Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Solvent-Free Synthesis of α-Aminophosphonates from N-Heterocycles, Activated Acetylenes, and Diphenyl Phosphite

Issa Yavari [a] , Anvar Mirzaei [a] & Loghman Moradi [a]
[a] Chemistry Department , Tarbiat Modares University , Tehran, Iran
Published online: 26 Jul 2010.

To cite this article: Issa Yavari , Anvar Mirzaei & Loghman Moradi (2010) Solvent-Free Synthesis of α-Aminophosphonates from N-Heterocycles, Activated Acetylenes, and Diphenyl Phosphite, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:16, 2407-2414, DOI: 10.1080/00397910903249598

To link to this article: http://dx.doi.org/10.1080/00397910903249598

Synthetic Communications®, 40: 2407–2414, 2010

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903249598

Taylor & Francis
Taylor & Francis Group

SOLVENT-FREE SYNTHESIS OF α-AMINOPHOSPHONATES FROM N-HETEROCYCLES, ACTIVATED ACETYLENES, AND DIPHENYL PHOSPHITE

Issa Yavari, Anvar Mirzaei, and Loghman Moradi
Chemistry Department, Tarbiat Modares University, Tehran, Iran

A three-component, uncatalyzed synthesis of α-aminophosphonates via the reaction of isoquinoline or benzothiazole with activated acetylenes in moderate to good yields under solvent-free conditions is described.

Keywords: Activated acetylene; α-aminophosphon; benzothiazole; diphenyl phosphite; isoquinoline; α-mercaptophosphonate

INTRODUCTION

Approaches to the synthesis of optically active or racemic α-aminophosphonates have been intensely investigated over the past few decades.[1,2] Because α-aminophosphonates are structural mimics of α-amino acids, some of these compounds exhibit very high potency in inhibiting enzymes that are involved in the metabolism of the corresponding amino acids. These compounds have already been found to act as antibacterial agents, neuroactive compounds, anticancer drugs, and pesticides,[3–6] and some of them have been commercialized.[7]

A number of synthetic methods for α-aminophosphonates have been developed. Of these, the nucleophilic addition of phosphites to imines, catalyzed by a base or an acid, is the most convenient. However, these reactions cannot be carried out in a one-pot operation with a carbonyl compound, an amine, and a dialkyl phosphite because the amine and water present during imine formation can decompose or deactivate the Lewis acid.[8–13]

N-Heterocycles are known to form zwitterions with activated acetylenes such as dimethyl acetylenedicarboxylate.[14] This type of zwitterion can be trapped by a variety of electrophiles and proton donors.[15] As part of our current studies on the development of new routes in heterocyclic synthesis,[16–18] we report a one-pot synthesis of diphenyl α-aminophosphonates **4**.

Received June 29, 2009.

Address correspondence to Issa Yavari, Chemistry Department, Tarbiat Modares University, P.O. Box 14115-175, Tehran, Iran. E-mail: yavarisa@modares.ac.ir

RESULTS AND DISCUSSION

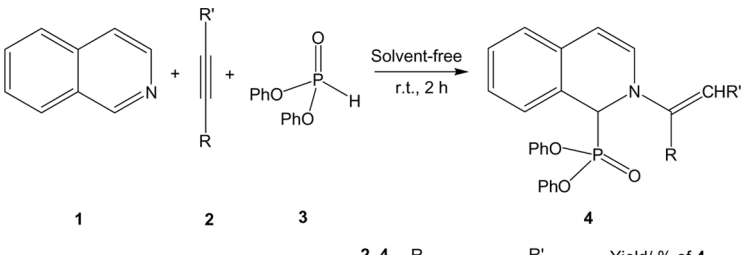
The reaction of isoquinoline (**1**) and activated acetylenes **2** in the presence of diphenyl phosphite (**3**), proceeded smoothly at rt and was complete within 2 h. The ^{1}H and ^{13}C NMR spectra of the crude products clearly indicated the formation of diphenyl α-aminophosphonates **4** in 60–90% yield (Scheme 1).

The structures of compounds **4** were deduced from their infrared (IR), ^{1}H NMR, and ^{13}C NMR spectra. For example, the ^{1}H NMR spectrum of **4a** exhibited signals for MeO (δ 3.70 and 3.97), CH (δ 5.65), and vinylic (δ 5.47, 5.98, and 6.36) H-atoms, along with multiplets for the aromatic H-atoms. The ^{1}H-decoupled ^{13}C NMR spectrum of **4a** showed 23 distinct resonances, in agreement with the proposed structure. The IR spectrum of **4a** displayed characteristic ester carbonyl and P=O bands. The ^{1}H NMR and ^{13}C NMR spectra of **4b–f** are similar to those for **4a** except for the ester moieties, which exhibited characteristic resonances in appropriate regions of the spectrum.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation (see Scheme 2). Presumably, the zwitterionic intermediate **5** formed from isoquinoline and activated acetylenes[14] is protonated by **3** to furnish intermediate **6**, which is attacked by **7** to produce **4**.

