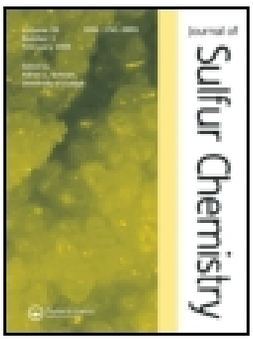

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Facile synthesis of novel 6-methyl-5-phenyl-2-sulfido-1,2,3,5-tetrahydro-4*H*[1,2] oxazolo[4′,5′:5,6]pyrano[2,3-*d*][1,3,2] diazaphosphinines

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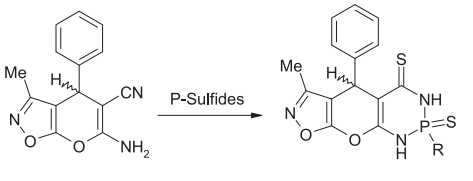
ABSTRACT

A number of 6-methyl-5-phenyl-2-sulfido-1,2,3,5-tetrahydro-4*H*[1,2] oxazolo[4′,5′: 5,6]pyrano[2,3-*d*][1,3,2]diazaphosphinines **4–11** were synthesized *via* an interaction of tetraphosphorus decasulfide and Lawesson's reagent under different conditions with 6-amino-3-methyl-4-phenyl-4*H*-pyrano[3,2-*d*][1,2]oxazole-5-carbonitrile (**3**). The reaction mechanisms for these products were discussed. Structures of the newly synthesized products were established on the basis of elemental analysis and spectral data.



R=SH, S Pyridinum, OEt, 4-MeOC$_6$H$_4$

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1,3,2-Diazaphosphinine; pyrano[3,2-*d*][1,2]oxazole; tetraphosphorus decasulfide; Lawesson's reagent

1. Introduction

The synthesis of phosphorus heterocycles, predominantly, phosphorus linked to an oxygen and nitrogen atoms gained considerable attention due to their broad spectrum of potent biological activities and pharmacological interest. Some of these heterocycles displayed anticancer [1], antimicrobial [2], insecticidal [3], herbicidal [4], and antibodies' properties [5]. Further, phosphorus heterocycles possessing multi-rings are found to be as stabilizers in polymers, as lubricant oil additives, and in organic synthesis as biocatalysts [6]. However, six-membered phosphorus heterocyclic rings have gained much attention since they are involved as intermediates in a number of synthetic, biological processes, and

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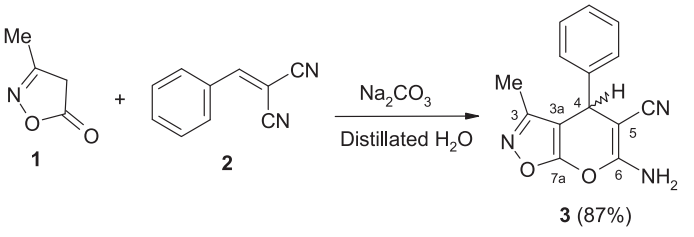
pharmaceutical fields [7]. Recently, researchers are showing interest towards the synthesis of 1,3,2-diazaphosphinine heterocycles due to their valuable biological importance and various applications in synthetic chemistry [8–10]. On the other hand, oxygen-containing heterocycles such as oxazole and pyran form very numerous and accessible groups of compounds with a broad spectrum of useful properties, which include anti-inflammatory, antibacterial, and anticancer [11–15]. Considering the above facts and our continuing research on the development of new biologically active heterocyclic organophosphorus compounds [16–18], we herein report an efficient method for the synthesis of novel 6-amino-3-methyl-4-phenyl-4*H*-pyrano[3,2-*d*][1,2]oxazole-5-carbonitrile (**3**) and chemical transformations into 1,3,2-diazaphosphinines possessing a pyrano[3,2-*d*][1,2] oxazole system *via* its reaction with some phosphorus sulfide reagents.

