3,5-DIAMINO-4-PHOSPHONOPYRAZOLEs As Precursors for the Synthesis of 3-AMINO-4-PHOSPHONO-5-PHENYLTHIOURLYPYRAZOLES and Phosphonated Pyrazolopyrimidines

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ABSTRACT: The synthesis of a series of pyrazolopyrimidine derivatives is described in two steps. The reaction of hydrazine with phosphoryl thioamide leads to the formation of 3,5-diamino-4-phosphopyrazoles. The latter react with several 1,3-diketones to give the corresponding phosphonated pyrazolopyrimidines.

Keywords: hydrazine, 3,5-diamino-4-phosphonopyrazole, phosphonated thiourlylpyrazole, phosphonated pyrazolopyrimidine.

INTRODUCTION

In the past decade, interest in pyrazole chemistry has significantly increased mainly due to the discovery of the interesting properties exhibited by a great number of pyrazole derivatives [1-5]. The condensation of these heterocycles with diketones gives rise to purine analogs pyrazolopyrimidines, which are of considerable chemical and pharmacological importance. Indeed, representatives of this type of heterocycles exhibit a wide range of biological activity [6,7] and some of pyrazolopyrimidines serve as efficient sedative-hypnotic and anxiolytic drugs like zaleplon (Sonata, hypnotic) [8], indiplon (hypnotic) [9], and ocinaplon (anxiolytic) [10]. These drugs are related to the class of nonbenzodiazepines, and their therapeutic effect is due to allosteric enhancement of the action of the inhibitory neurotransmitter GABA at the GABA_A receptor [8,9].

In view of our ongoing interest in the chemistry of pyrazolopyrimidines [11–13], we have now focused our attention on development of efficient routes to bicyclic compounds with pyrazolopyrimidine core bearing a (EtO)_2P(O) group. The synthetic routes for preparation of pyrazolo[1,5-al]pyrimidines involve the cyclocondensation of aminopyrazoles with 1,3-biselectrophiles such as 1,3-dicarbonyl compounds.

RESULTS AND DISCUSSION

The 3,5-diamino-4-phosphonopyrazoles 2 serve as key intermediates in the synthesis of 3-arylamino-4-diethylphosphono-5-phenylthiourlylpyrazole 3 (Scheme 1). They are prepared in one step by reacting 1 with hydrazine hydrate in boiling toluene.

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The structure of the aminopyrazole 2 was identified as the reaction product on the basis of its elemental analysis and spectroscopic data. Its IR spectrum displayed the lack of absorption band assignable to the C=N group and the presence of a new absorption band at 3444-3458 cm⁻¹ assignable to NH₂ group characteristics of the cyclic pyrazolic [14-18]. The ¹H NMR spectrum displayed a broad singlet at δ 6.78-6.88 ppm corresponding to the NH₂ protons. The ¹³C NMR spectrum was characterized by signals at 116-140 ppm assignable to aromatic carbons and a signal at 150 ppm corresponding to imine carbon. The ³¹P NMR spectrum was characterized by a resonance in the range 10.38 and 19.15 ppm. On the other hand, the 3,5-diamino-4-phosphonopyrazoles 2 were allowed to react with phenyl isothiocyanate in ethanol to afford 3-arylamino-4-diethylphosphono-5-phenylthiourylpyrazole 3. Spectral data were in favor of the proposed thiourylpyrazole structure 3. The IR spectra of compounds 3 revealed the absence of NH₂ absorption band and the presence of new absorption bands at 1285-1300 cm⁻¹ assignable to the C=S group. The ¹³C NMR spectrum was characterized by signal at 187.6-189.6 ppm assignable to C=S.