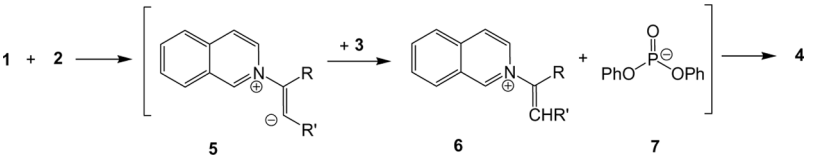
When the reaction was carried out in the presence of benzothiazole (**8**), diphenyl phosphonates **9** were obtained in moderate to good yields (Scheme 3).

In summary, we report a synthesis of dialkyl 2-[diphenoxyphosphoryl)-2(1-*H*)isoquimolinyl]-2-butendioates under noncatalytic and solvent-free conditions.

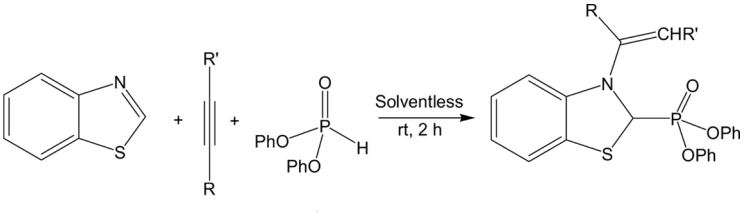


2, 4	R	R'	Yield/ % of 4
a	CO_2Me	CO_2Me	90
b	CO_2Et	CO_2Et	79
c	$CO_2{}^tBu$	$CO_2{}^tBu$	68
d	H	CO_2Me	89
e	H	CO_2Et	70
f	4-MeC_6H_4CO	4-MeC_6H_4CO	60

Scheme 1. Synthesis of diphenyl α-aminophosphonates **4**.



Scheme 2. A plausible mechanism for the formation of diphenyl α-aminophosphonates **4**.



2, 9	R	R'	Yield/ % of 9
a	CO_2Me	CO_2Me	80
b	CO_2Et	CO_2Et	70
c	$CO_2{}^tBu$	$CO_2{}^tBu$	65
d	H	CO_2Me	75

Scheme 3. Synthesis of diphenyl phosphonates **9**.

Under similar reaction conditions, benzothiazole led to dialkyl 2-[2-(diphenoxyphosphoryl)-1,3-benzothiazol-3(2*H*)-yl]-2-butendioates. The present procedure has the advantage that the reactants can be mixed without any prior activation or modification.

EXPERIMENTAL

Compounds **1**–**3** were obtained from Fluka and were used without further purification. Melting points were determined on an Electrothermal-9100 apparatus. IR spectra wee measured on a Shimadzu IR-460 spectrometer. ^1H and ^{13}C NMR spectra were measured on a Bruker DRX-500 Avance instrument in $CDCl_3$ at 500.1 and 125.7 MHz, respectively; δ in are stated in parts per million, and J in are stated in hertz. EI-MS (70 eV) were determined on a Finnigan-MAT-8430 mass spectrometer, in m/z. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer.

General Procedure for Synthesis of Compounds 4 and 9

Compound 2 (2 mmol) was added to a stirred solution of 0.47 g of diphenyl phosphite (2 mmol) and **1** or **8** (2 mmol) at rt. After completion of the reaction (1–2 h), as indicated by thin-layer chromatography (TLC; AcOEt/hexane, 2:1), the mixture was separated by column chromatography (SiO_2, Merck 230–240 mesh) using hexane/AcOEt 4:1 as eluent to afford the pure product.

Data

Dimethyl 2-[diphenoxyphosphoryl)-2(1*H*)isoquinolinyl]-2-butenedioate (4a). White powder, mp 157–159 °C, yield 0.46 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 2925, 1730 (C=O), 1693 (C=O), 1587, 1480, 1257 (P=O), 1149, 929, 764. ^1H NMR: δ = 3.70 (3H, s, MeO), 3.97 (3H, s, MeO), 5.47 (1H, d, $^5J_{PH} = 1.9$, CH), 5.65 (1H, d, $^2J_{PH} = 12.9$, CH), 5.98 (1H, d, $^3J_{HH} = 7.6$, CH), 6.36 (1H, d, $^3J_{HH} = 7.6$, 7.6, CH), 6.76 (2H, d, $^3J_{HH} = 8.4$, 2 CH), 7.03 (2H, d, $^3J_{HH} = 8.4$, 2 CH), 7.06–7.08

