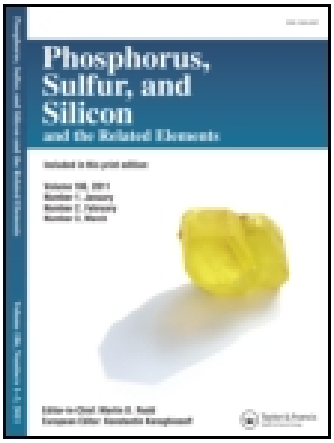


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Synthesis of New Phosphonate Derivatives of Naphtho[2,1-b[Pyran]3,2-e][1,2,4]Triazolo [1,5-c]Pyrimidines

Anis Romdhane [a] , Jean-François Gallard [b] , M'hamed Ali Hamza [a] & Hichem Ben Jannet [a]

[a] Laboratoire de Chimie Hétérocyclique, Produits Naturels et Réactivité, Equipe: Chimie Bio-Organique et produits Naturels, Département de Chimie, Faculté des Sciences de Monastir , Université de Monastir , Monastir , Tunisie

[b] Laboratoire de Chimie et de Biologie Structurales CNRS , Institut de Chimie des Substances Naturelles , Gif-sur-Yvette , France

Published online: 27 Mar 2012.

To cite this article: Anis Romdhane , Jean-François Gallard , M'hamed Ali Hamza & Hichem Ben Jannet (2012) Synthesis of New Phosphonate Derivatives of Naphtho[2,1-b[Pyran]3,2-e][1,2,4]Triazolo [1,5-c]Pyrimidines, Phosphorus, Sulfur, and Silicon and the Related Elements, 187:5, 612-618, DOI: 10.1080/10426507.2011.636109

To link to this article: http://dx.doi.org/10.1080/10426507.2011.636109

Phosphorus, Sulfur, and Silicon, 187:612–618, 2012

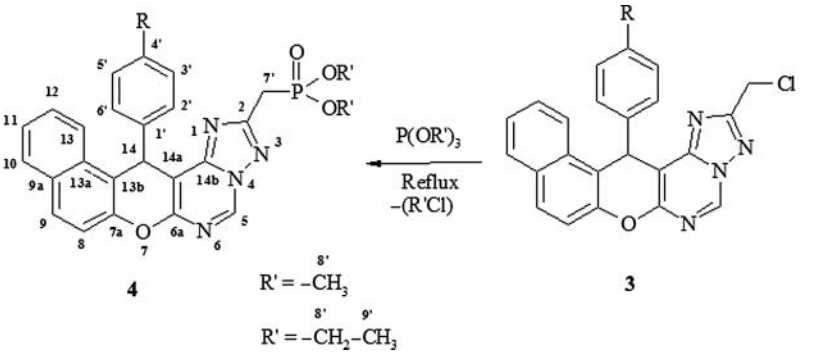
ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426507.2011.636109

SYNTHESIS OF NEW PHOSPHONATE DERIVATIVES OF NAPHTHO[2,1-*b*]PYRAN[3,2-*e*][1,2,4]TRIAZOLO [1,5-*c*]PYRIMIDINES

Anis Romdhane,[1] Jean-François Gallard,[2] M'hamed Ali Hamza,[1] and Hichem Ben Jannet[1]

[1]*Laboratoire de Chimie Hétérocyclique, Produits Naturels et Réactivité, Equipe: Chimie Bio-Organique et produits Naturels, Département de Chimie, Faculté des Sciences de Monastir, Université de Monastir, Monastir, Tunisie*
[2]*Laboratoire de Chimie et de Biologie Structurales CNRS, Institut de Chimie des Substances Naturelles, Gif-sur-Yvette, France*

GRAPHICAL ABSTRACT



Abstract *The synthesis of new naphthopyranotriazolopyrimidines phosphonates* ***4a–i*** *in good yields (74%–93%) has been accomplished via Michaelis–Arbusov rearrangement by the reaction of trialkyl phosphite with naphthopyranotriazolopyrimidines chloride* ***3a–e,*** *which were obtained from α-functionalized iminoethers* ***1*** *in two steps. The synthesized compounds* ***4a–i*** *were completely characterized by IR,* ^{1}H, ^{13}C, *and* ^{31}P *NMR and HRMS.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Naphthopyranotriazolopyrimidines phosphonates; Michaelis–Arbusov rearrangement; trialkyl phosphite; naphthopyranotriazolopyrimidines chloride; α-fonctionalized iminoethers

Received 7 September 2011; accepted 24 October 2011.

