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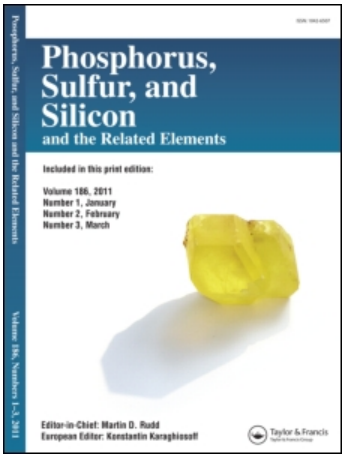

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An Efficient Route to New 1,2,4,3-Triazaphosphole-3-Oxide Derivatives

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AN EFFICIENT ROUTE TO NEW 1,2,4,3-TRIAZAPHOSPHOLE-3-OXIDE DERIVATIVES

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The condensation of hexamethylphosphorotriamide and bis-(dimethylamino) methylphosphonate with amidrazones 1 constitutes a new route to the synthesis of 1,2,4,3-triazaphosphole-3-oxide derivatives 3. Structures of all the synthesized compounds have been established by NMR (^1H, ^{13}C, ^{31}P) and IR spectroscopy, as well as by elemental analysis and MS spectral data for some products.

Keywords Amidrazones; bis-(dimethylamino) methylphosphonate; hexamethylphosphorotriamide; triazaphosphole

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INTRODUCTION

The synthesis of phosphonitrogenous heterocycles[1–3] is one of the aims of researchers in synthetic organic chemistry because of their large biological and pharmaceutical activities.[3–6] Triazaphosphole derivatives are a family of heterocyclic compounds that has attracted the interest of chemists due to their various applications as antibacterials[4] and cytoxicity[4] agents.

There are various methods[7–12] for the synthesis of 1,2,4,3-triazaphospholes, but most of them suffer from one or more disadvantages, such as the triazaphosphole derivatives can exist in several different isomeric forms depending on the type of substitution. We report in this article the selective synthesis of new triazaphosphole derivatives **3** by the reaction of amidrazones **1** with hexamethylphosphorotriamide or bis-(dimethylamino) methyl phosphonate.

RESULTS AND DISCUSSION

2-Aminobenzamidrazones **1**, which are the starting material for this work, were prepared from the condensation of hydrazine with 2-aminobenzonitrile in the presence of a catalytic amount of acetic acid. The chemical structure of compound **1** is in agreement with its spectral data. The IR spectrum of compound **1** exhibited the absorption bands for NH_2

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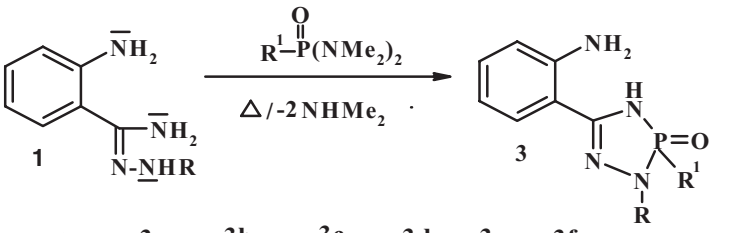

3	3a	3b	3c	3d	3e	3f
R	H	Me	Ph	H	Me	Ph
R^1	NMe_2	NMe_2	NMe_2	Me	Me	Me

Figure 1 Synthetic route of the formation of compound **3**.

and C=N (imine) and the absence of an absorption band of a CN group. ^{1}H NMR analysis confirmed the formation of compound **1** and showed the presence of new signals assigned to NH_2, NH, and protons of the methyl and phenyl introduced by the substituted hydrazine. ^{13}C NMR spectra showed the total absence of a signal related to CN (nitrile) group.

The reaction of compound **1** with phosphorylated reagents in dry toluene under reflux afforded triazaphosphole **3** (Figure 1).

The formation of triazaphospholes **3** was confirmed by ^{1}H, ^{13}C, and ^{31}P NMR spectra and IR spectroscopy as well as elemental analysis for some products (**3c** and **3d**). The ^{31}P NMR spectra showed the presence of a signal corresponding to phosphonate moiety (P=O) at 25 ppm when $R^1 = NMe_2$ and a signal at 38 ppm when $R^1 = Me$.

The IR spectrum of **3** showed absorption bands at 3230–3150 cm^{-1} (NH_2), 3350 cm^{-1} (NH), 1296–1308 cm^{-1} (P=O bonded) and strong bands in the region of 1090–1100 cm^{-1} indicating the presence of P-N groups. The ^{1}H NMR spectrum of **3** 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 groups coupled with phosphorus and were split into a doublet. The ^{13}C NMR spectra of **3** displayed the characteristic signals of all carbons and revealed two signals attributable to the carbons of P-N($\underline{C}H_3$)$_2$ of the two non-equivalent methyls of the NMe_2 group.

EXPERIMENTAL

IR spectra were recorded on Perkin Elmer Paragon 1000 PC spectrometer using a solution of $CHCl_3$. The spectra resolution was 4 cm^{-1}.