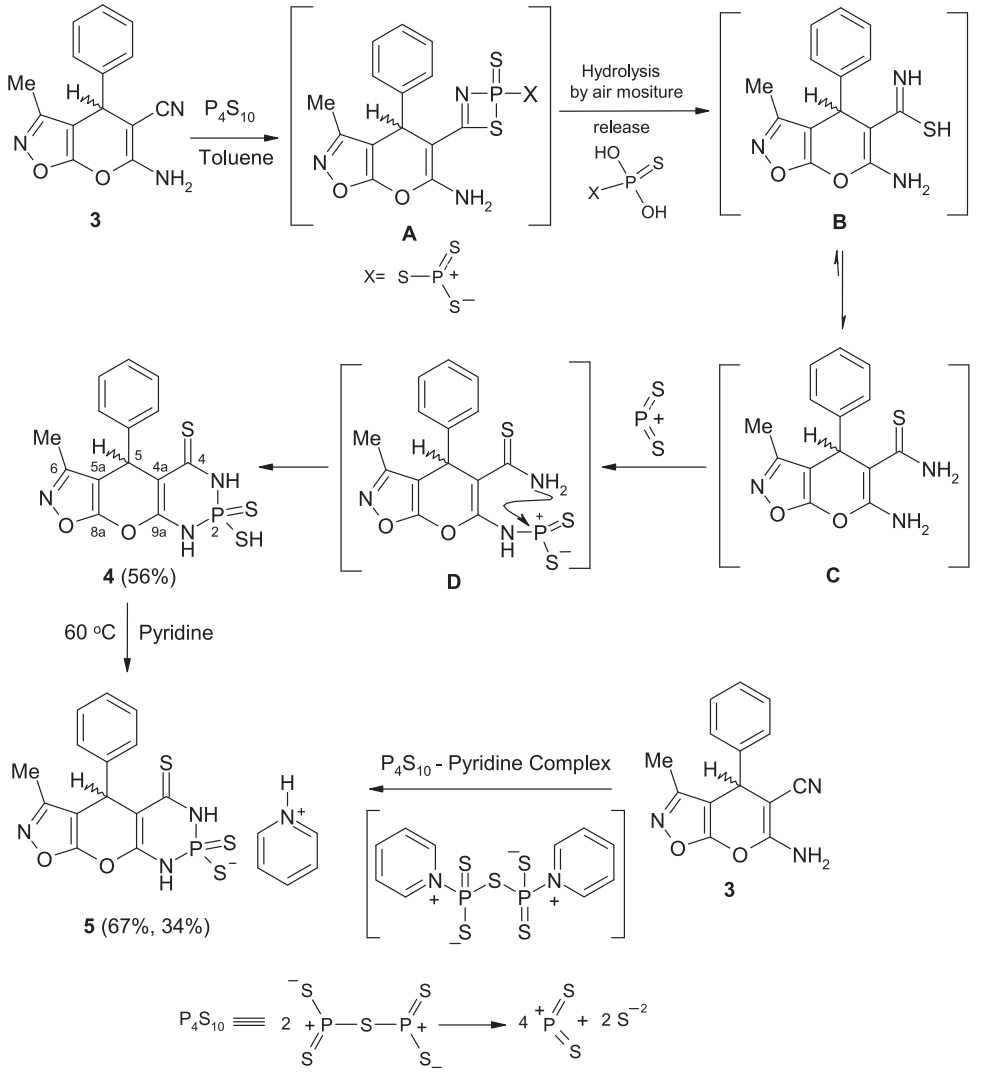
2. Results and discussion

The novel starting material 6-amino-3-methyl-4-phenyl-4*H*-pyrano[3,2-*d*][1,2] oxazole-5-carbonitrile (**3**) was synthesized in 87% yield by the reaction of 3-methyl-1,2-oxazol-5(4*H*)-one (**1**) with benzylidene-propanedinitrile (**2**) in distilled water containing a few amount of sodium carbonate as a catalyst (Scheme 1). The IR spectrum of compound **3** showed the NH_2 and C≡N functions at 3463, 3323, and 2197 cm^{-1}. Its ^{1}H-NMR spectrum revealed the characteristic H–4 and NH_2 protons as singlets at δ 4.96 and 6.69 ppm, respectively. Moreover, its ^{13}C-NMR spectrum displayed the carbon atoms of CH_3, C–4, and C≡N at δ 14.7, 26.6, and 109.2 ppm, respectively. Furthermore, the molecular ion peak of compound **3** was recorded at *m/z* 253, which confirmed the proposed structure.

The versatility of α-aminocarbonitrile substrate **3** is in great part due to its promptness to both electrophilic and nucleophilic attack. For this reason, we used it in the synthesis of 1,3,2-diazaphosphinine heterocycles *via* its reacting with tetraphosphorus decasulfide and Lawesson's reagent (LR) under different conditions especially they are known as powerful, mild, and versatile reagents for building phosphorus and sulfur heterocycles [19]. Thus, when compound **3** was treated with molar equivalents of tetraphosphorus decasulfide in dry toluene, the 6-methyl-5-phenyl-2-sulfanyl-2-sulfido-1,2,3,5-tetrahydro-4*H*-[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-*d*][1,3,2]diazaphosphinine-4-thione (**4**) was obtained in 56% yield (Scheme 2). The structure **4** was confirmed by elemental analysis, IR, ^{1}H-, ^{13}C-, ^{31}P-NMR, and mass spectra. Its IR spectrum revealed the absence of a strong band at 2197 cm^{-1}, and appearance of new C=S group at 1129 cm^{-1}. The ^{1}H-NMR spectrum of **4** gave signals at δ 3.70 ppm for the sulfanyl proton and two D_2O-exchangeable NH protons at δ 10.04 and 11.79 ppm. Its ^{13}C-NMR spectrum added a good support for the proposed



Scheme 1. Synthesis of 6-amino-3-methyl-4-phenyl-4*H*-pyrano[3,2-*d*][1,2]oxazole-5-carbonitrile (**3**).



