SYNTHESES OF 1-BENZYLOXYAMINOALKYLPHOSPHONATES

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Abstract- *A synthesis of 1-benzyloxyaminoalkylphosphonates was achieved via ionic hydrogenation of diethyl 1-benzyloxyiminoalkylphosphonates by triethylsilane-trifluoroacetic acid. Diethyl 1-benzyloxyaminomethylphosphonate, which could not prepared by reduction, was synthesized by a simple one pot reaction.*

INTRODUCTION

N-Hydroxyamino acids have been known for over 100 years but their derivatives have only recently been identified as constituents of natural products [1-4]. Hydroxylamine derivatives are found chiefly in metabolites of microorganisms.[3] Reviews of such hydroxamic acids have been given by Mikes,[1] Chimiac,[2] Neilands,[3] and Meahr.[4]

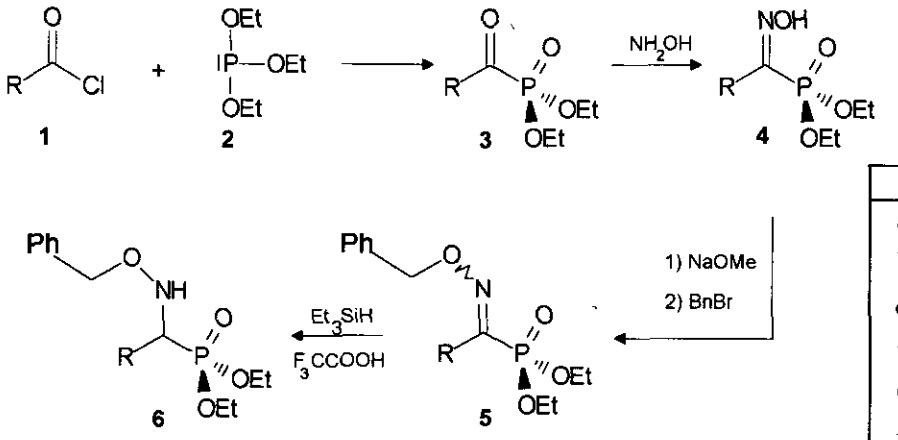
Although the biological role of these compounds is not completely clear, they have been reported to act as growth factors, antibiotics antitumour or fungistatic agents. [5] Moreover *N*-hydroxypeptides have been found in human and mouse tumours.[6]

Phosphonate analogs of amino acids, either isolated from nature or obtained synthetically, display a wide range of interesting properties which may have considerable economic and clinical potential.[7] In addition to phosphonoamino acids, their peptides also show interesting activity mainly antibacterial and as inhibitors of proteases.[8] Compounds containing phosphonate and *N*-hydroxyamino functions are until now poorly explored; only a few reports describe the synthesis of *N*-hydoxyaminoalkylphosphonates. Vasella obtained alkyl *N*-

glycosyl-*N*-hydroxyaminoalkylphosphonates in good yields and high diastereomeric excess by nucleophilic addition of lithium dialkylphosphite to *N*-glycosylnitrones. [9] Elhaddadi and co-workers reported a direct method of preparing 1-benzyloxyaminophosphonic acids by reaction of phosphorus trichloride with *O*-benzyloximes.[10] The present paper describes the results of our studies concerning the reduction of diethyl 1-benzyloxyiminoalkylphosphonates by triethylsilane-trifluoroacetic acid and the preparation of diethyl 1-benzyloxyaminomethylphosphonate *via* a simple one pot synthesis.

