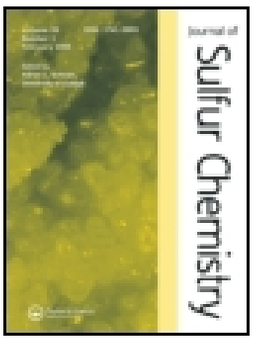

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Efficient synthesis of novel 2,3-dihydro-1,3,5,4-thiadiazaphosphole derivatives

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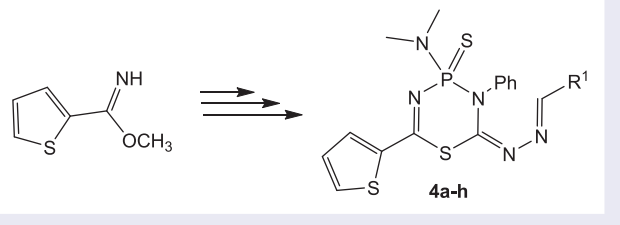
ABSTRACT

The condensation of various thiosemicarbazones with methyl thiophene-2-carboximidate afforded the corresponding intermediates **2a–2h**. Subsequent cyclization of the latter compounds with hexamethylphosphorous triamide constitutes a new route to the synthesis of novel highly functionalized thiadiazaphosphole derivatives **4a–4h**. This method offers significant advantages such as efficiency, high yields and mild reaction conditions.



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Thiosemicarbazones; hexamethylphosphorous triamide; iminoester; thiadiazaphospholes

1. Introduction

Although heterocyclic compounds of phosphorus have received considerable attention over the past three decades, there remain a number of interesting problems to be solved. Thus, the nitrogen- and sulfur-containing heterophospholes, especially including an [N—P—N] unit, have been less studied. It was found that some of the target compounds are useful not only as antibacterials [1] and cytoxic agents [1] but also in preparing two- and three-coordinate phosphorus cations.[2] Some examples of these derivatives possessing potent activity are shown in Figure 1.

Motivated by the aforementioned biological importance of these heterocyclic compounds which include [N—P—N] units and as continuation with our previous work on the synthesis of novel heterocyclic systems,[3–6] we report herein the synthesis of some new thiadiazaphospholes derivatives starting from methyl thiophene-2-carboximidate. Some characteristic properties of products have been also reported.

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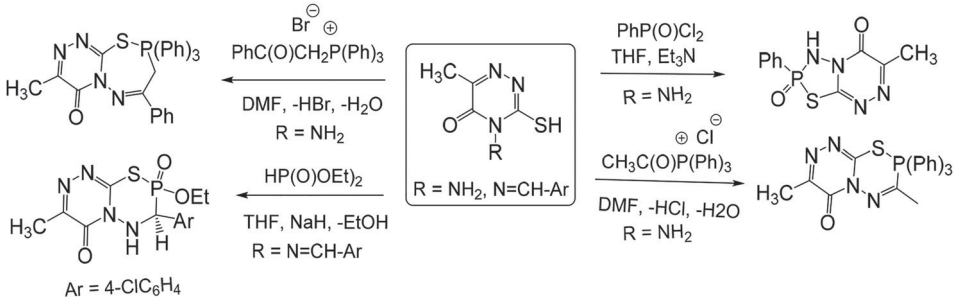


Figure 1. Synthetic route for some biologically active nitrogen- and sulfur-containing heterophospholes.

2. Results and discussion

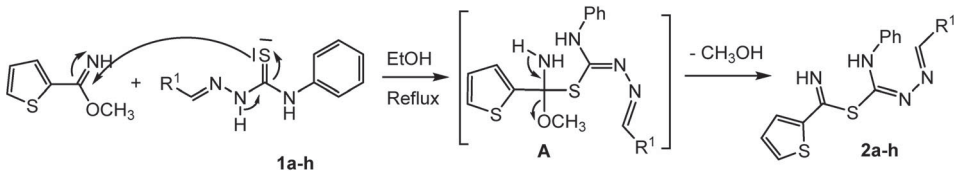
Iminoesters occupy a special position as important intermediates in synthesis because they provide building blocks for several types of heterocyclic systems.[7] As a result of the versatility of the title compounds as a synthetic entry point to fused heterocycles, we first investigated their behavior in reaction with some thiosemicarbazones. Second, the reactivity of the resulted intermediates **2a–2h** toward thiadiazaphospholes was studied.