3,5-Diaminopyrazoles are versatile reagents and have been extensively used as synthetic starting materials for the synthesis of several polysubstituted fused pyrazoles of potential biological activity [19-22]. It was thus of interest to study the reactivity of 5-aminopyrazole towards a variety of chemical reagents. The general literature procedure [24-26] for the synthesis of pyrazolo[1,5-a]pyrimidines involves cyclocondensation of aminopyrazoles with reagents having 1,3-electrophilic centers such as γ-diketones or enamines. Cyclocondensation of compounds 2 with diketones in boiling ethanol and the presence of a catalytic amount of acetic acid produced in each case a single product, as evidenced by TLC (Scheme 2).
The reaction products can be formulated as pyrazolo[1,5-a]pyrimidine derivatives 4, evidence for assigned structures being provided by analytical and spectroscopic data. For example, the IR spectrum of compound 4 showed the appearance of absorption bands at 3428, 1601 and 1535 cm\(^{-1}\) due to NH, C=N and C=C groups, respectively. The \(^1\)H NMR spectra for compounds 4a-h were characterized by the existence of pyrazolopyrimidine signals at $\delta$ 2.46 ppm and $\delta$ 6.82 ppm assignable to the protons of the methyl group and the ethylene proton respectively. The \(^1\)H NMR spectra for compounds 4i-l exhibited two additional signals at $\delta$ 2.46 and 2.54 ppm assignable to the protons of two methyl groups in pyrimidine ring and a singlet signal at $\delta$ 6.82 ppm for proton in the pyrimidine ring. Its \(^31\)P NMR spectrum showed a new signal between $\delta$ 6.66 and 10.19 ppm.

CONCLUSION

In conclusion, the objective of the present study was to synthesize of some new pyrazoles, thiourlypyrazoles and pyrazolopyrimidines. The structure of the compound was elucidated by \(^1\)H, \(^13\)C, \(^19\)F and \(^31\)P NMR and CHN analyses.

EXPERIMENTAL

Melting points were determined on a Koehler bank. IR spectra were recorded from KBr on a Perkin-Elmer 197 spectrometer; only structurally significant bands are reported. NMR spectra were recorded on a Bruker-A since spectrometer operating at 300 MHz for \(^1\)H, 75 MHz for \(^13\)C, 282 MHz for \(^19\)F and 121 MHz for \(^31\)P nuclei. Chemical shifts were measured relative to TMS in CDCl$_3$ as solvents. Materials: thin-layer chromatography (TLC): TLC plates (Merck, silica gel 60 F254 0.2 mm 200×200 nm); substances were detected using UV light at 254 nm. Analyzes were performed by the Service of elemental analyses (Perkin Elmer 2000 Analyzer carbon sulfur) at the National Institute of Physico-Chemical Analysis (INRAP) Biotechnopole Sidi Thabet, Tunisia.

Synthesis of 3,5-diamino-4-phenazopyrazoles 2.

A mixture of compound 1 (0.01 mol) and hydrazine hydrate 98% (0.01 mol) in toluene is refluxed for 22 h. After cooling the solvent is removed under reduced pressure and the residue recrystallized from ethanol to give the product 2.

2a:5-Amino-3-p-chlorophenylamino-4-diethylphosphonopyrazole. Yield 87% ; yellow powder; mp = 111 °C. \(^1\)H NMR (CDCl$_3$, 300 MHz) $\delta_{ppm}$: 1.15 (m, 6H); 4.10 (m, 4H); 6.78 (brs, 2H, NH$_2$); 6.93 (s, NH); 6.99 (s, NH); 7.00-7.20 (m, 4H$_{arom}$). \(^13\)C NMR (CDCl$_3$, 75 MHz) $\delta_{ppm}$: 15.9 (CH$_3$); 60.6 (CH$_2$); 76.6 (P-C=C); 119.7-138.2 (C$_{arom}$); 150.8 (NH$_2$C=); 152.3 (C=N). \(^31\)P NMR (CDCl$_3$, 121 MHz) $\delta_{ppm}$: 10.38. IR (KBr, ν cm$^{-1}$): NH$_2$ =3444, NH =3367, NH =3220, P=O =1265. Anal. For C$_{13}$H$_{15}$ClN$_3$O$_2$P: Calcd: %C= 45.82, %H= 5.22, %N= 16.25; Found: %C= 45.31, %H= 5.25, %N= 16.35.

