate / pet. ether (60-80°C) as eluent. The first fraction gave pale yellow crystals of 2-cyano-3-(4-methoxyphenyl)-thioacrylamide **4**: 55% yield, crystallized from ethyl acetate (mp., mixed mp. and comparative IR and MS spectra) (7). The second fraction yielded orange powder of 6-(4-methylsulfanyl-phenyl)-1,4-dithioxo-2,3-dithia-$1\lambda^5,4\lambda^5$-diphosphabicyclo-[2.2.0]hexane-5,5-dicarbonitrile **5**, 28% yield, mp. 200°C . IR (cm^{-1}): 720 (P=S); 1600 (C=C, aromatic); m/z 391[M$^+$+1].

Reaction of Nitrile 2 with Phosphorus pentasulfide.

A solution of nitrile **2** (5 mmol) and Phosphorus pentasulfide (5 mmol) in dry toluene (25 ml) was heated under reflux for 10 h. The solution was evaporated to dryness in presence of silica gel and subjected to column chromatography on silica gel, using ethyl acetate/petroleum ether (20/80 v/v) yielded yellow crystals of 2-cyano-3-(3,4-dimethoxy-phenyl)-thioacrylamide **6**, 80% yield, crystallized from ethyl aoetate, mp. 190-92°C (ethyl acetate). IR (cm^{-1}) : 3350, 3290 (NH_2); 2210 (CN); 1635 (C=C, ethylenic); 1560 (C=C, aromatic), 1240 (C=S). ^1H NMR: δ 3.95, 4.05 ppm (2s, 6H, 2(OCH_3); δ 7.45 ppm (s, 1Haromatic proton; 6.95, 7.60 ppm (2d, 2H aromatic protons); the D_2O-exchangeable proton (NH_2) appeared at δ 8.72 ppm. M/z 248 [M^+].

Similarly, 2-cyano-3-(3,4,5-trimethoxy-phenyl)thioacrylamide **7** was obtained as reddish brown crystals from the reaction of nitrile **3** with phosphorus pentasulfide under the same experimental conditions described above, 85% yield, crystallized from ethanol, mp. 178-80°C. IR (cm^{-1}): 3400, 3310 (NH_2); 2220 (CN); 1630 (C=C, ethelynic); 1570 (C=C, aromatic); 1250 (C=S). ^1H NMR: δ3.78 ppm (s, 3H, OCH_3); δ 3.85 (s,6H, 2OCH_3); δ 7.35 (s, 2H, aromatic protons); δ 8.05 (s, 1H, exocyclic proton); δ 10.12 (2H, NH_2 protons, exchangeable with D_2O). m/z 278 [M^+].

Reaction of Arylidenemalononitriles 1 with Lawesson's Reagent 10.

A mixture of the nitrile **1** (5 mmol) and **10** (5 mmol) in dry toluene (25 ml) was heated under reflux until no more of the starting materials could be detected (TLC) for (10- 12 h). The reaction mixture was evaporated on silica gel under reduced pressure. The solid product was applied to silica gel column using ethyl acetate / pet. ether (60-80°C) as eluent. The first fraction gave the thioacrylamide **4**, 30% yield (mp., mixed m.p. and comparative IR and MS) (7). The second fraction afforded yellow crystals of 3-cyano-2-(4-methoxy-phenyl)-4-(4-methylsulfanyl-phenyl)-2-thioxo-2λ^5-[1,2]thiaphosphetane-3-carbothioic acid amide **11**: 51% yield,, m.p. 178-80°C. IR (cm^{-1}): 3400, 3325 (NH_2), 2200 (CN), 1600 (C=C) aromatic. m/z 436[M^+].

Reaction of Arylidenemalononitriles 2 with Lawesson's Reagent 10.

Nitrile **2** (5 mmol) in dry toluene (25 ml) was heated under reflux after the addition of **10** (5 mmol) for 12 h. After evaporating the reaction mixture on silica gel in vacuum. The solid product was subjected to column chromatography on silica gel, using ethyl acetate /pet.ether (20/80 v/v). The first fraction yielded 30%of the thioacrylamide 6 (mp., mixed mp., comparative IR and Mass spectra). The second fraction gave 30% yield, yellow crystals of 4-(3,4-bis-methylsulfanyl-phenyl)-3-cyano-2-(4-methoxy-phenyl)-2-thioxo-2λ^5-[1,2]thiaphosphetane-3-carbothioic acid amide **13**: 55% yield of yellow crystals, m.p. 256-58°C crystallized from ethanol. IR (cm^{-1}): 3350, 3280 (NH_2); 1650 (C=C) aromatic; 1240 (C=S). m/z 482 [M^+].

Similarly, nitrile **3** reacted with **10** under the same experimental condition to give the thioacrylamide 7 in 75% yield, (mp., mixed mp. and comparative IR and MS spectra).

Reaction of Nitrile 3 with thiophenol.

To nitrile **3** (5 mmol) in dry toluene (25 ml) was added thiophenol (5 mmol). The mixture was refluxed for 8 h until no more of the starting materials could be detected (TLC). The toluene was evaporated *in vacuo* and the residue washed several times with ether to give compound **6**, 90% yield, yellow crystals, m.p. 82-85°C (ethanol/ether). IR (cm^{-1}): 2220 (CN), 1630 (C=C) aromatic. ^1H NMR: 3.85(s, 6H, 2OCH_3); 3.94 (s, 3H, OCH_3), 6.5 (s, 1H, exocyclic proton); 7.4 (m, 2H, aromatic proton). m/z 365 [M^+]

Reaction of Nitrile 3 with Benzvlmercaptan.

To nitrile **3** (5 mmol) in dry toluene (25 ml) was added benzylmercaptan (5 mmol). The mixture was refluxed for 10 h until no more of the starting materials could be detected (TLC). The toluene was evaporated *in vacuo* and the residue washed several times with ether to give 2-(3,4,5-trimethoxybenzyl)malononitrile 9 as a pale yellow crystals, crystallized from ethanol m.p. 198-200 °C (ethanol). IR (cm^{-1}): 2225 (CN), 1640 (C=C) aromatic. ^1H NMR: 2.5(d, 2H, CH_2); 3.76 (s, 6H, 2OCH_3); 3.85 (s, 3H, OCH_3); 7.35 (m, 2H, aromatic protons); 6.8 (t, 1H , $CH(CN)_2$). m/z 246 [M^+]

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