RESULTS AND DISCUSSION

The reduction of 1-oxyiminocarboxylic acids or esters by boron complexes is an attractive and simple route for the synthesis of the corresponding hydroxyamino compounds. While cyanoborohydrides are required for the reduction of 1-oxyiminocarboxylic acids, the use of borane amine complexes under acidic conditions is described for reduction of α-benzyloxyimino acids esters.[11] Application of this method using the corresponding 1-benzyloxyiminoalkylphosphonates,[12] however, was unsatisfactory; yields were low and the resulting products were mainly composed of unreacted 1-benzyloxyiminophosphonates, which hardly could be separated from the desired products.[13]



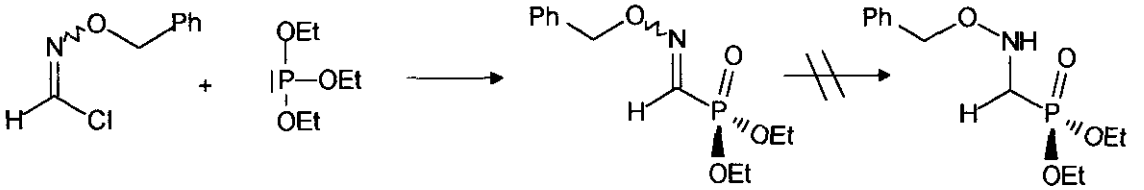
	R
a	Me
b	Et
c	iPr
d	iBu
e	Ph
f	Bn
g	CH_2CH_2Ph

Scheme 1

Recently Hiyama and co-workers reported the reduction of oximes with triethylsilane-trifluoracetic acid.[14] We were able to apply this method with a slight modification for the selective reduction of 1–benzyloxyiminoalkyl phosphonates (**5**) to the corresponding 1-benzyloxyaminoalkylphosphonates (**6**).

Reduction of **5** by 2 eq. of triethylsilane in trifluoracetic acid at 40°C afforded **6** in good yields (50 - 79%) as colourless oils, which were isolated by collumn chromatography on silica gel, using ether/pentane. The progress of reduction could be observed by ^{1}H-nmr spectroscopy. After evaporation of all volatile compounds under reduced pressure (40°C / 0.01 torr) monitoring by ^{1}H-nmr spectroscopy revealed slow decrease of the signal at δ= 5.2 - 5.3 ppm, attributed to the benzylic protons of **5** , and a concomitant growth of a singlet at δ = 4.7 - 4.8 ppm belonging to the benzylic protons of **6** .

Compound (**8**) could not be prepared according to Scheme 1 and was synthesized by the *Michaelis-Arbusov reaction* as depicted in Scheme 2; contrary to **5a - g** it was not possible to reduce **8** by ionic hydrogenation.

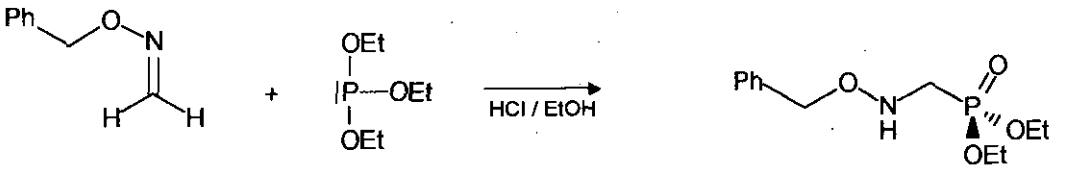


7 **2** **8** **9**

E/Z = 1:9

Scheme 2

Since no starting material was recovered, we are inclined to contribute this failure to decomposition of **8**. Consequently we sought a more mild and convenient way for the preparation of **9**. We found, that reaction of *O*-benzylformaldoxime (**10**) with triethylphosphite (**2**) in 0.5 M ethanolic HCl resulted in formation of diethyl 1-benzyloxyaminomethylphosphonate (**9**). It is especially noteworthy, that this reaction was limited to compound (**10**); attempts to prepare **5** by this method failed.