2b:5-Amino-3-benzylamino-4-diethylphosphonopyrazole. Yield 79% ; yellow powder; mp = 128 °C. \(^1\)H NMR (CDCl$_3$, 300 MHz) $\delta_{ppm}$: 1.25 (m, 6H); 4.26 (m, 4H); 4.38 (s, 2H); 6.81 (brs, 2H, NH$_2$); 6.98 (s, NH); 7.12 (s, NH); 7.21-7.48 (m, 5H$_{arom}$). \(^13\)C NMR (CDCl$_3$, 75 MHz) $\delta_{ppm}$: 16.2-16.5 (CH$_3$); 47 (CH$_2$); 61.9-63.8 (CH$_2$); 73.2 (P-C=C); 126.4-140.4 (C$_{arom}$); 151.4 (NH$_2$C=); 152.1 (C=C=N). \(^31\)P NMR (CDCl$_3$, 121 MHz) $\delta_{ppm}$: 13.67. IR (KBr, ν cm$^{-1}$): NH$_2$=3448, NH =3370, NH =3200, P=O =1262.

2c:5-Amino-4-diethylphosphono-3-phenylaminopyrazole. Yield 84% yellow powder; mp = 108 °C. \(^1\)H NMR (CDCl$_3$, 300 MHz) $\delta_{ppm}$: 1.30 (m, 6H); 4.20 (m, 4H); 6.88 (brs, 2H, NH$_2$); 6.91 (s, NH); 7.07 (s, NH); 7.20-7.38 (m, 5H$_{arom}$). \(^13\)C NMR (CDCl$_3$, 75 MHz) $\delta_{ppm}$: 16.1-16.3 (CH$_3$); 60.9-62.8 (CH$_2$); 73.1 (P-C=C); 116.4-140.4 (C$_{arom}$); 151.6 (NH$_2$C=); 152.1 (C=C=N). \(^31\)P NMR (CDCl$_3$, 121 MHz) $\delta_{ppm}$: 16.05. IR (KBr, ν cm$^{-1}$): NH$_2$=3458, NH =3360, NH =3210, P=O =1260. Anal. For C$_{13}$H$_{19}$N$_3$O$_2$P: Calcd: %C= 50.32, %H= 6.17, %N= 18.06; Found: %C= 50.31, %H= 6.12, %N= 18.00.

2d:5-Amino-3-cyclohexylamino-4-diethylphosphonopyrazole. Yield 82% ; yellow powder; mp = 139 °C. \(^1\)H NMR (CDCl$_3$, 300 MHz) $\delta_{ppm}$: 1.30 (m, 6H); 1.51-2.00 (m,11H-C$_{Hex}$); 4.20 (qd, 4H); 6.87 (brs, 2H, NH$_2$); 6.97 (s, NH); 7.00 (s, NH). \(^13\)C NMR (CDCl$_3$, 75 MHz) $\delta_{ppm}$: 16.2 (CH$_3$); 24.2-47.8 (C$_{Hex}$); 61.9-62.8 (CH$_2$); 74.1 (P-C=C); 151.5 (NH$_2$C=); 152.1 (C=C=N). \(^31\)P NMR (CDCl$_3$, 121 MHz) $\delta_{ppm}$: 19.15. IR (KBr, ν cm$^{-1}$): NH$_2$=3455, NH =3367, NH =3225, P=O =1261.
Synthesis of 3-amino-4-phosphono-5-phenylthiourlypyrazoles 3.

To a stirred solution of 3,5-diamino-4-phosphono pyrazoles 2 (0.01 mol) in ethanol (15 mL) is added phenyl isothiocyanate (0.01 mol). The mixture was stirred for 24 h at room temperature, the solvent is removed under reduced pressure and the residuce recrystallized from ethyl acetate to give the product 3.