The starting materials for this work were easily prepared according to the reported procedures. Methyl thiophene-2-carboximidate was synthesized by application of the Pinner synthesis.[8,9] Passage of dry HCl gas into an ethereal solution of thiophene-2-carbonitrile containing an equimolar amount of methanol for 1 h gave the hydrochloride salt. This was isolated as a crystalline solid and treated with sodium bicarbonate solution in ether at 0°C to provide free imidate in high overall yield (80%).

Thiosemicarbazones**1a–1h,** were synthesized in two steps. The first step was the preparation of 4-phenylthiosemicarbazide in 79% yield by the reaction of phenylisothiocyanate and hydrazine hydrate in ethanol at room temperature.[10] The reaction of 4-phenylthiosemicarbazide with various aromatic aldehydes in the presence of few drop of acetic acid (0.5 mL) at 79°C for 4 h leads to the corresponding 4-phenyl-3-thiosemicarbazone derivatives in good yields (73–91%).

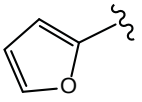
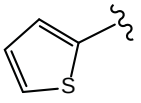
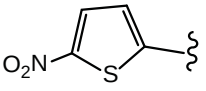
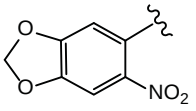
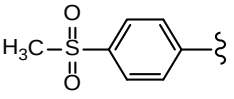
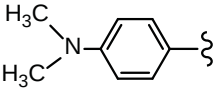
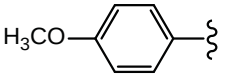
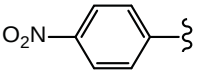
Straightforward reactions of iminoesters with hydrazine derivatives led us to presume that analogous reactions are possible with thiosemicarbazones. In fact, the condensation of 4-phenyl-3-thiosemicarbazones with methyl thiophene-2-carboximidate in absolute ethanol under reflux resulted in the formation of the key intermediates **2a–2h**. In order to demonstrate the efficiency and generality of this protocol, we examined the reactions of iminoester and various substituted thiosemicarbazones (Table 1). All substrates react to give the corresponding products **2a–2h** in good to excellent yields. We propose the mechanism shown in Scheme 1. Conjugate addition of **1a–1h** gives the intermediate **A**. Elimination of the methoxy group provides compounds **2a–2h**.

The chemical structures of compounds **2a–2h** are in agreement with their spectral data. The IR spectrum exhibited absorption bands at 3280 cm^{-1} (NH), and 1630 cm^{-1} (C=N), and the absence of an absorption band at 1265 cm^{-1} attributed to the C=S moiety. The ^1H NMR analysis confirmed the formation of products **2a–2h** and showed the presence of new signals assigned to NH, CH=N, and the protons of the phenyl introduced by the



Scheme 1. Proposed mechanism for the formation of compounds **2a–2h**.

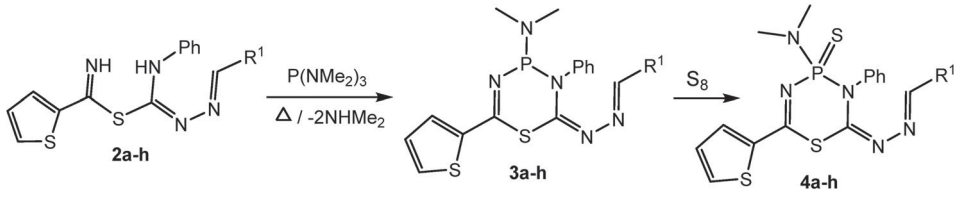
Table 1. Substrate scope studies

Entry	R^1	Product	Yield (%)[a]
1a		2a	79
1b		2b	80
1c		2c	77
1d		2d	74
1e		2e	81
1f		2f	78
1g		2g	87
1h		2h	85

[a]Isolated yield.

substituted thiosemicarbazones. In the ^{13}C NMR spectra, we observed greater than 95% disappearance of the signal around 52 ppm related to the methoxy group.

The key intermediates **2a–2h** possess several reactive sites; in particular the *N,N*-nucleophilic sites. They can partake in intermolecular condensation with electrophilic reagents. The bisnucleophilic character of **2a–2h** allows us to postulate that their reaction with hexamethylphosphorous triamide could constitute an easy access in to a new series of thiadiazaphospholes. Indeed, good yields of the title compounds have been obtained by the reaction of the intermediates **2a–2h** with hexamethylphosphorous triamide in dry toluene under reflux (Scheme 2 and Table 2).