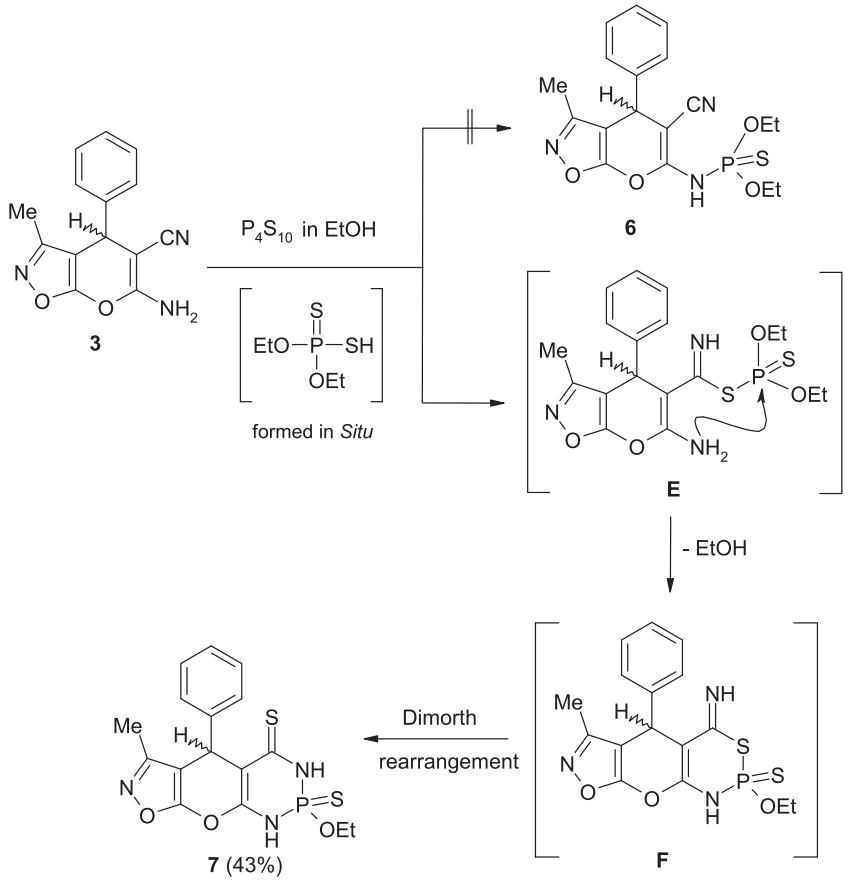
Scheme 2. Reaction of compound **3** with P_4S_{10} in dry toluene and pyridine.

structure and revealed the carbon atom of C = S at δ 186.3 ppm. The ^{31}P-NMR spectrum of compound **4** recorded a singlet at δ 35.1 ppm. Moreover, its mass spectrum recorded its expected molecular ion peak at *m/z* 381 (M^+, 22%). A possible explanation for the course of the formation of compound **4** is shown in Scheme 2. The reaction presumably proceeded in two steps. Firstly, the addition of P_4S_{10} on the nitrile group and conversion it into the thioamide group in the nonisolable intermediate **C** [20,21]. Secondly, heterocyclization of the neighboring amino groups through the reaction with PS_2 cation to give the novel oxazolopyranodiazaphosphinine system **4** (Scheme 2). Furthermore, when compound **3** was allowed to react with the P_4S_{10}–Pyridine complex in dry pyridine at 80°C, the pyridinium sulfide salt **5** was separated with 67% yield (Scheme 2) [22]. The isolated product **5** was also obtained *via* warming of compound **4** in a little amount of pyridine at 60°C (Scheme 2).

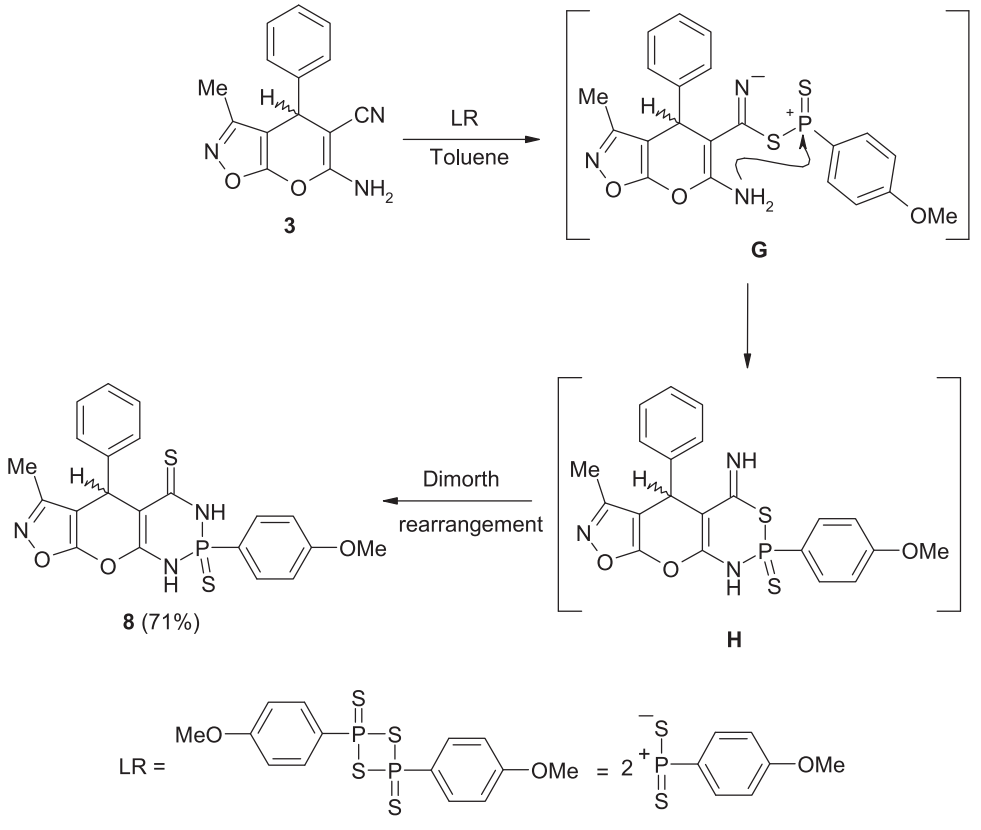
Elemental and mass spectral analysis of **5** led to an empirical formula $C_{19}H_{17}N_4O_2PS_3$. The ^{1}H- and ^{13}C-NMR spectra displayed the presence of the pyridine ring.