10 **2** **9**

Scheme 3

EXPERIMENTAL

Melting points were determined on an electrothermal digital melting point apparatus and are uncorrected. Ir spectra were recorded on a Carl Zeiss DMR4 spectrophotometer. ^{1}H- and ^{13}C-Nmr spectra were obtained with a Bruker WM-250 instrument using $CDCl_3$ as solvent unless otherwise indicated. All chemical shifts are reported in ppm downfield from internal tetramethylsilane; coupling constants J are given in Hz. ^{31}P-Nmr spectra were recorded on a Bruker AC 200 at 81.0 MHz (internal standard 85% H_3PO_4). EI-mass spectra were recorded on a Varian MAT 311A spectrometer (70eV).-

General procedure for preparation of 1-benzyloxyaminophosphonates (6):

To a solution of 10 mmol of 1-benzyloxyiminophosphonate[10] (**5**) (**5a**: 2.85 g, **5b**: 2.99 g, **5c**: 3.15 g, **5d**: 3.3 g, **5e:** 3.48 g, **5f:** 3.61 g, **5g:** 3.75 g) in trifluoroacetic acid (20 ml) under nitrogen was added 2.4 g (20 mmol) of triethylsilane . The pale yellow solution was stirred at 40°C for 12 h. Evaporation of all volatile compounds under reduced pressure (40°C/ 0.01 torr) afforded a pale yellow oil. The residue was taken up in ether and washed with 1M Na_2CO_3 (25 ml). The organic phase was dried over anhydrous Na_2SO_4, evaporated to dryness and the oily residue was chromatographed on silica gel with ether to give **6** as colorless oils.

Diethyl 1-benzyloxyaminoethylphosphonate (6a) - 1.9 g (66%) were obtained after chromatographic separation, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.30 (m, 6H, O-CH_2-CH_3), 1.38 (dd, $^{2}J_{PH}$= 16 Hz, $^{3}J_{HH}$= 7 Hz, 3H, **H-2**), 3.38(dq, $^{2}J_{PH}$= 14 Hz, $^{3}J_{HH}$= 7.1 Hz, 1H, **H-1**), 4.09 (m, 4H, O-CH_2-CH_3), 4.72 (s, 2H, O-CH_2-Ph), 6.85 (bs, 1H, **N-H**), 7.25 - 7.40 (m, 5H, H_{Ar}). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ=13.3 (s, **C-2**, $^{2}J_{PC}$= 0 Hz), 16.3 (d, $^{3}J_{PC}$= 3 Hz, O-CH_2-CH_3), 53.9 (d, $^{1}J_{PC}$= 146 Hz, **C-1**), 62.1 (d, $^{2}J_{PC}$= 6.5 Hz, O-CH_2-CH_3), 76.9 (s, O-CH_2-Ph), 127.9, 128.3, 128.5 (s, C_{Ar}), 137.5 (s, C_i). ^{31}P-Nmr ($CDCl_3$) δ= 24.8. Ir (film) ν= 3215(m) **N-H**, 3100(w), 3070(w), 3040(m), 2990(s), 2940(m), 2910(m), 2870(m), 1500(m), 1480(m), 1465(m,sh), 1455(s), 1395(m), 1370(s), 1235(vs) **P=O**, 1165(s), 1100(s, sh), 1055(vs) ,1030(vs) **P-O-C**, 970(vs), 920(m), 880(w), 800(s), 750(s), 700(s), 610(m) cm^{-1}. Anal. Calcd for $C_{13}H_{22}NO_4P$: C,54.35; H, 7.72; N, 4.88. Found: C, 54.08; H 7.81; N, 4.89.-

Diethyl 1-benzyloxyaminopropylphosphonate (6b) - 1.87 g (62%) were obtained after chromatographic separation, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.05 (t, $^{3}J_{HH}$= 7.5 Hz, 3H, **H-3**,), 1.30 (virt. q, 6H, O-CH_2-CH_3), 1.82 (m, 2H, **H-2**), 3.12 (ddd, $^{3}J_{HHa}$= 5.5 Hz, $^{3}J_{HHb}$= 7.5 Hz, $^{2}J_{PH}$= 15 Hz, 1H, **H-1**), 4.10 (m, 4H, O-CH_2-