(2H, m, 2 CH), 7.14–7.19 (3H, m, 3 CH), 7.24–7.32 (5H, m, 5 CH). ^{13}C NMR: δ = 51.3 (MeO), 53.2 (MeO), 57.8 (d, $^{1}J_{PC}$ = 155.2, P-CH), 92.8 (CH), 115.5 (CH), 119.9 (d, $^{3}J_{CP}$ = 4.2, 2 CH), 120.3 (d, $^{3}J_{CP}$ = 4.2, 2 CH), 123.7 (CH), 125.0 (CH), 125.1 (CH), 125.2 (d, $^{3}J_{CP}$ = 2.8, CH), 125.9 (CH), 127.6 (CH), 127.8 (d, $^{2}J_{CP}$ = 6.2, 6.2, C), 129.3 (d, $^{3}J_{CP}$ = 5.0, C), 129.4 (2 CH), 129.6 (2 CH), 130.9 (d, $^{3}J_{CP}$ = 3.8, C), 149.6 (CH), 150.1 (d, $^{2}J_{CP}$ = 10.5, C), 150.2 (d, $^{2}J_{CP}$ = 10.5, C), 164.6 (C=O), 164.8 (C=O). ^{31}P NMR: δ = 10.1. EI-MS: 505 (2, M^+), 376 (5), 317 (8), 285 (20), 272 (100), 223 (25), 129 (75), 94 (30), 77 (60), 39 (50). Anal. calc. for $C_{27}H_{24}NO_7P$ (505.46): C, 64.16; H, 4.79; N, 2.77. Found: C, 64.31; H, 4.70; N 2.80.

Diethyl 2-[diphenoxyphosphoryl)-2(1*H*)isoquinolinyl]-2-butenedioate (4b). White powder, mp 134–136 °C, yield 0.42 g (79%). IR (KBr) (ν_{max}/cm^{-1}): 2930, 1733 (C=O), 1690 (C=O), 1590, 1470, 1260 (P=O), 1150, 935, 754. ^{1}H NMR: δ = 1.26 (3H, t, $^{3}J_{HH}$ = 7.1, Me), 1.38 (3H, t, $^{3}J_{HH}$ = 7.1, Me), 3.70 (2H, q, $^{3}J_{HH}$ = 7.1, CH_2O), 3.97 (2H, q, $^{3}J_{HH}$ = 7.1, CH_2O), 5.45 (1H, d, $^{5}J_{PH}$ = 1.8, CH), 5.66 (1H, d, $^{2}J_{PH}$ = 13.0, CH), 5.96 (1H, d, $^{3}J_{HH}$ = 7.6, CH), 6.39 (1H, d, $^{3}J_{HH}$ = 7.6, 7.6, CH), 6.76 (2H, d, $^{3}J_{HH}$ = 8.4, 2 CH), 7.04–7.08 (4H, m, 4 CH), 7.13–7.19 (3H, m, 3 CH), 7.24–7.31 (5H, m, 5 CH). ^{13}C NMR: δ = 13.7 (Me), 14.2 (Me), 57.8 (d, $^{1}J_{PC}$ = 155.2, P-C), 59.9 (CH_2O), 62.5 (CH_2O), 93.2 (d, $^{3}J_{CP}$ = 2.9, CH), 111.3 (CH), 119.0 (d, $^{3}J_{CP}$ = 4.2, 2 CH), 120.3 (d, $^{3}J_{CP}$ = 4.4, 2 CH), 123.7 (CH), 125.0 (CH), 125.1 (CH), 125.2 (d, $^{3}J_{CP}$ = 3.0, CH), 126.0 (CH), 127.6 (d, $^{4}J_{CP}$ = 2.6, CH), 127.7 (d, $^{2}J_{CP}$ = 5.6, C), 129.3 (d, $^{3}J_{CP}$ = 3.4, C), 129.3 (2 CH), 129.5 (2 CH), 131.0 (d, $^{3}J_{CP}$ = 3.8, C), 149.6 (CH), 150.2 (d, $^{2}J_{CP}$ = 11.0, C), 150.3 (d, $^{2}J_{CP}$ = 11.0, 11.0, C), 164.1 (C=O), 166.3 (C=O). ^{31}P NMR: δ = 12.4. EI-MS: 533 (1, M^+), 404 (6), 331 (9), 285 (22), 300 (100), 237 (27), 129 (73), 94 (29), 77 (62), 39 (49). Anal. calc. for $C_{29}H_{28}NO_7P$ (533.51): C, 65.29; H. 5.29; N, 2.63. Found: C, 65.11; H, 5.23; N, 2.65.