Next, the reaction of compound **3** with *O*,*O*-diethyldithiophosphoric acid (formed in *situ* from reaction tetraphosphorus decasulfide with absolute ethanol) furnished the corresponding product **7** and not the expected **6** (Scheme 3). The structure of compound **7** was confirmed with mass spectrum which revealed the molecular ion peak at *m/z* 393 (M^+, 100%) and the ^{1}H- and ^{13}C-NMR spectra data displayed the presence of the characteristic ethoxy group. Mechanistically, the formation of the diazaphosphinine ring can be explained on the basis of an initial nucleophilic addition of thiol group at the nitrile group giving the nonisolable intermediate **E**, followed by an attack of the amino functional group at phosphorus atom. This intramolecular cyclization gave the nonisolable intermediate **F**, which in turn rearranged to the desired fused triheterocyclic system *via* a *Dimroth* rearrangement (Scheme 3).

Treatment of compound **3** with LR in dry toluene under reflux led to the formation 2-(4-methoxyphenyl)-6-methyl-5-phenyl-2-sulfido-1,2,3,5-tetrahydro-4*H*[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-*d*][1,3,2]diazaphosphinine-4-thione (**8**) (Scheme 4). To explain the formation of compound **8**, a plausible reaction mechanism is proposed in Scheme 4. Initially, due



Scheme 3. Reaction of compound **3** with P_4S_{10} in absolute ethanol.

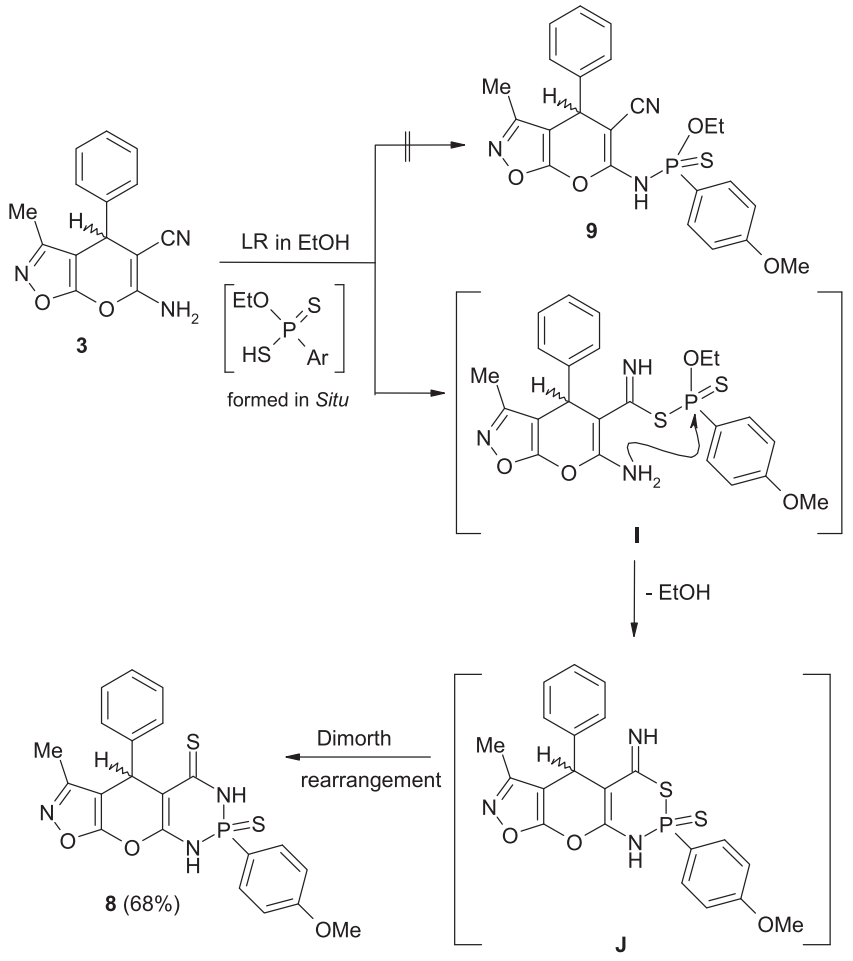


Scheme 4. Reaction of compound **3** with Lawesson's reagent in dry toluene.

to the stronger nucleophilicity of the sulfur anion in LR fragment, the nucleophilic addition of sulfur anion to the nitrile group resulted in the formation of intermediate **G**, which underwent the intramolecular cyclization of the amino group with phosphorus atom, followed by *Dimorth* rearrangement affording the final product (Scheme 4). The IR spectrum of compound **8** revealed the absence of the NH_2 and $C\equiv N$ groups of starting material **3** and the presence of the NH at 3424 cm^{-1} as a broad band. The ^{1}H-NMR spectrum showed the presence of two NH protons at δ 9.21 and 11.26 ppm, and the OCH_3 protons as a singlet at δ 3.85 ppm. Also, its ^{13}C-NMR spectrum supported the presence of the methoxy group at δ 55.6 ppm. Furthermore, its ^{31}P-NMR spectrum revealed a singlet at δ 52.3 ppm.