Address correspondence to Hichem Ben Jannet, Laboratoire de Chimie Hétérocyclique, Produits Naturels et Réactivité, Equipe: Chimie Bio-Organique et produits Naturels, Département de Chimie, Faculté des Sciences de Monastir, Université de Monastir, Avenue de l'Environnement, 5019 Monastir, Tunisie. E-mail: hichem.benjannet@yahoo.fr

INTRODUCTION

Phosphorus-containing compounds play a key role in living organisms as carriers of genetic information and important signaling, regulatory, energy transfer, and structural compounds.[1] Due to this pivotal role, biological important phosphorus compounds have become therapeutic targets in various modern medicinal techniques such as antisense[2] and antigene[3] approaches to modulation gene expression or a gene silencing technique using short interfering RNA.[4] On the other hand, heterocyclic phosphonates containing the P–C bond are not particularly abundant in nature. Their diverse biological activity[5,6] has, for a long time, attracted considerable synthetic[7] and pharmacological interest.[8]

The Michaelis–Arbuzov rearrangement, also known as the Arbusov reaction, is a very versatile way to form P–C bond from the reaction of an aryl/alkyl halide and trialkyl phosphite.[9] This reaction is one of the most extensively investigated and is widely used to prepare phosphonates, which are particularly important in connection with their remarkable biological and pharmacological activities. They have been widely used as antibacterial,[10] anti-HIV,[11] anti-inflammatory,[12] antiviral,[13] and antitumor[14] agents. Thus, a large number of new phophonate derivatives have been prepared hitherto with special attention to nitrogen heterocyclic compounds.[15–19] In this context, triazolopyrimidines, known by their medicinal, bactericidal, and fungicidal activities,[20–22] could be used as a source of nitrogen with access to new bioactive phosphonate derivatives.

In continuation of this fact and as a contribution to the search for efficient methodologies for the synthesis of new heterocyclic phosphonates, we prepared a series of novel naphthopyranotriazolopyrimidines dialkylphosphonates **4a–i**, since they would be expected to possess biological activity, via the Arbusov reaction of naphthopyranotriazolopyrimidines chloride **3a–e** with trialkyl phosphite.