3a: 3-p-Chlorophenylamino-4-diethylphosphono-5-phenylthiourlypyrazole. Yield 88%; white powder; mp = 166 °C. 1H NMR (CDCl₃, 300 MHz) δ ppm: 1.15 (m, 6H); 4.25 (m, 4H); 6.95 (s, NH); 7.12 (s, NH); 7.22-7.48 (m, 9H arom); 8.00 (s, NH); 9.10 (s, NH). 13C NMR (CDCl₃, 75 MHz) δ ppm: 16.1 (CH₃); 61.1 (CH₂); 72.7 (P-C=C); 116.3-138.9 (C arom); 152.1 (NH₂C=); 154.2 (C=N); 189.6 (C=S). 31P NMR (CDCl₃, 121 MHz) δ ppm: 13.62. IR (KBr, ν cm⁻¹): NH = 3348, NH = 3329, NH = 3320, P = 0 = 1261, C=S = 1285. Anal. For C₂₃H₂₃ClN₂O₃PS: Calcd: %C = 50.05, %H = 4.79, %N = 14.59; Found: %C = 50.20, %H = 4.85, %N = 14.69.

3b: Benzylationo-4-diethylphosphono-5-phenylthiourlypyrazole. Yield 89%; white powder; mp = 146 °C. 1H NMR (CDCl₃, 300 MHz) δ ppm: 1.20 (m, 6H); 4.25 (m, 4H); 4.38 (s, 2H); 6.91 (s, NH); 7.17 (s, NH); 7.20-7.48 (m, 10H arom); 8.19 (s, NH); 8.97 (s, NH). 13C NMR (CDCl₃, 75 MHz) δ ppm: 16.2 (CH₂); 47.2 (CH₂); 61.3 (CH₂); 71.7 (P-C=C); 116.8-138.9 (C arom); 155.1 (NH₂C=); 157.2 (C=N); 187.6 (C=S). 31P NMR (CDCl₃, 121 MHz) δ ppm: 12.57. IR (KBr, ν cm⁻¹): NH = 3358, NH = 3349, NH = 3337, NH = 3215, P = 0 = 1264, C=S = 1290. Anal. For C₂₃H₂₃N₂O₃PS: Calcd: %C = 54.89, %H = 5.70, %N = 15.24; Found: %C = 54.87, %H = 5.68, %N = 15.29.

3c: 4-Diethylphosphono-3-phenylamino-5-phenylthiourlypyrazole. Yield 75%; white powder; mp = 158 °C. 1H NMR (CDCl₃, 300 MHz) δ ppm: 1.25 (m, 6H); 4.20 (m, 4H); 6.92 (s, NH); 7.07 (s, NH); 7.20-7.48 (m, 10H arom); 8.17 (s, NH); 8.87 (s, NH). 13C NMR (CDCl₃, 75 MHz) δ ppm: 16.2 (CH₂); 62.3 (CH₂); 68.7 (P-C=C); 117.8-139.7 (C arom); 155.1 (NH₂C=); 157.2 (C=N); 188.6 (C=S). 31P NMR (CDCl₃, 121 MHz) δ ppm: 14.71. IR (KBr, ν cm⁻¹): NH = 3368, NH = 3359, NH = 3330, NH = 3210, P = 0 = 1260, C=S = 1300. Anal. For C₂₃H₂₃N₂O₃PS: Calcd: %C = 53.92, %H = 5.43, %N = 15.72; Found: %C = 53.90, %H = 5.40, %N = 15.69.

3d: 3-Cyclohexylamino-4-diethylphosphono-5-phenylthiourlypyrazole. Yield 82%; white powder; mp = 152 °C. 1H NMR (CDCl₃, 300 MHz) δ ppm: 1.15 (m, 6H); 1.51-2.15 (m, H cyc); 4.21 (m, 4H); 6.95 (s, NH); 7.00 (s, NH); 7.22-7.48 (m, 5H arom); 8.50 (s, NH); 9.12 (s, NH). 13C NMR (CDCl₃, 75 MHz) δ ppm: 16.1-16.3 (CH₃); 25.2-48.8 (C cyc); 61.2-62.4 (CH₂); 75.7 (P-C=C); 114.8-148.9 (C arom); 151.1 (NH₂C=); 153.2 (C=N); 187.6 (C=S). 31P NMR (CDCl₃, 121 MHz) δ ppm: 15.31. IR (KBr, ν cm⁻¹): NH = 3358, NH = 3349, NH = 3340, NH = 3220, P = 0 = 1264, C=S = 1295.