Scheme 2. Synthetic route for the title compounds **4a–4h**.

Table 2. Substrate scope studies

Entry	Product	Yield (%)[a]	Product	Yield (%)[a]
2a	**3a**	87	**4a**	82
2b	**3b**	86	**4b**	87
2c	**3c**	81	**4c**	84
2d	**3d**	87	**4d**	89
2e	**3e**	87	**4e**	81
2f	**3f**	83	**4f**	79
2g	**3g**	85	**4g**	90
2h	**3h**	81	**4h**	83

[a]Isolated yield.

The formation of thiadiazaphospholes **4a–4h** was confirmed by ^{1}H, ^{13}C, and ^{31}P NMR spectra and IR spectroscopy as well as elemental analysis. The ^{31}P NMR spectra showed the presence of a signal corresponding to the phosphonate moiety (P=S) at 80 ppm. The IR spectrum of **4a–4h** showed absorption bands at 1645 and 1587 cm^{-1} (C=N), 790 cm^{-1} (P=S) and strong bands in the region of 921–947 cm^{-1} indicating the presence of P-N groups. The ^{1}H NMR spectrum of compounds **4a–4h** revealed the presence of two types of methyl group protons in NMe_2 with different chemical shifts. Furthermore, the Me group protons of NMe_2 moiety coupled with phosphorus and were split into a doublet. Further support was obtained from the ^{1}H NMR spectra, where it did not display signs of the NH protons. On the other hand, the ^{1}H NMR spectra exhibited resonances assigned to the CH=N moiety appearing as a singlet at 8.21–8.47 ppm. The ^{13}C NMR spectra of thidiazaphospholes displayed the characteristic signals of all carbons and revealed two signals attributable to the carbons of P-N$(CH_3)_2$ of the two non-equivalent methyls of the NMe_2 group and a signal around 147 ppm attributed to the endocyclic C=N.

3. Conclusion

In summary, we have developed an efficient and general methodology for the synthesis of novel thiadiazaphospholes derivatives through the reaction of various thiosemicarbazones with methyl thiophene-2-carboximidate and cyclization of the obtained intermediates with hexamethylphosphoro triamide. The possible biological activities of the synthesized compounds are ongoing in our laboratory and will be reported in due course.

4. Experimental section

4.1. General

Melting points were measured with a Kofler hot-staged apparatus and are uncorrected. ^{1}H, ^{31}P and ^{13}C-NMR spectra were recorded with DMSO-d_6 as the solvent on a Bruker-300

spectrometer. The chemical shifts are reported in ppm relative to TMS (internal reference) for ^{1}H and ^{13}C-NMR and relative to 85% H_3PO_4 (external reference) for ^{31}P-NMR. The coupling constants are reported in Hz. For the ^{1}H-NMR, the multiplicities of signals are indicated by the following abbreviations: s: singlet, d: doublet, t: triplet. Elemental analyses were carried out on EI Elemental Vario EL apparatus. IR spectra were recorded on a Nicolet IR200 spectrometer. The progress of the reactions was monitored by thin layer chromatography (TLC).

4.2. Typical procedure for the synthesis of compounds (2a–2h)

A mixture of methyl thiophene-2-carboximidate (1.41 g, 0.01 mol) and appropriate thiosemicarbazones (0.01 mol) dissolved in absolute ethanol (50 mL) was refluxed for 6–8 h with continuous stirring. The solvent was evaporated under reduced pressure, and then the solid was triturated with cold water and cold absolute ethanol, dried and recrystallized from a mixture methanol-DMF (2:1).

4.2.1. (E)-N′-((E)-Furan-2-ylmethylene)-N-phenylcarbamohydrazonicthiophene-2-carbimidic thioanhydride (2a)

White solid, yield 79%, mp 220–222°C; IR (ν_{max}, cm^{-1}): 3280 and 3173 (NH), 3090 and 2800 (CH, furan ring), 1667 and 1625 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 6.66, 7.04, 7.88 (3H, furan ring), 7.11, 7.34, 7.48 (3H, thiophene ring), 7.33 (t, 1H, J = 7.2 Hz, ArH), 7.47 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.63 (d, 2H, J = 7.8 Hz, ArH), 8.02 (s, 1H, CH=N), 9.19 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 129.84, 131.45, 133.17 and 143.51 (thiophene ring), 140.87 (CH=N), 114.6, 117.25, 142.67 and 146.43 (furan ring), 126.10, 128.60, 126.71 and 139.20 (phenyl), 147.22 (C=NH), 154.53 (C=N). Anal. Calcd for $C_{17}H_{14}N_4OS_2$ (354.44): C, 57.61; H, 3.98; N, 15.81%. Found: C, 57.63; H, 3.95; N, 15.87%.