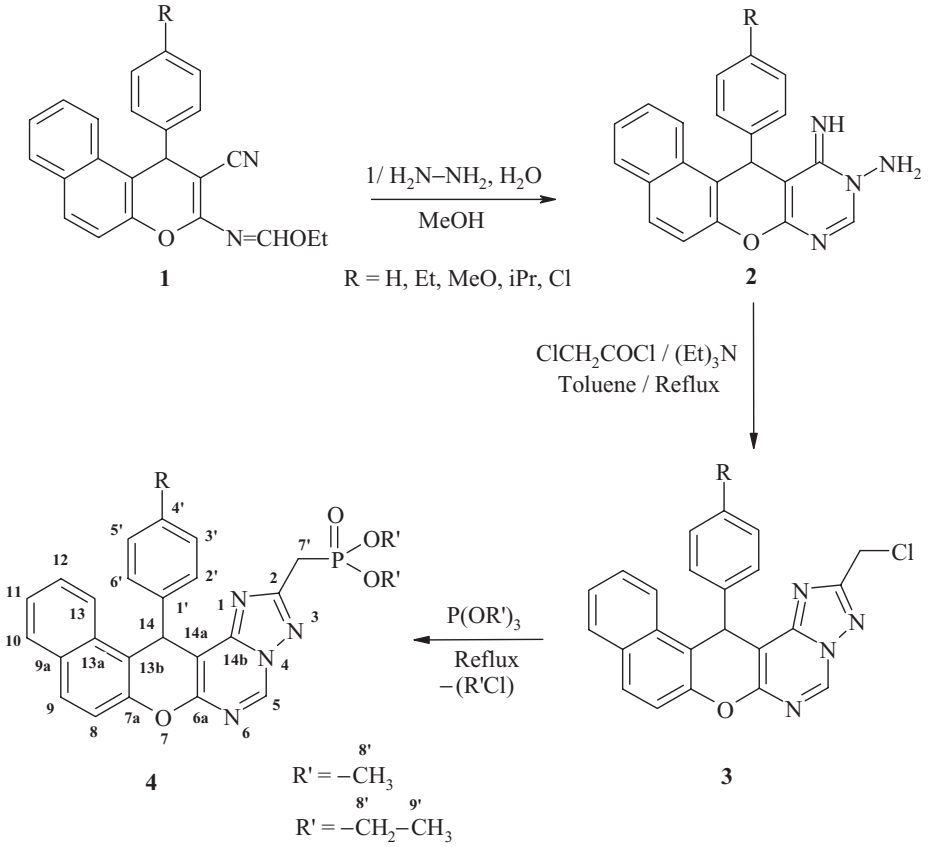
RESULTS AND DISCUSSION

According to the previously reported method,[23] we have synthesized a series of α-functionalized iminoethers **1a–e** and have subjected them to reaction with an aqueous solution of hydrazine in methanol at 0 °C to give the naphthopyranopyrimidines **2** (Scheme 1). The key intermediate, naphthopyranotriazolpyrimidines chloride **3**, was prepared according to the literature procedure,[24] through a cyclization reaction of binucleophiles **2** using chloroacetyl chloride.

The formation of new naphthopyranotriazolpyrimidines phosphonates **4a–i**, in good yields (Table 1) was carried out via Michaelis–Arbuzov rearrangement (Arbusov reaction) of naphthopyranotriazolpyrimidines chloride **3** with trialkyl phosphite. (Scheme 1)

In order to determine the best conditions for the preparation of compounds **4**, we examined the reaction under various conditions by changing the temperature and the solvent (toluene, xylene); we found that the best yields (Table 1) were obtained when compounds **3** were reacted under reflux with an excess of trialkyl phosphite used at the same time as a solvent. The reaction was conducted until TLC indicated that the starting materials have been completely converted to products **4**.

The structures of compounds **4** have been assigned from their analytical data, IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and mass spectroscopy (HR-ES-MS). In fact, the ^{1}H NMR spectra, of compounds **4** showed, in addition to the signals corresponding to the cyclic moiety protons that the CH_2 group ($H_{7'}$) was found as a doublet ($J = 21.6$–25.4 Hz) at a chemical shift of 3.56–3.85 ppm. The large splitting was a result of a two-bond coupling



Scheme 1

of being directly bonded to the phosphorus. We also detected the presence of a doublet at 3.84–3.88 ppm (J = 12.5–12.7 Hz), when R′ = Me, as a result of proton $H_{8'}$ coupled to the phosphorus group and a multiplet with chemical shift of 4.02–4.25 ppm, when R′ = Et, due to the coupling $H_{8'}$ with phosphorus and H_9.

Table 1 Yields of naphthopyranotriazolopyrimidines dialkylphosphonates **4a–i**

Product **4**	R	R′	Yield (%)
4a	H	Me	74
4b	H	Et	78
4c	Et	Me	82
4d	Et	Et	84
4e	MeO	Me	86
4f	MeO	Et	87
4g	iPr	Et	89
4h	Cl	Me	91
4i	Cl	Et	93

The ^{13}C NMR spectra of these compounds were also in agreement with the proposed structures. In fact, in addition of the signals corresponding to the carbons introduced by the intermediate **2**, we observed a doublet at 26.8–28.6 ppm with a very large coupling constant (161.2–161.9 Hz) as a result of being directly bonded of $C_{7'}$ to the phosphorus and two doublets at 53.2–72.7 ppm (J = 7.1–7.4 Hz) and 161.9–162.6 ppm (J = 9.3–9.7 Hz) from the coupling of phosphorus with $C_{8'}$ and C_2, respectively. Finally, when R′ = Et, we observed a doublet at 16.4 ppm (J = 6.9 Hz) results of carbon $C_{9'}$ being coupled to phosphorus. The ^{31}P NMR spectra of these compounds showed the signal corresponding to the phosphonyl group. The infrared spectra also revealed the presence of absorbance due to P=O band at 1220–1230 cm^{-1}. The HR-ES mass spectra showed essentially the ion peak $[M + H]^+$. Figures S 1–S6 (Supplemental Materials) show sample ^1H, ^{13}C, and ^{31}P NMR spectra for **4a**,**h**.