To a solution of compound 2 (0.01 mol) in ethanol (10 mL) and acetic acid (0.5 mL), an appropriate 1,3-diketone compounds (0.01 mol) is added. The reaction mixture is refluxed for 48 h, and then poured into crushed ice. The solid product is collected by filtration, dried and recrystallized in methanol to give compounds 4.

4a: 7-p-Chlorophenylamino-8-diethylphosphono-2-methyl-4-pyrazolopyrazol[1,5-alpyrimidine. Yield 64%; yellow powder; mp = 228 °C. 1H NMR (CDCl₃, 300 MHz) δ ppm: 1.25 (td, 6H); 2.55 (s, 3H); 3.85 (qd, 4H); 5.40 (s, 1H); 7.10-7.98 (m, 9H arom); 8.50 (s, NH). 13C NMR (CDCl₃, 75 MHz) δ ppm: 16.1-16.3 (CH₃); 24.3 (CH₃); 60.6-60.7 (CH₃); 72.9 (P-C=C); 107.4 (HC); 118.3-131.1 (CM arom); 145.7 (C=N); 157.1 (N-C=C); 160.8 (H₃C-C=N). 31P NMR (CDCl₃, 121 MHz) δ ppm: 10.19. IR (KBr, ν cm⁻¹): NH = 3264, C=C = 1246. Anal. For C₂₃H₂₃ClN₂O₃P: Calcd: %C = 58.66, %H = 5.10, %N = 11.90; Found: %C = 58.60, %H = 5.09, %N = 11.89.

4b: 7-Benzylamino-8-diethylphosphono-2-methyl-4-pyrazolopyrazol[1,5-alpyrimidine. Yield 81%; yellow powder; mp = 178 °C. 1H NMR (CDCl₃, 300 MHz) δ ppm: 1.25 (td, 6H); 2.24 (s, 3H); 3.89 (qd, 4H); 4.14 (s, 2H); 6.25 (s, 1H); 7.10-7.60 (m, 10H arom); 8.50 (s, NH). 13C NMR (CDCl₃, 75 MHz) δ ppm: 15.1-15.7 (CH₃); 24.3 (CH₃); 42.5 (CH₃); 60.9-60.7 (CH₃); 72 (P-C=C); 101.5 (HC); 124.4-131.8 (C arom); 142.7 (C=N); 147.7 (N-C=C); 159.2 (H₃C-C=N). 31P NMR (CDCl₃, 121 MHz) δ ppm: 8.22. IR (KBr, ν cm⁻¹): NH = 3344, C=C = 1236.
4c: 8-Diethylphosphono-2-methyl-4-phenyl-7-phenylaminopyrazolo[1,5-a]pyrimidine. Yield 77%; yellow powder; mp = 208 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.15 (td, 6H); 2.54 (s, 3H); 3.90 (qd, 4H); 6.35 (s, 1H); 7.10-7.88 (m, 10H arom); 8.60 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 16.1-16.2 (CH₃); 24.3 (CH₃); 60.6-60.7 (CH₂); 82 (P-C=C); 107.5 (HC); 117.4-138.4 (C arom); 146.7 (C=N); 157.1 (N-C=C); 160.2 (H=C=C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 9.35. IR (KBr, v cm⁻¹): NH = 3364, C=C = 1256.

4d: 7-Cyclohexylamino-8-diethylphosphono-2-methyl-4-phenylpyrazolo[1,5-a]pyrimidine. Yield 76%; yellow powder; mp = 199 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.00 (td, 6H); 1.41-2.10 (m, H c c h e x); 2.34 (s, 3H); 3.90 (qd, 4H); 6.40 (s, 1H); 7.10-7.88 (m, 5H arom); 8.20 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 16.31-16.40 (CH₃); 24.56 (CH₃); 25.45-52.23 (C_c שאינו); 60.67 (CH₂); 76.98 (P-C=C); 102.69 (HC); 125.91-131.40 (C arom); 149.05 (C=N); 155.19 (N-C=C); 169.40 (H=C=C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 6.92. IR (KBr, v cm⁻¹): NH = 3264, C=C = 1256.