CH_3), 4.72 (s, 1H, O-C**H**$_2$-Ph), 5.96 (br s, 1H, N-**H**), 7.12-7.40 (m, 5H, **H**$_{AR}$). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 11.1 (d, $^3J_{PC}$= 9.4 Hz, **C-3**), 16.2 (d, $^3J_{PC}$= 5.0 Hz, OCH_2-**C**H_3), 16.3 (d, $^3J_{PC}$= 5.0 Hz, OCH_2-**C**H_3), 20.7 (s, $^2J_{PC}$= 0 Hz, **C-2**), 60.0 (d, $^1J_{PC}$= 142.7 Hz, **C-1**), 61.7 (d, $^2J_{PC}$= 6.3 Hz, OCH_2-CH_3), 61.8 (d, $^3J_{PC}$= 6 Hz, OCH_2-CH_3), 76.5 (s, O-**C**H_2-Ph), 127.7, 128.2, 128.4, (s, **C**$_{Ar}$), 137.5 (s, **C**$_i$). ^{31}P-Nmr ($CDCl_3$) δ= 25.4. Ir (film) ν= 3230(m) **N-H**, 3090(w), 3070(m), 3040(m), 2980(vs), 2940(s), 2910(s), 2890(s), 1640(m), 1500(m), 1460(s), 1395(s), 1370(s), 1250(vs) **P=O**, 1230(s), 1165(s), 1100(s), 1050(vs, b) **P-O-C**, 1030(vs, b), 970(vs, b), 950(vs, b), 785(m),750(s), 700(s) cm^{-1}. Anal. Calcd for $C_{14}H_{24}NO_4P$: C, 55.81; H, 8.02; N, 4.65; P, 10.28. Found: C, 55.66; H 8.27; N, 4.62; P, 10.13.

Diethyl 1-benzyloxyamino-2-methylpropylphosphonate (6c) 2.50 g (79%) were obtained after chromatographic workup, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.06 (d, $^3J_{HH}$= 6 Hz, 3H, **H-3**), 1.10 (d, $^3J_{HH}$= 6 Hz, 3H, **H-4**), 1.29 (m, 6H, O-CH_2-**C**H_3), 2.29 (m, 1H, **H-2**), 3.08 (dd, $^2J_{PH}$= 16 Hz, $^3J_{HH}$= 5.5 Hz, 1H, **H-1**), 4.1 (m, 4H, O-C**H**$_2$-CH_3), 4.71 (s, 2H, O-C**H**$_2$-O), 6.05 (br s, 1H, **N-H**), 7.25-7.40 (m, 5H, H$_{Ar}$). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 16.3 (d, $^3J_{PC}$= 3.6 Hz, O-CH_2-**C**H_3), 16.4 (d, $^3J_{PC}$= 5.7 Hz, O-CH_2-**C**H_3), 18.9 (d, $^3J_{PC}$= 5.3 Hz, **C-3**), 20.8 (d, $^3J_{PC}$= 8.9 Hz, **C-4**), 27.5 (s, $^2J_{PC}$= 0 Hz, **C-2**), 61.7 (d, $^2J_{PC}$= 8.6 Hz, O-CH_2-CH_3), 64.6 (d, $^1J_{PC}$= 139.4 Hz, **C-1**), 76.1 (s, O-**C**H_2-Ph), 127.8, 128.3, 128.4 (s, **C**$_{Ar}$), 137.6 (s, **C**$_i$). ^{31}P-Nmr ($CDCl_3$) δ= 25.3. Ir (film) ν= 3240(w) **NH**, 3100(w), 3070(w), 3040(w),2980(m), 2940(m) 2910(m), 2870(m), 1650(w), 1500(w), 1475(m), 1455(m), 1390(m), 1370(m), 1250(s) **P=O**, 1165(m), 1100(m), 1050(s, sh) **P-O,** 1025(s) P-O, 960(s), 850(s), 790(m), 745(m), 700(s) cm^{-1}. Anal. Calcd for $C_{15}H_{26}NO_4P$: C,57.13; H, 8.31; N, 4.44; P, 9.82. Found: C, 57.0; H 8.21; N, 4.55; P,9.82.