Di(*t*-butyl) 2-[diphenoxyphosphoryl)-2(1*H*)isoquinolinyl]-2-butenedioate (4c). White powder, mp 136–138 °C, yield 0.40 g (68%). IR (KBr) (ν_{max}/cm^{-1}): 2932, 1725 (C=O), 1690 (C=O), 1600, 1490, 1237 (P=O), 1135, 923, 746. ^{1}H NMR: δ = 1.45 (9H, s, Me_3C), 1.59 (9H, s, Me_3C), 5.35 (1H, d, $^{5}J_{PH}$ = 1.6, CH), 5.64 (1H, d, $^{2}J_{PH}$ = 12.6, CH), 5.90 (1H, d, $^{3}J_{HH}$ = 7.6, CH), 6.46 (1H, d, $^{3}J_{HH}$ = 7.60, CH), 6.76 (2H, d, $^{3}J_{HH}$ = 8.4, 2 CH), 7.13–7.17 (4H, m, 4 CH), 7.19–7.21 (3H, m, 3 CH), 7.25–7.31 (5H, m, 5 CH). ^{13}C NMR: δ = 27.9 (Me_3C), 28.3 (Me_3C), 57.2 (d, $^{1}J_{PC}$ = 160.0, P-C), 83.7 (O*C*Me$_3$), 84.0 (O*C*Me$_3$), 94.9 (CH), 119.4 (CH), 120.0 (d, $^{3}J_{CP}$ = 4.2, 2 CH), 120.3 (d, $^{3}J_{CP}$ = 4.2, 2 CH), 123.7 (CH), 125.0 (CH), 125.2 (CH), 125.3 (d, $^{3}J_{CP}$ = 5.6, CH), 126.3 (CH), 127.5 (CH), 127.7 (d, $^{2}J_{CP}$ = 5.6, C), 129.2 (2 CH), 129.3 (C), 129.4 (2 CH), 131.3 (d, $^{3}J_{CP}$ = 3.0, C), 149.4 (CH), 150.0 (d, $^{2}J_{CP}$ = 11.4, C), 150.2 (d, $^{2}J_{CP}$ = 11.4, C), 163.0 (C=O), 165.6 (C=O). ^{31}P NMR: δ = 11.6. EI-MS: 589 (2, M^+), 460 (7), 359 (11), 285 (26), 356 (100), 265 (24), 129 (72), 94 (31), 77 (62), 39 (53). Anal. calc. for $C_{33}H_{36}NO_7P$ (589.62): C, 67.22; H, 6.15; N, 2.38. Found: C, 67.20; H, 6.20; N, 2.45.

Methyl (*E*)-3-[diphenoxyphosphoryl)-2(1*H*)isoquinolinyl]-2-propenoate (4d). White powder, mp 190–192 °C, yield 0.40 g (89%). IR (KBr) (ν_{max}/cm^{-1}): 1680 (C=O), 1615, 1583, 1257 (P=O), 1153, 993, 766. ^{1}H NMR: δ = 3.72 (3H, s, MeO), 5.30 (1H, dd, $^{3}J_{HH}$ = 13.5, $^{5}J_{PH}$ = 1.7, CH), 5.58 (1H, d, $^{2}J_{PH}$ = 12.8, CH),

5.88 (1H, d, $^3J_{HH} = 7.5$, CH), 6.45 (1H, d, $^3J_{HH} = 7.5$, CH), 6.83 (2H, d, $^3J_{HH} = 8.0$, 2 CH), 6.98 (2H, d, $^3J_{HH} = 8.0$, 2 CH), 7.04–7.17 (3H, m, 3 CH), 7.19–7.20 (2H, m, 2 CH), 7.23–7.31 (5H, m, 5 CH), 7.53 (1 , d, $^3J_{HH} = 13.5$, CH). ^{13}C NMR: δ = 51.0 (MeO), 58.8 (d, $^1J_{PC} = 160.0$, P-C), 92.5 (CH), 109.3 (CH), 119.9 (d, $^3J_{CP} = 4.2$, 2 CH), 120.1 (d, $^3J_{CP} = 4.2$, 2 CH), 123.2 (CH), 125.0 (CH), 125.1 (CH), 125.2 (d, $^3J_{CP} = 3.0$, CH), 127.4 (CH), 127.8 (d, $^2J_{CP} = 5.5$, C), 128.5 (CH), 129.3 (d, $^3J_{CP} = 3.2$, C), 129.5 (2 CH), 129.6 (2 CH), 131.4 (d, $^3J_{CP} = 3.6$, CH), 147.3 (CH), 150.1 (d, $^2J_{CP} = 10.6$, C), 150.2 (d, $^2J_{CP} = 10.6$, C), 168.5 (C=O). ^{31}P NMR: δ = 11.5. EI-MS: 447 (1, M^+), 318 (5), 259 (12), 214 (100), 165 (20), 129 (70), 94 (28), 77 (56), 39 (46). Anal. calc. for $C_{25}H_{22}NO_5P$ (447.42): C, 67.11; H, 4.96; N, 3.13. Found: C, 67.42; H, 4.87; N 3.05.