EXPERIMENTAL

All reactions were monitored by TLC using aluminium sheets of Merck silica gel 60 F_{254}, 0.2 mm. Column chromatography was performed on silica gel (70–230 mesh) using ethyl acetate and hexane mixture as eluents. Melting temperatures were determined on an Electrothermal 9002 apparatus and were reported uncorrected. NMR spectra were recorded on a Bruker AC-300 spectrometer at 300 MHz (^1H), 75 MHz (^{13}C), and 121 MHz (^{31}P). All chemical shifts were reported as δ values (ppm) relative to internal tetramethylsilane. Toluene was distilled from sodium prior to use. IR spectra were recorded on FTS-6000 BIO-RAD apparatus. Mass spectra were obtained with Micromass LCT (ESI technique, positive mode) spectrometers.

General Procedure for Preparation of Naphthopyranopyrimidinedialkyl Phosphonates 4a–i

In a typical procedure, the solution of naphthopyranotriazolopyrimidine **3** (1 mmol) and an excess of trialkylphosphite (10 mL) was refluxed for 6 h. The reaction evolution was checked by TLC. When all the starting material was consumed, the mixture was cooled to room temperature, then the precipitate formed was filtered, dried, and purified by silica gel column chromatography using petroleum ether–ethyl acetate (7:3).

Compound 4a: **2-methyldimethoxyphosphoryl-14-phenyl-4H-naphto[2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo [1,5-*c*]pyrimidine**: white solid; mp 258 °C–259 °C; IR (KBr, cm^{-1}) ν: 1630 (C=N), 1230 (P=O), 975 (P–O–C); ^1H NMR (300 MHz, $CDCl_3$): δ 3.67 (d, J_{P-H} = 25.2 Hz, 2H), 3.86 (d, J_{P-H} = 12.3 Hz, 3H), 3.88 (d, J_{P-H} = 12.7 Hz, 3H), 6.40 (s, 1H), 7.08–7.60 (m, $11H_{arom.}$), 9.08 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.7 (d, J_{P-C} = 161.6 Hz), 37.6, 53.3 (d, J_{P-C} = 7.4 Hz), 103.4, 114.9, 117.5, 123.4, 125.2, 127.2, 127.4, 128.3, 128.6, 128.9, 129.9, 130.8, 131.6, 138.1, 142.4, 148.5, 153.1, 154.2, 161.9 (d, J_{P-C} = 9.6 Hz); ^{31}P (120 MHz, $CDCl_3$): δ 24.5; HR-ES-MS $[M + H]^+$ calcd. for $(C_{25}H_{22}N_4O_4P)^+$: 473.1341; found: 473.1347.

Compound 4b: **2-methyldiethoxyphosphoryl-14-phenyl-4H-naphto[2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo [1,5-*c*]pyrimidine**: white solid; mp 254 °C–255 °C; IR (KBr, cm^{-1}) ν: 1625 (C=N), 1220 (P=O), 980 (P–O–C); ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 8.8 Hz, 6H), 3.85 (d, J_{P-H} = 25.3 Hz, 2H), **4.25–4.37** (m, 4H), 6.32 (s, 1H), 7.12–8.08 (m, $11H_{arom.}$), 9.10 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.4 (d, J_{P-C} = 6.9 Hz),

27.8 (d, $J_{P-C} = 161.2$ Hz), 37.6, 62.7 (d, $J_{P-C} = 7.4$ Hz), 103.4, 115.1, 117.5, 123.4, 125.2, 127.2, 127.4, 128.3, 128.6, 128.7, 129.9, 130.8, 131.6, 138.1, 142.5, 148.6, 153.2, 154.1, 162.4 (d, $J_{P-C} = 9.5$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 21.9; HR-ES-MS $[M + H]^+$ calcd. for $(C_{27}H_{26}N_4O_4P)^+$: 501,1674; found: 501.1668.