4.2.2. (E)-N-Phenyl-N′-((E)-thiophen-2-ylmethylene)carbamohydrazonicthiophene-2-carbimidic thioanhydride (2b)

White solid, yield 80%, mp 243–245°C; IR (ν_{max}, cm^{-1}): 3267 and 3125 (NH), 2780 and 3081 (CH, thiophene ring), 1661 and 1637 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 7.18, 7.31, 7.44, 7.55, 7.75 and 7.80 (6H, thiophene ring), 7.36 (t, 1H, J = 7.2 Hz, ArH), 7.51 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.61 (d, 2H, J = 7.8 Hz, ArH), 8.52 (s, 1H, CH=N), 8.89 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 128.03, 129.80, 130.61, 131.12, 132.02, 133.21, 142.58 and 143.78 (thiophene ring), 139.17 (CH=N), 126.63, 126.81, 128.33 and 136.77 (phenyl), 148.01 (C=NH), 153.46 (C=N). Anal. Calcd for $C_{17}H_{14}N_4S_3$ (370.50): C, 55.11; H, 3.81; N, 15.12%. Found: C, 55.13; H, 3.76; N, 15.16%.

4.2.3. (E)-N′-((E)-(5-nitrothiophen-2-yl)methylene)-N-phenylcarbamohydrazonic thiophene-2-carbimidic thioanhydride (2c)

White solid, yield 77%, mp 261–264°C; IR (ν_{max}, cm^{-1}): 3272 and 3143 (NH), 2783 and 3097 (CH, thiophene ring), 1643 and 1611 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 7.22, 7.40, 7.59, 7.72 and 7.85 (5H, thiophene ring), 7.34 (t, 1H, J = 7.2 Hz, ArH), 7.55 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.67 (d, 2H, J = 7.8 Hz, ArH), 8.31 (s, 1H, CH=N), 9.06

(br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 127.80, 128.91, 130.62, 131.79, 132.93, 143.61 and 150.70 (thiophene ring), 143.3 (CH=N), 126.44, 126.12, 128.42 and 137.15 (phenyl), 149.13 (C=NH), 154.03 (C=N). Anal. Calcd for $C_{17}H_{13}N_5O_2S_3$ (415.50): C, 49.14; H, 3.15; N, 16.86%. Found: C, 49.19 H, 3.12; N, 16.91%.

4.2.4. (E)-N′-((E)-(6-Nitrobenzo[d][1,3]dioxol-5-yl)methylene)-N-phenylcarbamohydrazonic thiophene-2-carbimidic thioanhydride (2d)

Yellow solid, yield 74%, mp 217–219°C; IR (ν_{max}, cm^{-1}): 3283 and 3123 (NH), 2812 and 3092 (CH, thiophene ring), 1656 and 1618 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 6.25 (s, 2H, CH_2), 7.09, 7.37, 7.51 (3H, thiophene ring), 7.21 (t, 1H, J = 7.2 Hz, ArH), 7.37 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.57 (d, 2H, J = 7.8 Hz, ArH), 7.61 (s, 1H, ArH), 8.17 (s, 1H, CH=N), 8.52 (s, 1H, ArH), 9.21 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 104.20 (CH_2), 128.77, 131.13, 132.95 and 143.23 (thiophene ring), 140.87 (CH=N), 128.42, 126.44, 126.12, 139.52, 143.04, 149.11 and 152.34 (C_{arom}), 148.80 (C=NH), 155.12 (C=N). Anal. Calcd for $C_{22}H_{19}N_5O_2S_2$ (449.54): C, 58.78; H, 4.26; N, 15.58%. Found: C, 58.79 H, 4.19; N, 15.63%.