Diethyl 1-benzyloxyamino-3-methylbutylphosphonate (6d) 2.4 g (73%) were obtained after chromatographic separation, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 0.88 (d, 3H, $^3J_{HH}$= 7.5 Hz, **H-4**), 0.91 (d, $^3J_{HH}$= 7.5 Hz, 3H, **H-5**), 1.29 (virt. q, 6H, O-CH_2-**C**H_3), 1.39-1.72 (m, 2H, **H-2**), 1.79-1.96 (m, 1H, **H-3**), 3.21 (ddd, $^3J_{HHa}$= 9.7 Hz, $^3J_{HHb}$= 4.6 Hz, $^2J_{PH}$= 14.3 Hz, 1H, **H-1**), 4.08 (m, 4H, O-C**H**$_2$-CH_3), 4.69 (s, 2H, O-C**H**$_2$-Ph), 5.93 (bs, 1H, N-**H**), 7.25-7.40 (m, 5H, **H**$_{AR}$). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 16.2 (d, $^3J_{PC}$= 5 Hz, O-CH_2-**C**H_3), 16.3 (d, $^3J_{PC}$= 4.7 Hz, O-CH_2-**C**H_3), 21.5 (s, **C-4**), 23.1 (s,**C-5**), 24.8 (d, $^3J_{PC}$= 10.8 Hz, **C-3**), 36.3 (d, $^2J_{PC}$= 0 Hz, **C-2**), 56.5 (d, $^1J_{PC}$= 142.9 Hz, **C-1**), 61.7 (d, $^2J_{PC}$= 3 Hz, O-CH_2-CH_3), 61.8 (d, $^2J_{PC}$= 6 Hz, O-CH_2-CH_3,), 76.6 (s, O-**C**H_2-Ph), 127.7, 128.1, 128.4, (s, **C**$_i$). Ir (film) ν= 3230(**N-H**), 3090(w), 3065(w), 3035(w), 2960(s), 2940(s, sh), 2870(m), 1500(w), 1470(m), 1455(m), 1390(m), 1370(m), 1300(w), 1240(s) **P=O**, 1210(m, sh), 1170(m), 1100(m, sh), 1065(vs, sh) , 1030(vs) **P-O-C**; 980(vs), 750(m), 700(m) cm^{-1}. Anal. Calcd for $C_{16}H_{28}NO_4P$: C,58.35; H, 8.56; N, 4.25; P,9.40. Found: C, 58.21; H 8.52; N, 4.28; P, 9.24.

Diethyl benzyloxyaminobenzylphosphonate (6e) - 2.75 g (79%) were obtained after chromatographic separation, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.12 (t, $^3J_{PH}$= 6.9 Hz, 3H, O-CH_2-CH_3), 1.24 (t, $^3J_{PH}$= 6.9 Hz, 3H, O-CH_2-CH_3), 3.71-4.08 (m, 4H, O-CH_2-CH_3), 4.48 (d, $^2J_{PH}$= 20.4 Hz, $^4/_5$ v. 1H, **H-1**), 4.63 (virt. d, J= 8.4 Hz, 2H, O-CH_2-Ph), 4.64 (d, $^2J_{PH}$= 26.9 Hz, $^1/_5$ v. 1H, **H-1**), 6.25 (br s, 1H, N-**H**), 7.15 - 7.50 (m, 5H, H_{Ar}). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 16.2 (d, $^3J_{PC}$= 5.9 Hz, O-CH_2-CH_3), 16.3 (d, $^3J_{PC}$= 5.9 Hz, O-CH_2-CH_3) , 62.9 (d, $^1J_{PC}$= 143.7 Hz, **C-1**), 76.7 (s, O-CH_2-Ph), 127.9, 128.1, 128.1, 128.3, 128.4, 128.5, 128.7 (s, C_{Ar}), 134.8 (d, $^2J_{PC}$= 5 Hz, **C-2**), 137.5 (s, C_i). Ir (film) ν= 3230(m) **N-H**, 1495(m), 1475(w), 1455(m), 1390(m), 1370(m), 1250(s) **P=O**, 1180(w), 1165(m), 1100(m), 1050(vs), 1025(vs) **P-O-C**, 970(s), 915(m), 850(w), 795(m), 750(s), 700(s) cm^{-1}. Anal. Calcd for $C_{13}H_{22}NO_4P$: C,61.88; H, 6.92; N, 4.01. Found: C, 61.59; H 6.86; N, 4.31.