Compound 4c: **2-methyldimethoxyphosphoryl-14-(4-ethyl)phenyl-4H-naphto [2,1-*b*] pyrano[3,2-*e*][1,2,4] triazolo[1,5-*c*]pyrimidine**: white solid; mp 224 °C–225 °C; IR (KBr, cm^{-1}) ν: 1625 (C=N), 1225 (P=O), 985 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (t, $J = 8.8$ Hz, 3H), 2.53 (q, $J = 8.8$ Hz, 2H), 3.70 (d, $J_{P-H} = 25.2$ Hz, 2H), 3.83 (d, $J_{P-H} = 12.2$ Hz, 3H), 3.85 (d, $J_{P-H} = 12.5$ Hz, 3H), 6.36 (s, 1H), 6.92–8.10 (m, $10H_{arom.}$), 9.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.2, 27.1 (d, $J_{P-C} = 161.8$ Hz), 28.3, 37.7, 53.2 (d, $J_{P-C} = 7.2$ Hz), 103.7, 115.1, 117.5, 123.5, 125.2, 127.3, 128.0, 128.2, 128.6, 129.8, 130.9, 131.6, 137.9, 139.8, 143.1, 148.5, 153.3, 154.1, 162.1 (d, $J_{P-C} = 9.7$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 24.5; HR-ES-MS $[M + H]^+$ calcd. for $(C_{27}H_{26}N_4O_4P)^+$: 501.1738; found: 501.1733.

Compound 4d: **2-methyldiethoxyphosphoryl-14-(4-ethyl)phenyl-4H-naphto[2, 1-*b*] pyrano[3,2-*e*][1,2,4] triazolo[1,5-*c*]pyrimidine**: white solid; mp 254 °C–255 °C; IR (KBr, cm^{-1}) ν: 1635 (C=N), 1230 (P=O), 980 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (t, $J = 8.8$ Hz, 3H), 1.16 (t, $J = 8.2$ Hz, 6H), 2.51 (q, $J = 8.8$ Hz, 2H), 3.66 (d, $J_{P-H} =$ 25.4 Hz, 2H), **4.14–4.21** (m, 4H), 6.40 (s, 1H), 7.01–8.02 (m, $10H_{arom.}$), 9.05 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.1, 16.4 (d, $J_{P-C} = 6.9$ Hz), 27.3 (d, $J_{P-C} = 161.3$ Hz), 28.3, 37.2, 62.7 (d, $J_{P-C} = 7.1$ Hz), 103.7, 115.2, 117.5, 123.4, 125.2, 127.4, 128.1, 128.2, 128.6, 129.8, 130.8, 131.6, 137.9, 139.8, 143.1, 148.5, 152.9, 154.2, 162.1 (d, $J_{P-C} = 9.5$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 21.9; HR-ES-MS $[M + H]^+$ calcd. for $(C_{29}H_{30}N_4O_4P)^+$: 529.2008; found: 529.2014.

Compound 4e: **2-methyldimethoxyphosphoryl-14-(4-methoxy)phenyl-4H-naph to[2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine**: white solid; mp 262 °C–263 °C; IR (KBr, cm^{-1}) ν: 1630 (C=N), 1220 (P=O), 990 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.63 (d, $J_{P-H} = 21.6$ Hz, 2H), 3.66 (s, 3H), 3.84 (d, $J_{P-H} = 12.4$ Hz, 3H), 3.86 (d, J_{P-H} = 12.7 Hz, 3H), 6.36 (s, 1H), 6.69–7.96 (m, $10H_{arom.}$), 9.08 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.8 (d, $J_{P-C} = 161.3$ Hz), 36.7, 53.2 (d, $J_{P-C} = 7.4$ Hz), 55.1, 103.7, 113.9, 115.1, 117.5, 123.5, 125.2, 127.4, 128.6, 129.4, 129.8, 130.8, 131.6, 134.8, 137.9, 148.4, 153.0, 154.1, 158.6, 161.8 (d, $J_{P-C} = 9.5$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 24.5; HR-ES-MS $[M + H]^+$ calcd. for $(C_{26}H_{24}N_4O_5P)^+$: 503.1317; found: 503.1323.

Compound 4f: **2-methyldiethoxyphosphoryl-14-(4-methoxy)phenyl-4H-naphto [2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine**: white solid; mp 268 °C–269 °C; IR (KBr, cm^{-1}) ν: 1615 (C=N), 1230 (P=O), 995 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (t, $J = 8.8$ Hz, 6H), 3.60 (d, $J_{P-H} = 22.3$ Hz, 2H), 3.66 (s, 3H), **4.02–4.17** (m, 4H), 6.25 (s, 1H), 6.60–7.82 (m, $10H_{arom.}$), 8.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.4 (d, $J_{P-C} = 6.9$ Hz), 27.8 (d, $J_{P-C} = 161.2$ Hz), 36.7, 55.1, 62.7 (d, $J_{P-C} = 7.1$ Hz), 103.7, 113.9, 115.2, 117.5, 123.4, 125.1, 127.3, 128.6, 129.4, 129.8, 130.8, 131.6, 134.8, 137.9, 148.5, 153.1, 153.9, 158.5, 162.3 (d, $J_{P-C} = 9.3$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 22.0; HR-ES-MS $[M + H]^+$ calcd. for $(C_{28}H_{28}N_4O_5P)^+$: 531.1601; found: 531.1608.