^{1}H, ^{13}C, and ^{31} P NMR spectra were recorded in $CDCl_3$ as solvent containing TMS (tetramethylsilane) on a Brüker 300 spectrometer (^{1}H: 300 MHz, ^{13}C: 75.47 MHz, ^{31}P: 121.49 MHz). The chemical shifts (δ)) are reported in ppm relative to TMS (internal reference) for ^{1}H and ^{13}C and relative to 85% H_3PO_4 (external reference) for ^{31}P.

Melting points were determined using a Büchi melting point apparatus and are uncorrected. Elemental microanalysis was performed on a Perkin-Elmer CHN-2400 analyzer apparatus.

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Synthesis of 2-Aminobenzamidrazones 1

To a solution of anthranilonitrile (0.01 mol) in ethanol (10 mL), hydrazine (0.015 mol) and a few drops of acetic acid were added. The reaction mixture was refluxed for 12 h and then allowed to reach room temperature. The solvent was evaporated from the vacuum pump, and the resulting solid was filtered, washed several times with diethyl ether, and recrystallized from ethanol. Compound **1a** obtained was chromatographed on a silica gel column using a mixture of ethyl acetate and petroleum ether (4:6) as eluent.

1a: Mp = 50°C. Yield = 93%. IR ($CHCl_3$), ν (cm^{-1}): ν (NH_2) = 3320–3400; ν (NH) = 3460. ^{1}H NMR ($CDCl_3$): δ 4.38 (s, 6H, NH_2); 6.60–7.28 (m, 4H, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 115.23; 117.75; 117.90; 132.32; 134.04; 149.78.

1b: Mp = 52°C. Yield = 94%. IR ($CHCl_3$), ν (cm^{-1}): ν (NH_2) = 3320–3400, ν (NH) = 3455. ^{1}H NMR ($CDCl_3$): δ 4.60 (broad s, 5H, NH, NH_2); 3.10 (s, 3H, CH_3); 6.40–7.25 (m, 4H, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 38.60; 117.34; 118.48; 128.50; 129.29; 131.98; 146.85; 150.78.

1c: Oil. Yield = 90%. IR ($CHCl_3$), ν (cm^{-1}): ν (NH_2) = 3325–3400, ν (NH) = 3465. ^{1}H NMR ($CDCl_3$): δ 4.30 (broad s, 5H, NH, NH_2); 6.40–7.25 (m, 9H, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 115.34, 118.00, 119.43, 119.77, 128.50, 129.29, 131.98, 134.56, 146.85, 151.42.

Synthesis of 1,2,4,3-Triazaphosphole-3-oxide Derivatives

A mixture of aminobenzamidrazone **1** (1.0 mmol) and hexamethylphosphorotriamide or bis-(dimethylamino) methylphosphonate (1.0 mmol) dissolved in anhydrous toluene (10 mL) was heated under reflux for 24 h. After evaporating off the solvent in vacuum, the resulting solid product was recrystallized from CCl_4 (**3c**, **3d**, **3e**, **3f**), and the oil obtained (**3a** and **3b**) was purified by column chromatography using silica gel (60–120 mesh) with ethyl acetate:petroleum ether (3:7) as eluent.

3a: Oil. Yield = 60%. IR ($CHCl_3$), ν (cm^{-1}): ν (C=N) = 1635; ν (NH_2) = 3230–3150; ν (NH) = 3350; ν (P=O) = 1296. ^{1}H NMR ($CDCl_3$): δ 2.35 (d, $^3J_{PH}$ = 5.5 Hz, 3H, N-$\underline{CH_3}$); 2.52 (d, $^3J_{PH}$ = 5.5 Hz, 3H, N-$\underline{CH_3}$); 4.81 (broad s, 4H, $N\underline{H}$, $N\underline{H_2}$); 6.50–7.16 (m, $4H_{arom}$). ^{13}C NMR ($CDCl_3$): δ 35.88 (d, $^2J_{PC}$ = 9.2 Hz, $N\underline{C}H_3$); 36.22 (d, $^2J_{PC}$ = 6.0 Hz, $N\underline{C}H_3$); 115.22; 116.11; 117.53; 131.42; 133.30; 150.74; 169.96. ^{31}P NMR ($CDCl_3$): δ 25.09. Calcd for $C_9H_{14}N_5PO$:%C: 45.18;%H: 5.85;%N: 29.28; found:%C: 45.10;%H: 5.80;%N: 29.15.