Ethyl (*E*)-3-[diphenoxyphosphoryl-2(1*H*)isoquinolinyl]-2-propenoate (4e). White powder, mp 128–130 °C, yield 0.32 g (70%). IR (KBr) (ν_{max}/cm^{-1}): 1684 (C=O), 1613, 1584, 1477, 1258 (P=O), 1153, 936, 766. ^{1}H NMR: δ = 1.26 (3H, t, $^3J_{HH} = 7.1$, Me), 4.15 (2H, q, $^3J_{HH} = 7.1$, CH_2O), 5.27 (1H, dd, $^3J_{HH} = 13.5$, $^5J_{PH} = 2.0$, CH), 5.56 (1H, d, $^2J_{PH} = 12.5$, CH), 5.85 (1H, d, $^3J_{HH} = 7.5$, CH), 6.43 (1H, d, $^3J_{HH} = 7.5$, CH), 6.81 (2H, d, $^3J_{HH} = 8.5$, 2 CH), 6.97 (2H, d, $^3J_{HH} = 8.5$, 2 CH), 7.01–7.10 (3H, m, 3 CH), 7.14–7.17 (2H, m, 2 CH), 7.20–7.28 (5H, m, 5 CH), 7.50 (1H, d, $^3J_{HH} = 13.5$, CH). ^{13}C NMR: δ = 14.5 (Me), 58.8 (CH, d, $^1J_{PC} = 158.0$, P-C), 59.7 (CH_2O), 93 (CH), 109.2 (CH), 120.0 (d, $^3J_{CP} = 4.2$, 2 CH), 120.2 (d, $^3J_{CP} = 4.2$, 2 CH), 123.2 (CH), 125.0 (CH), 125.1 (CH), 125.2 (d, $^3J_{CP} = 3.0$, CH), 127.4 (CH), 127.9 (d, $^2J_{CP} = 5.5$, C), 128.7 (CH), 129.3 (d, $^3J_{CP} = 3.4$, C), 129.5 (2 CH), 129.6 (2 CH), 131.5 (d, $^3J_{CP} = 3.7$, CH), 147.1 (CH), 150.2 (d, $^2J_{CP} = 11.1$, C), 150.3 (d, $^2J_{CP} = 10.5$, C), 168.1 (C=O). ^{31}P NMR: δ = 9.3. EI-MS: 461 (2, M^+), 332 (6), 273 (10), 228 (100), 179 (23), 129 (68), 94 (29), 77 (55), 39 (46). Anal. calc. for $C_{26}H_{24}NO_5P$ (461.45): C, 67.67; H, 5.24; N, 3.04. Found: C, 67.72; H, 5.20; N, 2.90.

Diphenyl {2-[(*E*)-1-(4-methylbenzoyl)-3-(4-metylphenyl)-3-oxo-1-propenyl]-1,2-dihydro-1-isoquinolinyl}phosphonate (4f). White powder, mp 159–161 °C, yield 0.38 g (60%). IR (KBr) (ν_{max}/cm^{-1}): 2923, 1664 (C=O), 1593 (C=O), 1513, 1480, 1268 (P=O), 1177, 933, 756. ^{1}H NMR: δ = 2.35 (3H, s, Me), 2.37 (3H, s, Me), 5.86 (1H, d, $^2J_{PH} = 7.9$, CH), 6.05 (1H, broad, CH), 6.74 (2H, d, $^3J_{HH} = 7.8$, 2 CH), 6.97–7.08 (4H, m, 4 CH), 7.11–7.19 (6H, m, 6 CH), 7.20–7.27 (6H, m, 6 CH), 7.29–7.41 (4H, m, 4 CH), 7.77 (2H, d, $^3J_{HH} = 7.8$, 2 CH). ^{13}C NMR: δ = 21.2 (Me), 21.8 (Me), 59.0 (d, $^1J_{PC} = 181.0$, P-CH), 115.4 (CH), 119.9 (CH), 120.0 (CH), 120.1 (d, $^3J_{CP} = 3$, 2 CH), 120.4 (d, $^3J_{CP} = 3$, 2 CH), 120.7 (CH), 125.4 (CH), 125.5 (CH), 126.3 (C), 127.2 (C), 127.8 (CH), 128.2 (2 CH), 128.6 (2 CH), 128.7 (CH), 129.1 (2 CH), 129.4 (2 CH), 129.5 (2 CH), 129.7 (C), 129.8 (2 CH), 129.9 (CH), 130.0 (C), 130.1 (C), 130.2 (C), 133.4 (CH), 142.9 (C), 150.1 (C), 150.2 (C), 156.4 (C=O), 187.4 (C=O). ^{31}P NMR: δ = 13.2. EI-MS: 625 (1, M^+), 496 (14), 392 (100), 377 (3), 283 (22), 129 (65), 94 (25), 77 (66), 39 (45). Anal. calc. for $C_{39}H_{32}NO_5P$ (625.66): C, 74.87; H, 5.16; N, 2.24. Found: C, 74.99; H, 5.10; N, 2.30.