4.2.5. (E)-N′-((E)-4-(methylsulfonyl)benzylidene)-N-phenylcarbamohydrazonic thiophene-2-carbimidic thioanhydride (2e)

White solid, yield 81%, mp 247–249°C; IR (ν_{max}, cm^{-1}): 3264 and 3150 (NH), 2793 and 3060 (CH, thiophene ring), 1663 and 1631 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 3.22 (s, 3H, CH_3), 7.10, 7.36, 7.47 (3H, thiophene ring), 7.24 (t, 1H, J = 7.2 Hz, ArH), 7.39 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.63 (d, 2H, J = 7.8 Hz, ArH), 7.95 (d, 2H, J = 8.4 Hz, ArH), 8.15 (d, 2H, J = 8.4 Hz, ArH), 8.22 (s, 1H, CH=N), 8.97 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 43.8 (CH_3), 129.02, 131.24, 132.76 and 143.12 (thiophene ring), 141.02 (CH=N), 126.11, 126.73, 128.62, 128.70 and 139.44 (C_{arom}), 149.30 (C=NH), 156.03 (C=N). Anal. Calcd for $C_{20}H_{18}N_4O_2S_3$ (442.57): C, 54.28; H, 4.10; N, 12.66%. Found: C, 54.35; H, 4.09; N, 12.73%.

4.2.6. (E)-N′-((E)-4-(Dimethylamino)benzylidene)-N-phenylcarbamohydrazonic thiophene-2-carbimidic thioanhydride (2f)

Yellow solid, yield 78%, mp 198–200°C; IR (ν_{max}, cm^{-1}): 3281 and 3122 (NH), 2782 and 3081 (CH, thiophene ring), 1668 and 1644 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.96 (s, 6H, $2CH_3$), 7.14, 7.36, 7.50 (3H, thiophene ring), 7.23 (t, 1H, J = 7.2 Hz, ArH), 7.34 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.53 (d, 2H, J = 7.8 Hz, ArH), 7.59 (d, 2H, J = 8 Hz, ArH), 7.83 (d, 2H, J = 8.4 Hz, ArH), 8.33 (s, 1H, CH=N), 9.17 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 21.21 (CH_3), 129.20, 131.11, 133.17 and 143.40 (thiophene ring), 143.11 (CH=N), 126.33, 127.80, 128.91, 129.24, 137.81 and 141.64 (C_{arom}), 148.19 (C=NH), 153.56 (C=N). Anal. Calcd for $C_{21}H_{21}N_5S_2$ (407.55): C, 61.89; H, 5.19; N, 17.18%. Found: C, 61.83; H, 5.22; N, 17.15%.

4.2.7. (E)-N′-((E)-4-Methoxybenzylidene)-N-phenylcarbamohydrazonicthiophene-2-carbimidicthioanhydride (2g)

White solid, yield 87%, mp 187–189°C; IR (ν_{max}, cm^{-1}): 3287 and 3144 (NH), 2796 and 3065 (CH, thiophene ring), 1659 and 1633 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 3.86 (s, 3H, OCH_3), 6.86 (d, 2H, J = 8.8 Hz, ArH), 7.11, 7.36, 7.49 (3H, thiophene ring),

7.22 (t, 1H, J = 7.2 Hz, ArH), 7.37 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.45 (d, 2H, J = 8.8 Hz, ArH), 7.51 (d, 2H, J = 7.8 Hz, ArH), 8.37 (s, 1H, CH=N), 9.07 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 55.44 (CH_3), 129.82, 131.45, 133.27 and 143.50 (thiophene ring), 140.12 (CH=N), 125.32, 126.78, 128.6, 129.43, 137.53 and 159.45 (C_{arom}), 149.12 (C=NH), 152.31 (C=N). Anal. Calcd for $C_{20}H_{18}N_4OS_2$ (394.51): C, 60.89; H, 4.60; N, 14.20%. Found: C, 60.86; H, 4.63; N, 14.19%.

4.2.8. (E)-N′-((E)-4-Nitrobenzylidene)-N-phenylcarbamohydrazonic thiophene-2-carbimidic thioanhydride (2h)

Yellow solid, yield 85%, mp 267–269°C; IR (ν_{max}, cm^{-1}): 3277 and 3132 (NH), 2801 and 3052 (CH, thiophene ring), 1664 and 1632 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 7.21, 7.33, 7.52 (3H, thiophene ring), 7.26 (t, 1H, J = 7.2 Hz, ArH), 7.41 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, ArH), 7.57 (d, 2H, J = 7.8 Hz, ArH), 7.68 (d, J = 8.8 Hz, 2H, ArH), 8.12 (d, J = 8.8 Hz, 2H, ArH), 8.16 (1H, s, CH=N), 9.23 (br s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 129.89, 131.32, 133.01 and 142.98 (thiophene ring), 144.11 (CH=N), 126.78, 128.60, 129.44, 137.53, 142.31 and 151.65 (C_{arom}), 147.88 (C=NH), 153.97 (C=N). Anal. Calcd for $C_{19}H_{15}N_5O_2S_2$ (409.48): C, 55.73; H, 3.69; N, 17.10%. Found: C, 55.72; H, 3.66; N, 17.17%.