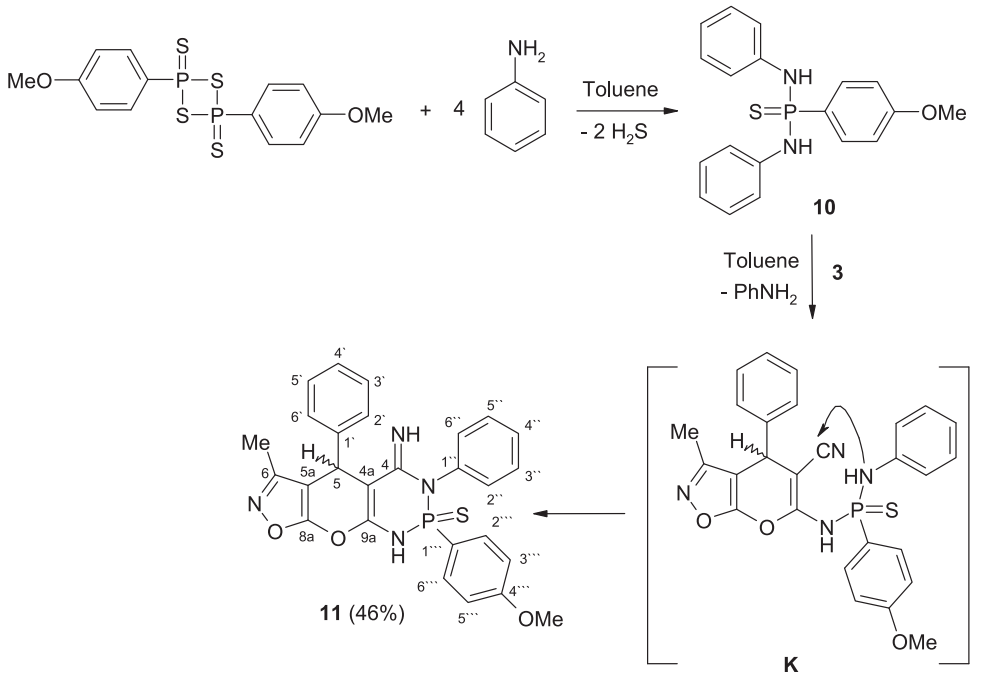
When the previous reaction was carried out in absolute ethanol instead of toluene, we found that the isolated product was compound **8**. The proposed mechanism for the formation of compound **8** by this method suggested that LR reagent may react with absolute ethanol to give the nonisolable 4-$MeOC_6H_4P(S)(SH)(OEt)$ which reacted with starting material **3** according to the mechanism shown in Scheme 5.

The final point in this work was the treatment of compound **3** with *P*-(4-methoxyphenyl)-*N*,*N*′-diphenylphosphonothioic diamide (**10**) which was prepared from the reaction of LR with fourth folds of distilled aniline according to the reported method [23]. The reaction of the latter compound **10** with α-aminocarbonitrile **3** in dry toluene required 16 h to give the isolated product **11** (46% yield) in a pure form. The formation of



Scheme 5. Reaction of compound **3** with Lawesson's reagent in absolute ethanol.

the latter compound can be interpreted in terms of nucleophilic attack by the amino group on the phosphorus atom of reagent **10** to give with concomitant elimination of an aniline moiety formed the nonisolable intermediate **K**, followed by ring closure through the addition of NH on the nitrile group. The participation of both amino and nitrile groups was evident if we consider the disappearance of the corresponding signals from ^{1}H- and ^{13}C-NMR spectra, respectively. Further, the ^{1}H-NMR spectrum of product **11** exhibited characteristic signals at δ 9.61 and 11.07 ppm attributable to NH protons, multiplets at δ 6.81–7.67 ppm easily attributable to the aromatic protons introduced by the aniline used and LR and a singlet at δ 3.88 ppm relative to the methoxy group. Unambiguous proof for the obtained product **11** was aroused from its ^{13}C-NMR data. Particularly, a new methoxy group introduced by the LR at δ 54.3 ppm and a singlet at δ 157.2 ppm attributable to the C = NH. The ^{31}P-NMR spectra of this compound reinforce the above by showing the phosphorus atom signal at δ 48.3 ppm. The mass spectrum was in agreement with the molecular formula (Scheme 6).



Scheme 6. Reaction of compound **3** with phosphonothioic diamide **10** in dry toluene.