Compound 4g: **2-methyldiethoxyphosphoryl-14-(4-isopropyl)phenyl-4H-naphto[2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine**: white solid; mp 228 °C–229 °C; IR (KBr, cm^{-1}) ν: 1625 (C=N), 1225 (P=O), 985 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.12 (d, $J = 6.8$ Hz, 6H), 1.39 (t, $J = 8.2$ Hz, 6H), **2.72–2.82** (m, 1H), 3.56 (d, $J_{P-H} = 22.5$ Hz, 2H), **4.12–4.24** (m, 4H), 6.36 (s, 1H), 6.92–8.19 (m, $10H_{arom.}$), 9.11 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.4 (d, $J_{P-C} = 6.9$ Hz), 23.7, 27.8 (d, $J_{P-C} =$

161.2 Hz), 33.5, 37.1, 62.7 (d, $J_{P-C} = 7.1$ Hz), 103.7, 115.3, 117.5, 123.5, 125.1, 126.6, 127.3, 128.1, 128.6, 128.9, 129.7, 130.9, 131.6, 137.9, 147.6, 148.6, 153.1, 154.1, 162.2 (d, $J_{P-C} = 9.5$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 22.1; HR-ES-MS $[M + H]^+$ calcd. for $(C_{30}H_{32}N_4O_4P)^+$: 543.2183; found: 543.2176.

Compound 4h: **2-methyldimethoxyphosphoryl-14-(4-chloro)phenyl-4H-naphto [2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine**: white solid; mp 262 °C–263 °C; IR (KBr, cm^{-1}) ν: 1615 (C=N), 1215 (P=O), 980 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.61 (d, $J_{P-H} = 21.6$ Hz, 2H), 3.82 (d, $J_{P-H} = 12.3$ Hz, 3H), 3.86 (d, $J_{P-H} = 12.5$ Hz, 3H), 6.34 (s, 1H), 7.03–7.85 (m, $10H_{arom.}$), 9.11 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.8 (d, $J_{P-C} = 161.9$ Hz), 37.1, 53.2 (d, $J_{P-C} = 7.4$ Hz), 102.9, 114.2, 117.5, 123.2, 125.3, 127.5, 128.7, 128.8, 129.7, 130.2, 130.6, 131.6, 133.1, 138.2, 140.9, 148.5, 153.1, 154.1, 162.1 (d, $J_{P-C} = 9.6$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 24.6; HR-ES-MS $[M + H]^+$ calcd. for $(C_{25}H_{21}ClN_4O_4P)^+$: 507.0989; found: 507.0995.

Compound 4i: **2-methyldiethoxyphosphoryl-14-(4-chloro)phenyl-4H-naphto [2,1-*b*] pyrano[3,2-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine**: white solid; mp 258 °C–259 °C; IR (KBr, cm^{-1}) ν: 1615 (C=N), 1230 (P=O), 995 (P–O–C); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51 (t, $J = 8.2$ Hz, 6H), 3.62 (d, $J_{P-H} = 25.1$ Hz, 2H), **4.08–4.21** (m, 4H), 6.35 (s, 1H), 6.35–7.92 (m, $10H_{arom.}$), 9.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.4 (d, $J_{P-C} = 6.9$ Hz), 27.8 (d, $J_{P-C} = 161.5$ Hz), 37.1, 62.7 (d, $J_{P-C} = 7.4$ Hz), 102.9, 114.3, 117.6, 123.2, 125.3, 127.5, 128.4, 128.7, 129.7, 130.1, 130.7, 131.6, 133.1, 138.2, 141.0, 148.6, 153.2, 153.8, 162.6 (d, $J_{P-C} = 9.4$ Hz); ^{31}P (121 MHz, $CDCl_3$): δ 22.0; HR-ES-MS $[M + H]^+$ calcd. for $(C_{27}H_{25}N_4ClO_4P)^+$: 535.1305; found: 535.1300.