Dimethyl 2-[2-(diphenoxyphosphoryl)-1,3-benzothiazol-3(2*H*)-yl]-2-butenedioate (9a). White powder, mp 150–152 °C, yield 0.41 g (80%). IR (KBr)

(ν_{max}/cm^{-1}): 2920, 1730 (C=O), 1725 (C=O), 1504, 1475, 1258 (P=O), 940, 749. ^{1}H NMR: δ = 3.59 (3H, s, MeO), 3.66 (3H, s, MeO), 5.89 (1H, broad, CH), 6.34 (2H, d, $^3J_{HH}$ = 8, 2 CH), 6.39 (1H, d, $^2J_{PH}$ = 11.4, CH), 6.92–6.95 (2H, m, 2 CH), 7.01–7.04 (2H, m, 2 CH), 7.05–7.10 (3H, m, 3 CH), 7.19–7.24 (5H, m, 5 CH). ^{13}C NMR: δ = 52.5 (MeO), 52.9 (MeO), 63.5 (d, $^1J_{PC}$ = 178.0, P-CH), 99.9 (CH), 110.9 (CH), 119.8 (d, $^3J_{CP}$ = 4.4, 2 CH), 119.9 (d, $^3J_{CP}$ = 4.4, 2 CH), 120.2 (CH), 120.3 (CH), 125.5 (d, $^4J_{CP}$ = 4.0, CH), 125.7 (CH), 129.1 (CH), 129.5 (2 CH), 129.6 (2 CH), 129.7 (C), 141.4 (C), 143.4 (C), 150.2 (d, $^2J_{CP}$ = 10.0, C), 150.4 (d, $^2J_{CP}$ = 9.6, C), 163.7 (C=O), 163.8 (C=O). ^{31}P NMR: δ = 14.3. EI-MS: 511 (1, M$^+$), 509 (7), 452 (12), 278 (100), 192 (22), 160 (23), 135 (16), 94 (28), 77 (32), 39 (21). Anal. calc. for $C_{25}H_{22}NO_7PS$ (511.48): C, 58.71; H, 4.34; N, 2.74. Found: C, 58.80; H, 4.30; N, 2.68.

Diethyl 2-[2-(diphenoxyphosphoryl)-1,3-benzothiazol-3(2*H*)-yl]-2-butenedioate (9b). White powder, mp 129–131 °C, yield 0.38 g (70%). IR (KBr) (ν_{max}/cm^{-1}): 2910, 1726 (C=O), 1677 (C=O), 1514, 1478, 1255 (P=O), 933, 751. ^{1}H NMR: δ = 1.11 (3H, t, $^3J_{HH}$ = 9.8, Me), 1.18 (3H, t, $^3J_{HH}$ = 9.8, Me), 4.10 (2H, q,$^3J_{HH}$ = 9.8, CH_2O), 4.25 (2H, q, $^3J_{HH}$ = 9.8, CH_2O), 6.37 (1H, d, $^5J_{PH}$ = 7.96, CH), 6.43 (1H, d, $^2J_{PH}$ = 11.5, CH), 6.80 (1H, m, CH), 6.93–6.96 (2H, m, 2 CH), 7.04–7.16 (6H, m, 6 CH), 7.23–7.30 (5H, m, 5 CH). ^{13}C NMR: δ = 13.7 (Me), 13.8 (Me), 61.1 (CH_2O), 62.4 (CH_2O), 63.5 (d, $^1J_{PC}$ = 178.5, P-CH), 111.1 (CH), 120.2 (d, $^3J_{CP}$ = 1.4, 2 CH), 120.3 (d, $^3J_{CP}$ = 1.5, 2 CH), 121.5 (CH), 121.8 (CH), 124.6 (CH), 125.0 (d, $^4J_{CP}$ = 2.4, CH), 125.4 (CH), 125.5 (CH), 129.4 (2 CH), 129.5 (2 CH), 129.7 (C), 139.6 (C), 143.6 (C), 150.2 (d, $^2J_{CP}$ = 10.5, C), 150.5 (d, $^2J_{CP}$ = 9.8, 9.8, C), 163.2 (C=O), 163.3 (C=O). ^{31}P NMR: δ = 12.9. EI-MS: 539 (1, M$^+$), 537 (5), 466 (13), 306 (100), 206 (20), 160 (20), 135 (18), 94 (25), 77 (30), 39 (20). Anal. calc. for $C_{27}H_{26}NO_7PS$ (539.54): C, 60.11; H, 4.86; N, 2.60. Found: C, 59.95; H, 4.75; N, 2.66.