3b: Oil. Yield = 70%. IR ($CHCl_3$), ν (cm^{-1}): ν (C=N) = 1630; ν (NH_2) = 3235–3120; ν (NH) = 3350; ν (P=O) = 1296. ^{1}H NMR ($CDCl_3$): δ 2.38 (d, $^3J_{PH}$ = 4.9 Hz, 3H, N-$\underline{CH_3}$); 2.50 (d, $^3J_{PH}$ = 4.9 Hz, 3H, N-$\underline{CH_3}$); 3.20 (s, 3H, N-$\underline{CH_3}$); 4.80 (broad s, 3H, $N\underline{H_2}$, $N\underline{H}$); 6.05–7.16 (m, $4H_{arom}$). ^{13}C NMR ($CDCl_3$): δ 35.70 (d, $^2J_{PC}$ = 3.0 Hz, $N\underline{C}H_3$); 36.12 (d, $^2J_{PC}$ = 7.0 Hz, $N\underline{C}H_3$); 39.70 ($N\underline{C}H_3$); 116.25; 116.59; 116.92; 130.65; 133.31; 149.44; 169.00. ^{31}P NMR ($CDCl_3$): δ 25.60. m/e (Relative intensity)%: 253 (5); 193 (50); 165 (20); 150 (30); 135(47); 109(35); 92(42); 76(14).

3c: Mp: 175°C. Yield = 73%. IR ($CHCl_3$), ν (cm^{-1}): ν (C=N) = 1635; ν (NH_2) = 3230–3140; ν (NH) = 3330; ν (P=O) = 1296. ^{1}H NMR (($CDCl_3$): δ 2.22 (d, $^3J_{PH}$ = 5.0 Hz, 3H, N-$\underline{CH_3}$); 2.10 (d, $^3J_{PH}$ = 4.9 Hz, 3H, N-$\underline{CH_3}$); 5.00 (broad s, 3H, $N\underline{H_2}$, $N\underline{H}$); 6.10–7.20 (m, $4H_{arom}$). ^{13}C NMR ($CDCl_3$) : δ 36.07 (d, $^2J_{PC}$ = 6.0 Hz, $N\underline{C}H_3$); 36.12 (d, $^2J_{PC}$ = 7 Hz, $N\underline{C}H_3$); 111.59; 116.11; 117.63; 122.34; 128.04; 128.53; 129.17; 140.42; 147.06; 164.72. ^{31}P NMR ($CDCl_3$): δ 25.10. Calcd for $C_{15}H_{18}N_5PO$:%C: 57.14;%H: 5.71;%N: 22.22; found:%C: 57.00;%H: 5.68;%N: 22.00.

3d: Mp: 180°C. Yield = 80%. IR ($CHCl_3$), ν (cm^{-1}): ν (C=N) = 1635; ν (NH) = 3354; ν (NH_2) = 3230–3150; ν (P=O) = 1308. ^{1}H NMR ($CDCl_3$): δ 1.30 (d, $^2J_{PH}$ = 11.0 Hz, 3H, P-C$\underline{H}_3$); 4.72 (broad s, 3H, N$\underline{H}_2$, N$\underline{H}$); 6.60–7.70 (m, $4H_{arom}$). ^{13}C NMR ($CDCl_3$): δ 13.12 (N$\underline{C}H_3$); 114.82; 117.77; 118.98; 119.30; 131.70; 134.33; 145.00; 150.27. ^{31}P NMR ($CDCl_3$): δ 38.08. Calcd for $C_8H_{11}N_4PO$:%C: 45.71;%H: 5.23;%N: 26.66; found:%C: 45.60;%H: 5.20;%N: 26.56.

3e: Mp: 200°C. Yield = 80%. IR ($CHCl_3$), ν (cm^{-1}): ν (C=N) = 1630; ν (NH) = 3354; ν(NH_2) = 3230–3140; ν (P=O) = 1308. ^{1}H NMR ($CDCl_3$): δ 1.30 (d, $^2J_{PH}$ = 10.0Hz, 3H, P-C$\underline{H}_3$); 2.60 (s, 3H, N-C$\underline{H}_3$); 4.90 (broad s, 3H, N$\underline{H}_2$, N$\underline{H}$); 6.50–7.60 (m, $4H_{arom}$). ^{13}C NMR ($CDCl_3$): δ 11.72 (N$\underline{C}H_3$); 28.98; 115.17; 117.83; 121.12; 131.90; 133.90; 143.77; 150.54. ^{31}P NMR ($CDCl_3$): δ 38.80. MS: m/e (Relative intensity)%: 224(1); 209 (55); 162(10); 150(30); 135(37); 109(30); 92(48); 76(24).

3f: Mp: 192°C. Yield = 82%. IR ($CHCl_3$), ν (cm^{-1}): ν (C=N) = 1632; ν (NH) = 3350; ν(NH_2) = 3225–3130; ν (P=O) = 1307. ^{1}H NMR ($CDCl_3$): δ 1.32 (d, $^2J_{PH}$ = 12.0 Hz, 3H, P-C$\underline{H}_3$); 4.68 (broad s, 3H, N$\underline{H}_2$, N$\underline{H}$); 6.62–7.31 (m, $9H_{arom}$). ^{13}C NMR ($CDCl_3$): δ 14.24 (N$\underline{C}H_3$); 116.80; 119.71; 121.36; 128.81; 131.3; 133.35; 142.01; 148.78. ^{31}P NMR ($CDCl_3$): δ 34.20.

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