4.3. General synthetic procedure for thiadiazaphosphole derivatives

To a well-stirred solution of compounds **(2a–2b)** (2 mmol) in anhydrous toluene (15 mL) was added hexamethylphosphoroustriamide (2 mmol). The mixture was heated under reflux for 12 h. Silica gel TLC indicated the completion of the reaction. The solvent was evaporated under reduced pressure, and the residue was purified on silica gel preparative TLC using ethyl acetate as eluent.

A mixture of compounds **(3a–3b)** (1 mmol), S_8 (5 mmol) and anhydrous toluene (10 mL) was refluxed for 4 h, and then cooled. The sulfur excess was filtered off, and the solvent was removed under reduced pressure. Flash column chromatography on silica gel using petroleum ether as eluant affords **(4a–4b)**.

4.3.1. (E)-4-(Dimethylamino)-2-(((E)-furan-2-ylmethylene)hydrazono)-3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4a)

Whitesolid, yield 82%, mp 177–179°C; IR (ν_{max}, cm^{-1}): 790 (P=S), 926 (P-N), 1645 and 1587 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.31 (d, $^3J_{PH}$ = 5.2 Hz, 3H, NCH_3), 2.51 (d, $^3J_{PH}$ = 5.2 Hz, 3H, NCH_3), 6.62, 7.05, 7.90 (3H, furan ring), 7.21, 7.35, 7.61 (3H, thiophene ring), 7.22 (t, 1H, J = 7.4 Hz, ArH), 7.07 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.44 (d, 2H, J = 7.8 Hz, ArH), 8.42 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-d_6): δC 35.76 (d, $^2J_{PC}$ = 9.1 Hz, NCH_3), 36.16 (d, $^2J_{PC}$ = 5.8 Hz, NCH_3), 128.14, 130.95, 133.05 and 142.44 (thiophene ring), 143.17 (CH=N), 115.13, 117.27, 142.43 and 146.42 (furan ring), 126.20, 128.01, 128.74 and 138.41 (phenyl), 144.72 and 161.08 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 79.21.Anal. Calcd for $C_{19}H_{18}N_5OPS_3$ (459.54): C, 49.66; H, 3.95; N, 15.24%. Found: C, 49.69; H, 3.91; N, 15.31%.

4.3.2. (E)-4-(Dimethylamino)-3-phenyl-6-(thiophen-2-yl)-2-(((E)-thiophen-2-ylmethylene) hydrazono)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4b)

Whitesolid, yield 87%, mp 217–219°C; IR (ν_{max}, cm^{-1}): 797 (P=S), 933 (P-N), 1648 and 1591 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.38 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 2.52 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 7.10, 7.33, 7.40, 7.51, 7.67 and 7.78 (6H, thiophene ring), 7.29 (t, 1H, J = 7.4 Hz, ArH), 6.98 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.48 (d, 2H, J = 7.8 Hz, ArH), 8.37 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-d_6): δC 35. 61 (d, $^2J_{PC}$ = 3 Hz, NCH_3), 36.12 (d, $^2J_{PC}$ = 7.3 Hz, NCH_3), 128.14, 129.80, 130.42, 131.33, 132.11, 133.20, 142.50 and 143.24 (thiophene ring), 141.02 (CH=N), 125.6, 128.31, 130.17 and 133.50 (phenyl), 146.32 and 162.31 (C=N).^{31}P NMR (121.5 MHz, DMSO-d_6): δ 80.01. Anal. Calcd for $C_{19}H_{18}N_5PS_4$ (475.60): C, 47.98; H, 3.81; N, 14.73%. Found: C, 47.92; H, 3.87; N, 14.72%.