4e: 7-Phenylamino-8-diethylphosphono-2-methyl-4-trifluoromethylpyrazolo[1,5-a]pyrimidine. Yield 77%; yellow powder; mp = 168 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.15 (td, 6H); 2.64 (s, 3H); 4.10 (qd, 4H); 5.85 (s, 1H); 7.10-7.88 (m, 5H arom); 8.60 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 15.9 (CH₃); 17.3 (CH₃); 60.6-61.7 (CH₂); 76 (P-C=C); 102.5 (HC); 124.9-131.4 (C arom); 141.7 (C=N); 147.1 (N-C=C); 164.2 (H=C=C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 7.35. ^19F NMR (CDCl₃, 282 MHz) δ ppm: -66. IR (KBr, v cm⁻¹): NH = 3367, C=C = 1276.

4f: 7-Benzylamino-8-diethylphosphono-2-methyl-4-trifluoromethylpyrazolo[1,5-a]pyrimidine. Yield 69%; yellow powder; mp = 166 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.25 (td, 6H); 2.40 (s, 3H); 4.10 (qd, 4H); 4.40 (s, 2H); 6.30 (s, 1H); 7.10-7.38 (m, 5H arom); 8.20 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 15.9 (CH₃); 17.4 (CH₃); 43.5 (CH₃); 60.5-61.9 (CH₂); 76 (P-C=C); 102.7 (HC); 119.3-132.6 (C arom); 141.9 (C=N); 142.4 (N-C=C); 169.9 (H=C=C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 8.56. ^19F NMR (CDCl₃, 282 MHz) δ ppm: -64. IR (KBr, v cm⁻¹): NH = 3364, C=C = 1236.

4g: 7-Chlorophenylamino-8-diethylphosphono-2-methyl-4-trifluoromethylpyrazolo[1,5-a]pyrimidine. Yield 88%; yellow powder; mp = 171 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.10 (td, 6H); 2.54 (s, 3H); 4.10 (qd, 4H); 6.25 (s, 1H); 7.10-7.88 (m, 4H arom); 8.45 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 15.9-16.2 (CH₃); 19.3 (CH₃); 60.6-62.7 (CH₂); 74 (P-C=C); 104.5 (HC); 124.9-132.4 (C arom); 143.7 (C=N); 149.1 (N-C=C); 162.2 (H=C-C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 8.35. ^19F NMR (CDCl₃, 282 MHz) δ ppm: -62. IR (KBr, v cm⁻¹): NH = 3361, C=C = 1266.

4h: 7-Chloropyridinylamino-8-diethylphosphono-2-methyl-4-trifluoromethylpyrazolo[1,5-a]pyrimidine. Yield 79%; yellow powder; mp = 175 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.19 (td, 6H); 1.32-2.15 (m, H c c h e x); 2.40 (s, 3H); 4.00 (qd, 4H); 6.25 (s, 1H); 8.36 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 15.9-16.3 (CH₃); 18.3 (CH₃); 25.4-54.2 (C c c h e x); 60.4-61.7 (CH₂); 74 (P-C=C); 103.5 (HC); 143.7 (C=N); 148.1 (N-C=C); 168.2 (H=C-C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 8.75. ^19F NMR (CDCl₃, 282 MHz) δ ppm: -62. IR (KBr, v cm⁻¹): NH = 3367, C=C = 1286.

4i: 8-Diethylphosphono-2,4-dimethyl-7-phenylaminopyrazolo[1,5-a]pyrimidine. Yield 75%; yellow powder; mp = 188 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.15 (td, 6H); 2.50 (s, 3H); 2.65 (s, 3H); 4.10 (qd, 4H); 6.25 (s, 1H); 7.20-7.38 (m, 5H arom); 8.60 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 16.2-16.3 (CH₃); 17.5 (CH₂); 23.2 (CH₃); 60.9-62.2 (CH₂); 82 (P-C=C); 108 (HC); 116.4-140.4 (C arom); 148.7 (C=N); 157.4 (N-C=C); 157.6 (N-C=C); 160.4 (H=C-C=N). ^31P NMR (CDCl₃, 121 MHz) δ ppm: 10.15. IR (KBr, v cm⁻¹): NH = 3360, C=C = 1260.