Di(*t*-butyl) 2-[2-(diphenoxyphosphoryl)-1,3-benzothiazol-3(2*H*)-yl]-2-butenedioate (9c). White powder, mp 127–129 °C, yield 0.39 g (65%). IR (KBr) (ν_{max}/cm^{-1}): 2928, 1724 (C=O), 1726 (C=O), 1516, 1486, 1253 (P=O), 955, 769. ^{1}H NMR: δ = 1.40 (9H, s, *Me*$_3$C), 1.57 (9H, s, *Me*$_3$C), 6.41 (1H, d, $^2J_{PH}$ = 14.5, CH), 6.78 (1H, d, $^5J_{PH}$ = 5.0, CH), 7.08 (1H, m, CH), 7.19–7.24 (2H, m, 2 CH), 7.25–7.27 (6H, m, 6 CH), 7.32–7.35 (5H, m, 5 CH). ^{13}C NMR: δ = 27.8 (*Me*$_3$C), 27.9 (*Me*$_3$C), 63.5 (d, $^1J_{PC}$ = 178.2, P-CH), 82.1 (O*C*Me$_3$), 83.4 (O*C*Me$_3$), 111.4 (CH), 120.1 (d, $^3J_{CP}$ = 4.9, 2 CH), 120.7 (d, $^3J_{CP}$ = 4.5, 2 CH), 121.3 (CH), 121.7 (CH), 123.3 (CH), 125.0 (CH, d, $^4J_{CP}$ = 5, CH), 125.5 (CH), 125.6 (CH), 129.7 (2 CH), 129.8 (2 CH), 126.3 (C), 139.7 (C), 13.9 (C), 149.9 (d, $^2J_{CP}$ = 7.6, C), 150.5 (d, $^2J_{CP}$ = 7.4, C), 162.4 (C=O), 162.9 (C=O). ^{31}P NMR: δ = 12.8. EI-MS: 594 (2, M$^+$), 494 (11), 362 (100), 234 (23), 160 (25), 135 (17), 94 (29), 77 (32), 39 (24). Anal. calc. for $C_{31}H_{34}NO_7PS$ (594.64): C, 62.51; H, 5.75; N, 2.35. Found: C, 62.45; H, 5.65; N, 2.41.

Methyl (*E*)-3-[2-(diphenoxyphosphoryl)-1,3-benzothiazol-3(2*H*)-yl]-2-propenoate (9d). White powder, mp 145–147 °C, yield 0.34 g (75%). IR (KBr) (ν_{max}/cm^{-1}): 2900, 1695, (C=O), 1577, 1462, 1249 (P=O), 1159, 911, 731. ^{1}H NMR: δ = 3.72 (3H, s, MeO), 5.59 (1H, dd, $^3J_{HH}$ = 13.5, $^5J_{PH}$ = 1.2, CH), 5.88 (1H, d, $^2J_{PH}$ = 5.2, CH), 6.95 (2H, d, $^3J_{HH}$ = 9.8, CH), 6.98–7.02 (4H, m, 4 CH),

7.1–7.15 (4H, m, 4 CH), 7.21–7.26 (4H, m, 4 CH), 7.83 (1H, d, $^{3}J_{HH} = 13.5$, CH). ^{13}C NMR: $\delta = 51.19$ (MeO), 61.5 (d, $^{1}J_{PC} = 181.1$, P-CH), 95.9 (CH), 112.4 (CH), 120.0 (d, $^{3}J_{CP} = 4.2$, 2 CH), 120.1 (d, $^{3}J_{CP} = 4.4$, 2 CH), 122.7 (CH), 124.7 (CH), 125.4 (d, $^{4}J_{CP} = 5.4$, CH), 126.5 (CH), 127.3 (CH), 129.5 (C), 129.7 (2 CH), 129.8 (2 CH), 141.4 (C), 143.4 (CH), 150.2 (d, $^{2}J_{CP} = 10.5$, C), 150.4 (d, $^{2}J_{CP} = 9.8$, C), 168.4 (C=O). ^{31}P NMR: $\delta = 11.4$. EI-MS: 453 (1, M^{+}), 451 (8), 394 (12), 220 (100), 192 (20) 160 (19), 135 (22), 94 (26), 77 (31), 39 (21). Anal. calc. for $C_{23}H_{20}NO_5PS$ (453.45): C, 60.92; H, 4.45; N, 3.09. Found: C, 60.85; H, 4.51; N, 3.12.