Diethyl 1-benzyloxyamino-2-phenylethylphosphonate (6f) - 2.35 g (65%) were obtained after chromatographic separation, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.32(virt. t, J= 7.6 Hz, 3H, O-CH_2-CH_3), 1.38 (virt.t, 3H, O-CH_2-CH_3), 3.10 - 3.32 (m, 2H, **H-2**), 3.57 (ddd, $^2J_{PH}$= 15.5 Hz, $^3J_{HHa}$= 5.3 Hz, $^3J_{HHb}$= 8.5 Hz, 1H, **H-1**), 4.17 (m, 4H, O-CH_2-CH_3), 4.80 (s, 2H, O-CH_2-Ph), 6.98 (br s, 1H, N-**H**), 7.15-7.38 (m, 10H, H_{Ar}). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 16.1 (d, $^3J_{PC}$= 2.6Hz, O-CH_2-CH_3), 16.2 (d, $^3J_{PC}$= 2.9 Hz, O-CH_2-CH_3)), 33.1 (s, $^2J_{PC}$= 0 Hz, **C-2**), 59.8 (d, $^2J_{PC}$= 148 Hz, **C-1**), 61.7 (d, $^2J_{PC}$= 6.7 Hz, O-CH_2-CH_3), 61.9 (d, $^2J_{PC}$= 6.5 Hz, O-CH_2-CH_3) , 76.2 (s, O-CH_2-Ph), 126.3, 127.6, 128.1, 128.2, 128.2, 129.2, 129.5 (s, C_{Ar}), 137.3 (s, C_i), 137.7 (d, $^3J_{PC}$= 11.6 Hz, **C-3**). Ir (film) ν= 3240(w) **N-H**, 3100(w), 3070(m), 3040(m), 2990(s), 2940(m), 2920(m), 2870(m), 1610(w), 1500(s), 1480(m, sh), 1455(s), 1445(m), 1395(m), 1370(m), 1250(vs) **P=O**, 1165(m), 1100(s, sh), 1055(vs, sh) 1030(vs) **P-O-C**, 840(w), 790(s), 750(s), 700(s) cm^{-1}.. Anal. Calcd for $C_{13}H_{22}NO_4P$: C,63.65; H, 7.47; N, 3.71; P, 8.21. Found: C, 63.62; H 7.43; N, 3.72; P, 8.08.