4j: 7-Benzylamino-8-diethylphosphono-2,4-dimethyl-7-phenylaminopyrazolo[1,5-a]pyrimidine. Yield 57%; yellow powder; mp = 192 °C. ^1H NMR (CDCl₃, 300 MHz) δ ppm: 1.25 (td, 6H); 2.52 (s, 3H); 2.67 (s, 3H); 4.10 (qd, 4H); 4.28 (s, 2H); 6.35 (s, 1H); 7.20-7.38 (m, 5H arom); 8.61 (s, NH). ^13C NMR (CDCl₃, 75 MHz) δ ppm: 16.1-16.3 (CH₃); 17.5 (CH₃); 23. (CH₃); 47.2 (CH₂); 60.9-62.2 (CH₂); 79.9 (P-C=C); 108.1 (HC), 115.4-140.4
(C\textsubscript{arom}); 149.7 (C=N); 156.4 (N=C=C); 157.6 (N=C=C); 159.9 (H\textsubscript{2}C-C=N). \textsuperscript{31}P NMR (CDCl\textsubscript{3}, 121 MHz) \(\delta\) ppm: 6.66. IR (KBr, v cm\textsuperscript{-1}): NH = 3365, C=C = 1255.

4k: 7-p-Chlorophenylamino-8-diethylphosphono-2,4-dimethylpyrazolo[1,5-a]pyrimidine. Yield 87%; yellow powder; mp = 182 °C. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz) \(\delta\) ppm: 1.20 (td, 6H); 2.55 (s, 3H); 2.70 (s, 3H); 4.13 (qd, 4H); 6.30 (s, 1H); 7.20-7.58 (m, 4H \textsubscript{arom}); 8.60 (s, NH). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz) \(\delta\) ppm: 12.6-16.4 (CH\textsubscript{3}); 17.1 (CH\textsubscript{3}); 22.2 (CH\textsubscript{3}); 61.9-63.2 (CH\textsubscript{2}); 81.5 (P-C=C); 106.3 (HC); 116.4-142.4 (C\textsubscript{arom}); 148.6 (C=N); 157.6 (N=C=C); 157.8 (N=C=C); 159.9 (H\textsubscript{2}C-C=N). \textsuperscript{31}P NMR (CDCl\textsubscript{3}, 121 MHz) \(\delta\) ppm: 9.15. IR (KBr, v cm\textsuperscript{-1}): NH = 3365, C=C = 1266.

4l: 7-Cyclohexylamino-8-diethylphosphono-2,4-dimethylpyrazolo[1,5-a]pyrimidine. Yield 59%; yellow powder; mp = 194 °C. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz) \(\delta\) ppm: 1.20 (td, 6H); 1.41-2.25 (m, H\textsubscript{c-hex}); 2.49 (s, 3H); 2.64 (s, 3H); 4.10 (qd, 4H); 6.45 (s, 1H); 8.60 (s, NH). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz) \(\delta\) ppm: 16.2-16.5 (CH\textsubscript{3}); 17.5 (CH\textsubscript{3}); 23.2 (CH\textsubscript{2}); 25.2-48.8 (C\textsubscript{hex}); 60.9-62.2 (CH\textsubscript{2}); 76 (P-C=C); 107.2 (HC); 147.7 (C=N); 157.3 (N=C-C); 157.9 (N=C-C); 160.2 (H\textsubscript{2}C-C-N). \textsuperscript{31}P NMR (CDCl\textsubscript{3}, 121 MHz) \(\delta\) ppm: 8.46. IR (KBr, v cm\textsuperscript{-1}): NH = 3364, C=C = 1255.

REFERENCES