REFERENCES

1. Thomas, A. A.; Sharpless, K. B. The catalytic asymmetric aminohydroxylation of unsaturated phosphonates. *J. Org. Chem.* **1999**, *64*, 8379–8385.
2. Albrecht, S.; Defoin, A.; Salomon, E.; Tarnus, C.; Wetterholmb, A.; Haeggstro, J. Z. Synthesis and structure–activity relationships of novel nonpeptidic metallo aminopeptidase inhibitors. *Bioorg. Med. Chem.* **2006**, *14*, 7241–7257.
3. Joossens, J.; Veken, P. V.; Surpateanu, G.; Anne, A. M.; El-Sayed, I.; Ali, O. M.; Augustyns, K.; Haemers, A. Diphenyl phosphonate inhibitors for the urokinase-type plasminogen activator: Optimization of the P4 position. *J. Med. Chem.* **2006**, *49*, 5785–5793.
4. Qi, X.; Lee, S. H.; Kwon, J. Y.; Kim, Y.; Kim, S. J.; Lee, Y. S.; Yoon, J. Aminobromination of unsaturated phosphonates. *J. Org. Chem.* **2003**, *68*, 9140–9143.
5. Ntai, I.; Manier, M. L.; Hachey, D. L.; Bachmann, B. O. Biosynthetic origins of C-P bond containing tripeptide K-26. *Org. Lett.* **2005**, *7*, 2763–2765.
6. Joly, G. D.; Jacobsen, E. N. Thiourea-catalyzed enantioselective hydrophosphonylation of imines: Practical access to enantiomerically enriched α-amino phosphonic acids. *J. Am. Chem. Soc.* **2004**, *126*, 4102–4103.
7. Berlicki, L.; Kafarski, P. Computer-aided analysis and design of phosphonic and phosphinic enzyme inhibitors as potential drugs and agrochemicals. *Curr. Org. Chem.* **2005**, *9*, 1829–1950.
8. Azizi, N.; Saidi, M. R. Synthesis of tertiary α-amino phosphonate by one-pot, three-component coupling mediated by LPDE. *Tetrahedron* **2003**, *59*, 5329–5332.
9. Xu, F.; Luo, Y. W. J.; Shen, Q.; Chen, H. Facile one-pot synthesis of phosphonates using lanthanide chloride as catalyst. *Heteroat. Chem.* **2006**, *17*, 389–392.
10. Bioton, L. D.; Villemin, D.; Lohier, J. F.; Sopkova, J.; Jaffr, P. A. Synthesis of triazolylalkylphosphonate starting from ω-azidoalkylphosphonates or α-alkynylphosphonates. *Tetrahedron* **2007**, *63*, 9677–9684.
11. Xu, F.; Luo, Y.; Deng, M.; Shen, Q. One-pot synthesis of α-amino phosphonates using samarium diiodide as a catalyst precursor. *Eur. J. Org. Chem.* **2003**, *24*, 4728–4730.
12. Vanderhoydonck, B.; Stevens, C. V. Conjugate addition to 1-phosphono-2-aza-1,3-butadienes: Synthesis of phosphonylated γ-lactams. *J. Org. Chem.* **2005**, *70*, 191–198.
13. Atherton, F. R.; Hassal, C. H.; Lambert, R. W. Synthesis and structure–activity relationships of antibacterial phosphonopeptides incorporating (l-aminoethy1)phosphonic acid and (aminomethy1)phosphonic acid. *J. Med. Chem.* **1986**, *29*, 29–40.
14. Dillinger, H. J.; Fengler, G.; Schumann, D.; Winterfeldt, E. Additionen an die dreifachbindung—XXII: Das thermodynamisch kontrollierte addukt aus tert.butylisonitril und acetylendicarbonester. *Tetrahedron* **1974**, *30*, 2561–2564.
15. Yavari, I.; Moradi, L.; Mokhtarporiani-Sanandej, A.; Mirzaei, A. Efficient synthesis of trialkyl 3-phenylbuta-1,3-diene-1,2,4-tricarboxylates by a novel one-pot multicomponent reaction. *Helv. Chim. Acta* **2006**, *90*, 392–394.

16. Yavari, I.; Zabarjad-Shiraz, N.; Partovi, T. Stereoselective synthesis of new phosphorylated *N,N′*-dimethylbarbituric acids. *Synth. Commun.* **2002**, *32*, 2763–2769.
17. Yavari, I.; Sabbaghan, M. A synthesis of functionalized pyrroles by reaction of 3,4-diacetylhexane-2,5-dione with primary amines in water. *Synth. Commun.* **2007**, *37*, 1791–1800.
18. Yavari, I.; Mirzaei, A.; Moradi, L.; Mokhtarporiani-Sanandej, A. Efficient synthesis of trialkyl (*E*)-3-[3-oxo-2–3,4-dihydro-2-(1*H*)-quinoxalinylidene]-prop-1-ene-1,2,3 tricarboxylates. *Synth. Commun.* **2007**, *37*, 1195–1200.