3. Conclusion

Facile routes were achieved to synthesize novel 6-methyl-5-phenyl-2-sulfido-1,2,3,5-tetrahydro-4*H*[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-*d*][1,3,2]diazaphosphinines in one step starting from 6-amino-3-methyl-4-phenyl-4*H*-pyrano[3,2-*d*][1,2]oxazole-5-carbonitrile (**3**) with some phosphorus sulfides in different solvents. We hope that this approach may be valuable to others seeking novel synthetic fragments with unique properties for medicinal chemistry.

4. Experimental

4.1. General remarks

The melting point was determined in an open capillary tube on a digital Stuart SMP-3 apparatus. Infrared spectra were measured on an FT-IR (Nicolet IS10) spectrophotometer using KBr disks and a Perkin-Elmer 293 spectrophotometer using KBr disks. The ^{1}H- and ^{13}C-NMR spectra were measured on a Gemini-300BB spectrometer (400 and 100 MHz), using DMSO-d_6 as a solvent and TMS (δ) as an internal standard. ^{31}P-NMR spectra were measured on a Bruker (162 MHz) spectrophotometer using DMSO-d_6 as a solvent, TMS as an internal standard, and 85% H_3PO_4 as an external reference. Mass spectra were recorded on a Gas Chromatographic GCMSqp 1000 ex Shimadzu instrument at 70 eV. Elemental microanalysis was performed on Perkin-Elmer 2400II at the Chemical War department, Ministry of Defense. The purity of the synthesized compounds was checked by thin layer chromatography (TLC) and elemental microanalysis.

4.2. Synthesis of 6-amino-3-methyl-4-phenyl-4H-pyrano[3,2-d][1,2]oxazole-5-carbonitrile (3)

A mixture of 3-methyl-1,2-oxazol-5(4*H*)-one (**1**) (0.5 g, 5 mmol) and benzylidenepropanedinitrile (**2**) (0.77 g, 5 mmol) in distilled water (25 ml) containing 0.1 g of sodium carbonate was stirred at 60°C for 3 h. The formed solid was filtered off, washed with water several times and crystallized from ethanol to give yellow crystals in 87% yield; mp 194–196°C. IR (KBr), (ν_{max}, cm^{-1}): 3463, 3323 (NH_2), 2930 ($C–H_{aliph}$), 2197 (C≡N), 1663 (NH_{def}), 1593 (C=N), 1522 (C=C). ^{1}H-NMR (400 MHz, DMSO-d_6): 2.35 (s, 3H, CH_3), 4.96 (s, 1H, H–4), 6.69 (s, 2H, NH_2), 7.61–7.76 (m, 5H, Ph–H). ^{13}C-NMR (100 MHz, DMSO-d_6): 14.7 (CH_3), 26.6 (C–4), 72.9 (C–5), 109.2 (C≡N), 118.1 (C–3a), 125.5 (C–3′,5′), 128.9 (C–4′), 131.1 (C–2′,6′), 134.6 (C–1′), 143.9 (C–3), 152.1 (C–7a), 162.2 (C–6). MS (*m/z*, I %): 253 (M^+, 8%). Anal. Calcd for $C_{14}H_{11}N_3O_2$ (253.26): C, 66.40%; H, 4.38%; N, 16.59%. Found: C, 66.09%; H, 4.12%; N, 16.23%.

4.3. Synthesis of 6-methyl-5-phenyl-2-sulfanyl-2-sulfido-1,2,3,5-tetrahydro-4H-[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-d][1,3,2]diazaphosphinine-4-thione (4)

A mixture of tetraphosphorus decasulfide (1.11 g, 2.5 mmol) and compound **3** (0.63 g, 2.5 mmol) in dry toluene (40 ml) was heated under reflux for 5 h. The formed solid on heating was filtered off and recrystallized from diluted ethanol to give orange crystalline solid in 56% yield; mp 160−162°C. IR (KBr), (ν_{max}, cm^{-1}): 3400, 3300 (br, 2 NH), 3050 ($C–H_{arom}$), 2925 ($C–H_{aliph}$), 2605 (br, SH), 1599 (C=N), 1573 (C=C), 1129 (C=S), 1049 (O–C), 691 (P=S). ^{1}H-NMR (400 MHz, DMSO-d_6): 2.37 (s, 3H, CH_3), 3.70 (br, 1H, SH), 4.89 (s, 1H, H–5), 7.28–7.32 (m, 2H, Ph–H), 7.40–7.48 (m, 3H, Ph–H), 10.04 (brs, 1H, NH), 11.79 (brs, 1H, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): 15.2 (CH_3), 25.9 (C–5), 79.5 (C–4a), 119.6 (C–5a), 124.3 (C–3′,5′), 127.4 (C–4′), 130.7 (C–2′,6′), 134.8 (C–1′), 142.2 (C–6), 153.0 (C–8a), 161.4 (C–9a), 186.3 (C–4). ^{31}P-NMR (162 MHz, DMSO-d_6): 35.1 ppm. MS (*m/z*, I %): 381 (M^+, 22%). Anal. Calcd for $C_{14}H_{12}N_3O_2PS_3$ (381.44): C, 44.08%; H, 3.17%; N, 11.02%; S, 25.22%. Found: C, 43.82%; H, 2.84%; N, 10.74%; S, 24.88%.