4.3.3. (E)-4-(Dimethylamino)-2-(((E)-(5-nitrothiophen-2-yl)methylene)hydrazono)-3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4c)

White solid, yield 84%, mp 241–243°C; IR (ν_{max}, cm^{-1}): 790 (P=S), 932 (P-N), 1652 and 1584 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.34 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 2.48 (d, $^3J_{PH}$ = 4.9 Hz, 3H, NCH_3), 7.19, 7.32, 7.53, 7.61 and 7.91 (5H, thiophene ring), 7.28 (t, 1H, J = 7.4 Hz, ArH), 7.33 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.47 (d, 2H, J = 7.8 Hz, ArH), 8.21 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-d_6): δC 36.06 (d, $^2J_{PC}$ = 6 Hz, NCH_3), 36.12 (d, $^2J_{PC}$ = 7 Hz, NCH_3), 128.11, 128.70, 130.16, 132.10, 133.23, 142.37, 143.24 and 153.30 (thiophene ring), 139.93 (CH=N), 127.12, 128.32, 128.96, 129.54 and 135.22 (phenyl), 147.09 and 161.40 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 77.92.Anal. Calcd for $C_{19}H_{17}N_6O_2PS_4$ (520.59): C, 43.84; H, 3.29; N, 16.14%. Found: C, 43.85; H, 3.33; N, 16.20%.

4.3.4. (E)-4-(Dimethylamino)-2-(((E)-(6-nitrobenzo[d][1,3]dioxol-5-yl)methylene) hydrazono) -3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4d)

Yellow solid, yield 89%, mp 291–293°C; IR (ν_{max}, cm^{-1}): 794 (P=S), 930 (P-N), 1648 and 1574 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.24 (d, $^3J_{PH}$ = 4.9 Hz, 3H, NCH_3), 2.44 (d, $^3J_{PH}$ = 4.9 Hz, 3H, NCH_3), 6.22 (s, 2H, CH_2), 7.09, 7.35, 7.53 (3H, thiophene ring), 7.23 (t, 1H, J = 7.4 Hz, ArH), 7.37 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.52 (d, 2H, J = 7.8 Hz, ArH), 7.61 (s, 1H, ArH), 8.33 (1H, s, CH=N), 8.53 (s, 1H, ArH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 35.96 (d, $^2J_{PC}$ = 6.1 Hz, NCH_3), 36.43 (d, $^2J_{PC}$ = 7 Hz, NCH_3), 105.03 (CH_2), 128.72, 131.21, 133.01 and 143.21 (thiophene ring), 142.23 (CH=N), 124.95, 126.52, 128.76, 140.87, 143.12, 150.28 and 152.14 (C_{arom}), 148.54 and 159.88 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 78.87.Anal. Calcd for $C_{22}H_{19}N_6O_4PS_3$ (558.58): C, 47.31; H, 3.43; N, 15.05%. Found: C, 47.34; H, 3.44; N, 15.09%.

4.3.5. (E)-4-(Dimethylamino)-2-(((E)-4-(methylsulfonyl)benzylidene)hydrazono)-3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4e)

White solid, yield 81%, mp 195–197°C; IR (ν_{max}, cm^{-1}): 792 (P=S), 928 (P-N), 1652 and 1575 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.41 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 2.55 (d, $^3J_{PH}$ = 4.9 Hz, 3H, NCH_3), 3.18 (s, 3H, CH_3), 7.08, 7.39, 7.62 (3H, thiophene ring), 7.28 (t, 1H, J = 7.4 Hz, ArH), 7.33 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.51 (d, 2H, J = 7.8 Hz, ArH), 7.90 (d, 2H, J = 8.4 Hz, ArH), 8.11 (d, 2H, J = 8.4 Hz, ArH), 8.21 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-d_6): δC 35.32 (d, $^2J_{PC}$ = 6 Hz, NCH_3), 36.07 (d, $^2J_{PC}$ = 7.2 Hz, NCH_3), 42.92 (CH_3), 128.68, 132.03, 133.44 and 142.97 (thiophene ring), 143.09 (CH=N), 125.93, 127.13, 128.44, 128.89, 137.74 and 140.53 (C_{arom}), 145.78 and 159.05 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 79.12.Anal. Calcd for $C_{22}H_{22}N_5O_2PS_4$ (547.66): C, 48.25; H, 4.05; N, 12.79%. Found: C, 48.22; H, 4.09; N, 12.84%.