REFERENCES

1. Westheimer, F. H. *Science, New Series* **1987,** 235, 1173-1178.
2. Uhlmann, E.; Peyman, A. *Chem. Rev.* **1990,** 90(4), 543-584.
3. Helene, C. *Anti-cancer Drug Des*. **1991,** 6(6), 569-584.
4. Nawrot, B.; Sipa, K. *Curr. Top. Med. Chem.* **2006,** 6(9), 913-925.
5. Elderfield, R. *Heterocyclic Comp*. **1952,** 4(1), 125-129.
6. Meth-Cohn, O.; Narine, B. *Tetrahedron Lett*. **1978,** 12, 2045-2048.
7. Ali, M. M.; Tasneem, R. K. C.; Saiprakash, P. K. *Synlett* **2001,** 2, 251-253.
8. Patel, H. V.; Vyas, K. V.; Fernandes, P. S. *Indian J. Chem.* **1990,** 29(B), 836-842.
9. Sukhova, N. M.; Lidak, M. Zidermane, A.; Pelevina, P. S.; Voronia, S. S. *Khim. Farm. Zh.* **1989,** 23, 1226-1229.
10. Atherton, F. R.; Hassal, C. H.; Lambert, R. W. *J. Med. Chem.* **1986,** 29, 29-40.
11. Alonso, E.; Solis, A.; Del Pozo, C. *Synlett* **2000,** 5, 698-700.
12. Wafaa, M. A.; Azza, A. K.; Abeer, A. S. *Eur. J. Med. Chem.* **2010,** 45, 5217-5224.
13. (a) Zhoo, J.; Fan, H. T.; Song, B. A.; Jin, L. H.; Bhadury, P.; Hu, D. Y.; Yang, S. *Phosphorus, Sulfur Silicon Relat. Elem.* **2011,** 186, 81-87; (b) Yang, X.; Song, B. A.; Jin, L. H.; Wei, X.; Bhadury, P.; Li, X. X.; Yang, S.; Hu, D. Y. *Sci. China Chem.* **2011,** 54, 103-109.
14. Liu, J. Z.; Song, B. A.; Fan H. T.; Bhadury, P.; Wan, X.; Hu, D. Y.; Zeng, S. *Eur. J. Med. Chem.* **2010,** 45, 5108-5112.
15. Francesca, C.; Maria, L. G.; Elena, P.; Marinella, V. *Tetrahedron* **2001,** 57, 5455-5459.
16. Yan Chang, S.; Yuming, Z.; Jei, S. *J. Fluorine Chem*. **2002,** 116, 157-161.
17. Francisco, P.; Ana Maria, O. R.; Eduardo M. D. M.; Marta, R.; Jaione, P. *Tetrahedron* **2003,** 59, 2617-2623.
18. Lise, D. B.; Didier, V.; Jean-Francois, L.; Jane, S.; Paul-Alin, J. *Tetrahedron* **2007,** 63, 9677-9684.

19. Narayanna, R. M. V.; Sivakumar, B.; Balakrishna, A.; Reddy, C. S.; Nayak, S. K.; Reddy, C. D. *ARKIVOK* **2007,** XV, 246-254.
20. Rashad, A. E.; Mohamed, M. S.; Zaki, M. E. A.; Fatahala, S. S. *Archiv Der. Pharmazie* **2006,** 339(12), 664-669.
21. Chern, J. H.; Shia, K. S.; Hsu, T. A. *Bioorg. Med. Chem. Lett.* **2004,** 14(10), 2519-2525.
22. Dolakva, P.; Dracinsky, M.; Masojodkova, M.; Solinova, V.; Kasicka, V.; Holy, A. *J. Eur. Med. Chem.* **2009,** 44(6), 2408-2424.
23. Fakher, C.; Mehdi, M.; Mansour, S. *Heterocyclic Commun*. **2006,** 9, 401-404.
24. (a) Kamar, M.; Fakher, C.; Abdelouahid, S.; José, M.; Mansour, S. *Heterocyclic Lett.* **2011,** 2, 96-105; (b) Fakher, C.; Mehdi, M.; Hédi, B. M.; Leila, C. G.; Mansour, S. *Eur. J. Med. Chem.* **2007,** 42, 715-718.