4.4. Synthesis of pyridinium 6-methyl-5-phenyl-2-sulfido-4-thioxo-1,2,3,5-tetrahydro-4H-[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-d][1,3,2]diazaphosphinine-2-sulfide (5)

Method A: A solution of compound **4** (0.15 g) in dry pyridine (5 ml) was warmed at 60°C for 15 min. After cooling, the mixture was poured into cold water and neutralized with diluted 5% hydrochloric acid. The formed solid was filtered off, washed with water and crystallized from diluted dioxane to give yellow solid in 67% yield; mp 156−157°C.

Method B: A solution of tetraphosphorus decasulfide (1.11 g, 2.5 mmol) in pyridine (20 ml) was heated under reflux for 2 h to form the pyridine complex. A solution of compound **3** (0.63 g, 2.5 mmol) in dry pyridine (10 ml) was added to the above solution and further under reflux for 6 h. After cooling, the mixture was poured into cold water and neutralized with diluted 5% hydrochloric acid. The formed solid was filtered off, washed with water, and crystallized from diluted dioxane to give yellow solid in 34% yield; mp 155−156°C. IR (KBr), (ν_{max}, cm^{-1}): 3421 (br, 2 NH), 3030 ($C–H_{arom}$), 2934 ($C–H_{aliph}$), 1594 (C=N), 1540 (C=C), 1126 (C=S), 1025 (O–C), 692 (P=S). ^{1}H-NMR (400 MHz,

DMSO-d_6): 2.43 (s, 3H, CH_3), 5.03 (s, 1H, H–5), 7.33–7.49 (m, 5H, Ar–H), 7.57–7.62 (m, 2H, Ar–H), 7.69–7.72 (m, 2H, Ar–H), 7.95 (d, 1H, Ar–H), 8.56 (s, 1H, NH), 9.79 (brs, 1H, NH), 11.06 (brs, 1H, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): 15.4 (CH_3), 27.3 (C–5), 78.5 (C–4a), 118.9 (C–5a), 123.6 (C–β,$\beta'_{pyridine}$), 125.4 (C–3′,5′), 128.3 (C–4′), 132.4 (C–2′,6′), 133.5 (C–$\gamma_{pyridine}$), 135.2 (C–1′), 140.3 (C–$\alpha_{pyridine}$), 144.8 (C–6), 151.3 (C–8a), 161.1 (C–9a), 182.5 (C–4). MS (*m/z*, I %): 460 (M^+, 6%). Anal. Calcd for $C_{19}H_{17}N_4O_2PS_3$ (460.43): C, 49.56%; H, 3.69%; N, 12.17%; S, 20.86%. Found: C, 49.22%; H, 3.31%; N, 11.89%; S, 20.51%.

4.5. Synthesis of 2-ethoxy-6-methyl-5-phenyl-2-sulfido-1,2,3,5-tetrahydro-4H-[1,2] oxazolo[4′,5′:5,6]pyrano[2,3-d][1,3,2]diazaphosphinine-4-thione (7)

A solution of tetraphosphorus decasulfide (1.11 g, 2.5 mmol) in absolute ethanol (30 ml) was heated under reflux for 1 h to give *O*,*O*-diethyldithiophosphoric acid *in situ*. Compound **3** (0.63 g, 2.5 mmol) was added to the previous ethanolic solution. The mixture was heated under reflux for 14 h. The reaction mixture was concentrated into its half volume and left to cool. The formed solid was filtered off and recrystallized from diluted ethanol to give orange solid in 43% yield; mp 173−175°C. IR (KBr), (ν_{max}, cm^{-1}): 3421 (br, 2 NH), 3050 (C–H_{arom}), 2934 (C–H_{aliph}), 1593 (C=N), 1552 (C=C), 1131 (C=S), 1025, 1006 (O–C), 758 (P=S). ^{1}H-NMR (400 MHz, DMSO-d_6): 1.14 (t, 3H, J = 7.2 Hz, CH_3), 2.32 (s, 3H, CH_3), 3.40 (q, 2H, J = 7.2 Hz, OCH_2), 4.98 (s, 1H, H–5), 7.20–7.30 (m, 2H, Ph–H), 7.47 (d, 1H, J = 8.4 Hz, Ph–H), 7.64–7.73 (m, 2H, Ph–H), 9.07 (s, 1H, NH), 11.71 (brs, 1H, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): 15.2 (CH_3), 17.7 (CH_3), 28.3 (C–5), 56.8 (OCH_2), 80.2 (C–4a), 116.9 (C–5a), 123.5 (C–3′,5′), 128.7 (C–4′), 132.2 (C–2′,6′), 135.1 (C–1′), 144.4 (C–6), 152.1 (C–8a), 161.7 (C–9a), 183.6 (C–4). MS (*m/z*, I %): 393 (M^+, 100%). Anal. Calcd for $C_{16}H_{16}N_3O_3PS_2$ (393.43): C, 48.85%; H, 4.10%; N, 10.68%; S, 16.30%. Found: C, 48.53%; H, 3.85%; N, 10.27%; S, 16.01%.