4.3.6. (E)-4-(Dimethylamino)-2-(((E)-4-(dimethylamino)benzylidene)hydrazono)-3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4f)

Yellow solid, yield 79%, mp 157–159°C; IR (ν_{max}, cm^{-1}): 791 (P=S), 921 (P-N), 1663 and 1587 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.25 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 2.49 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 2.91 (s, 6H, $2CH_3$), 7.21, 7.41, 7.57 (3H, thiophene ring), 7.31 (t, 1H, J = 7.4 Hz, ArH), 7.41 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.57 (d, 2H, J = 7.8 Hz, ArH), 8.38 (s, 1H, CH=N), 7.62 (d, 2H, J = 8 Hz, ArH), 7.79 (d, 2H, J = 8.4 Hz, ArH). ^{13}C NMR (125 MHz, DMSO-d_6): δC 20.98 (CH_3), 36.01 (d, $^2J_{PC}$ = 6.2 Hz, NCH_3), 36.22 (d, $^2J_{PC}$ = 7 Hz, NCH_3), 129.12, 131.31, 133.76 and 143.21 (thiophene ring), 143.12 (CH=N), 125.75, 127.32, 128.15, 134.12, 140.87 and 142.55 (C_{arom}), 147.31 and 160.21 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 80.23.Anal. Calcd for $C_{23}H_{25}N_6PS_3$ (512.64): C, 53.89; H, 4.92; N, 16.39%. Found: C, 53.92; H, 4.87; N, 16.44%.

4.3.7. (E)-4-(Dimethylamino)-2-(((E)-4-methoxybenzylidene)hydrazono)-3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4g)

White solid, yield 90%, mp 268–270°C; IR (ν_{max}, cm^{-1}): 798 (P=S), 947 (P-N), 1656 and 1565 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.22 (d, $^3J_{PH}$ = 4.9 Hz, 3H, NCH_3), 2.55 (d, $^3J_{PH}$ = 5 Hz, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 7.01 (d, 2H, J = 8.8 Hz, ArH), 7.16, 7.38, 7.58 (3H, thiophene ring), 7.25 (t, 1H, J = 7.4 Hz, ArH), 7.41 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.57 (d, 2H, J = 7.8 Hz, ArH), 7.61 (d, 2H, J = 8.8 Hz, ArH), 8.47 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-d_6): δC 35.77 (d, $^2J_{PC}$ = 6.2 Hz, NCH_3), 36.24 (d, $^2J_{PC}$ = 7 Hz, NCH_3), 56.04 (CH_3), 127.24, 132.33, 133.09 and 142.89 (thiophene ring), 144.65 (CH=N), 125.98, 126.43, 129.32, 131.19 140.12 and 154.65 (C_{arom}), 147.66 and 163.23 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 75.98.Anal. Calcd for $C_{22}H_{22}N_5OPS_3$ (499.60): C, 52.89; H, 4.44; N, 14.02%. Found: C, 52.94; H, 4.40; N, 14.09%.

4.3.8. (E)-4-(Dimethylamino)-2-(((E)-4-nitrobenzylidene)hydrazono)-3-phenyl-6-(thiophen-2-yl)-2,3-dihydro-1,3,5,4-thiadiazaphosphole-4-sulfide (4h)

Yellow solid, yield 83%, mp 231–233°C; IR (ν_{max}, cm^{-1}): 789 (P=S), 927 (P-N), 1658 and 1592 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δH 2.29 (d, $^3J_{PH}$ = 5.2 Hz, 3H, NCH_3),

2.51 (d, $^{3}J_{PH}$ = 5.2 Hz, 3H, NCH_3), 7.27, 7.39, 7.58 (3H, thiophene ring), 7.29 (t, 1H, J = 7.4 Hz, ArH), 7.35 (dd, 2H, J = 7.8 Hz, J = 7.4 Hz, ArH), 7.59 (d, 2H, J = 7.8 Hz, ArH), 7.66 (d, J = 8.8 Hz, 2H, ArH), 8.10 (d, J = 8.8 Hz, 2H, ArH), 8.24 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-d_6): δC 35.93 (d, $^{2}J_{PC}$ = 6 Hz, NCH_3), 36.67 (d, $^{2}J_{PC}$ = 7 Hz, NCH_3), 129.03, 131.43, 133.21 and 142.94 (thiophene ring), 143.73 (CH=N), 126.44, 128.43, 131.02, 138.12, 142.56 and 152.87 (C_{arom}), 146.43 and 162.17 (C=N). ^{31}P NMR (121.5 MHz, DMSO-d_6): δ 80.19.Anal. Calcd for $C_{21}H_{19}N_6O_2PS_3$ (514.57): C, 49.02; H, 3.72; N, 16.33%. Found: C, 49.08; H, 3.67; N, 16.37%.

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