4.6. Synthesis of 2-(4-methoxyphenyl)-6-methyl-5-phenyl-2-sulfido-1,2,3,5-tetrahydro-4H-[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-d][1,3,2]diazaphosphinine-4-thione (8)

Method A: LR (1.0 g, 2.5 mmol) was added to a solution of compound **3** (0.63 g, 2.5 mmol) in dry toluene (30 ml). The mixture was heated under reflux for 7 h. The solution was concentrated to its half volume and left to cool. The oily product was treated with petroleum ether to give the precipitate which was filtered off and recrystallized from diluted ethanol to give orange solid in 71% yield; mp 103−104.

Method B: A solution of LR (1.0 g, 2.5 mmol) in absolute ethanol (30 ml) was heated under reflux for 2 h. Compound **3** (0.63 g, 2.5 mmol) was added to the previous ethanolic solution. The mixture was heated under reflux for 11 h. The reaction mixture was concentrated into its half volume and left to cool. The formed solid was filtered off and recrystallized from diluted ethanol to give orange solid in 68% yield; mp 105−106°C. IR (KBr), (ν_{max}, cm^{-1}): 3424 (br, 2 NH), 3020 (C–H_{arom}), 2934, 2838 (C–H_{aliph}), 1601 (C=N), 1573 (C=C), 1127 (C=S), 1027 (O–C), 692 (P=S). ^{1}H-NMR (400 MHz, DMSO-d_6): 2.42 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 4.97 (s, 1H, H–5), 6.86 (t, 2H, J = 7.2 Hz, H-3″,5″), 7.60–7.63 (m, 2H, Ph–H), 7.69–7.74 (m, 3H, Ph–H), 7.90 (d, 2H, J = 7.2 Hz, H-2″,6″), 9.21 (s, 1H, NH), 11.26 (s, 1H, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): 14.3 (CH_3), 28.1 (C–5), 55.6 (OCH_3),

79.9 (C–4a), 113.8 (C-3″,5″), 116.4 (C–5a), 123.0 (C–3′,5′), 127.7 (C–4′), 130.4 (C–2′,6′), 130.9 (d, J = 160 Hz, C–1″), 132.4 (C–2″,6″), 133.6 (C–1′), 141.4 (C–6), 150.5 (C–4″), 151.3 (C–8a), 164.4 (C–9a), 183.1 (C–4). ^{31}P-NMR (162 MHz, DMSO-d_6): 52.3 ppm. MS (m/z, I %): 455 (M^+, 5%). Anal. Calcd for $C_{21}H_{18}N_3O_3PS_2$ (455.50): C, 55.38%; H, 3.98%; N, 9.23%; S, 14.08%. Found: C, 55.02%; H, 3.71%; N, 8.98%; S, 13.87%.

4.7. Synthesis of 3,5-diphenyl-4-imino-2-(4-methoxyphenyl)-6-methyl-2-sulfido-1,2,3,5-tetrahydro-4H-[1,2]oxazolo[4′,5′:5,6]pyrano[2,3-d][1,3,2]diazaphosphinine (11)

A mixture of LR (0.5 g, 1.25 mmol) and distillated aniline (0.5 ml, 5 mmol) in dry toluene was heated under reflux for 4 h. Compound **3** (0.63 g, 2.5 mmol) was added to the previous mixture. The mixture was further heated under reflux for 16 h. The reaction mixture was concentrated into its half volume and left to cool. The formed solid was filtered off, washed with petroleum ether, and recrystallized from diluted ethanol to give pale brown solid in 46% yield; mp 140−142°C. IR (KBr), (ν_{max}, cm^{-1}): 3420 (br, 2 NH), 3035 (C–H_{arom}), 2956, 2839 (C–H_{aliph}), 1602 (C=N), 1573 (C=C), 1028 (O–C), 655 (P=S). ^{1}H-NMR (400 MHz, DMSO-d_6): 2.39 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 4.98 (s, 1H, H–5), 6.81 (d, 2H, J = 7.2 Hz, H–3‴,5‴), 6.93–6.97 (m, 5H, Ph–H), 7.17 (t, 1H, J = 6.4 Hz, Ph–H), 7.32–7.40 (m, 3H, Ph–H), 7.48–7.57 (m, 1H, Ph–H), 7.67 (d, 2H, J = 8.0 Hz, H–2‴,6‴), 9.61 (brs, 1H, NH), 11.07 (brs, 1H, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): 15.4 (CH_3), 27.9 (C–5), 54.3 (OCH_3), 79.7 (C–4a), 112.8 (C–3‴,5‴), 115.0 (C–5a), 122.9 (C–3″,5″), 124.2 (C–3′,5′), 125.0 (C–4″), 127.1 (C–4′), 130.6 (d, J = 140 Hz, C–1‴), 132.0 (C–3″,5″), 133.3 (C–2‴,6‴), 134.4 (C–2′,6′), 135.2 (C–1′), 139.9 (C–1″), 142.9 (C–6), 149.3 (C–4‴), 151.2 (C–8a), 157.2 (C–4), 160.9 (C–9a). ^{31}P-NMR (162 MHz, DMSO-d_6): 48.3 ppm. MS (m/z, I %): 514 (M^+, 11%). Anal. Calcd for $C_{27}H_{23}N_4O_3PS$ (514.55): C, 63.03%; H, 4.51%; N, 10.89%; S, 6.23%. Found: C, 62.78%; H, 4.24%; N, 10.51%; S, 5.96%.

Disclosure statement

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