Diethyl 1-benzyloxyamino-3-phenylpropylphosphonate (6g) - 2.05 g (54%) were obtained after chromatographic separation, colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.28 (m, 6H, O-CH_2-CH_3), 2.09 (m, 2H, **H-2**), 2.82 (m, 2H, **H-3**), 3.19 (ddd, $^3J_{HHa}$= 6 Hz, $^3J_{HHb}$= 6 Hz, $^2J_{PH}$= 17 Hz, 1H, **H-1**), 4.09 (m, 4H, O-CH_2-CH_3), 4.75 (s, 2H, O-CH_2-Ph), 7.15 - 7.40 (m, 10H, H_{Ar}). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 16.4 (d, $^3J_{PC}$= 6.5 Hz, O-CH_2-CH_3), 29.1 (s, $^2J_{PC}$= 0 Hz, **C-2**), 32.6 (d, $^3J_{PC}$= 11.6 Hz, **C-3**), 57.8 (d, $^1J_{PC}$= 142 Hz, **C-1**), 61.9 (d, $^2J_{PC}$= 5.5 Hz, O-CH_2-CH_3), 76.7 (s, O-CH_2-Ph), 126.0, 127.0, 128.3, 128.4, 128.5 (s, C_{Ar}), 137.5 (s, C_i), 141.5 (s, **C-4**). Ir (film) ν= 3240(m) **N-H**, 3090(w), 3060(w), 3030(s), 2980(vs), 2960(vs), 2940(vs, sh), 2910(vs), 2880(s), 1610(w), 1495(m), 1455(m), 1455(m), 1415(m, sh), 1390(m), 1370(m), 1235(s) **P=O**, 1165(m), 1100(m, sh), 1050(s, sh), 1025(s), 965(s), 910(m, sh), 860(m), 790 (m, sh), 735(s), 695(s), 600(m)

cm^{-1}.. Anal. Calcd for $C_{20}H_{28}NO_4P$: C,63.65; H, 7.47; N, 3.71; P, 8.21. Found: C, 63.62; H 7.43; N, 3.72; P, 8.08.-

***Preparation of diethyl benzyloxyiminomethyl phosphonate* (8)**

1.69 g (10 mmol) *N*-Benzyloxyformhydroxamic chloride[15] (**7**) and 1.66 g (10 mmol) triethylphosphite (**2**) were stirred at 160°C for 2 h under nitrogen. The crude product was chromatographed on silica gel, using ether/ n-hexane (9:1) to give **8** as colorless oil. yield: 1.1 g (40%). ^{1}H-Nmr ($CDCl_3$) *Z*-isomer: δ= 2.90 (m, 6H, O-CH_2-$\mathbf{C}H_3$), 4.14 (m, 4H, O-$\mathbf{C}H_2$-CH_3), 5.29 (s, 2H, O-$\mathbf{C}H_2$-Ph), 7.10 (d, $^2J_{PH}$= 37 Hz, 1H, **H-1**), 7.28 - 7.42 (m, 5H, $\mathbf{H}_{Ar}$). *E*-isomer: δ= 2.90 (m, 6H, O-CH_2-$\mathbf{C}H_3$), 4.14 (m, 4H, O-$\mathbf{C}H_2$-CH_3), 5.22 (s, 2H, O-$\mathbf{C}H_2$-Ph), 7.28 - 7.42 (m, 5H, $\mathbf{H}_{Ar}$), 7.59 (d, $^2J_{PH}$= 36.5 Hz, 1H, **H-1**). ^{13}C-Nmr ($CDCl_3$, {^{1}H}). *Z*-isomer: δ= 16.2 (d, $^3J_{PC}$= 7 Hz, O-CH_2-$\mathbf{C}H_3$), 62.58 (d, $^2J_{PC}$= 23.4 Hz, O-$\mathbf{C}H_2$-CH_3), 77.55 (s, O-$\mathbf{C}H_2$-Ph), 128.1, 128.2, 128.4, (s, C_{Ar}), 136.6 (s, C_i), 141.76 (d, $^1J_{PC}$= 161.6 Hz, **C-1**). *E*-isomer: δ= 16.2 (d, $^3J_{PC}$= 7 Hz, O-CH_2-$\mathbf{C}H_3$), 62.58 (d, $^2J_{PC}$= 23.4 Hz, O-$\mathbf{C}H_2$-CH_3), 77.43 (s, O-$\mathbf{C}H_2$-Ph), 128.1, 128.2, 128.4, (s, $\mathbf{C}_{Ar}$), 136.6 (s, $\mathbf{C}_i$), 141.83 (d, $^1J_{PC}$= 219.6 Hz, **C-1**). .Ir (film) ν= 3110(w), 3100(w), 3070(w), 3040(w), 3090(s), 2940(s), 2910(s), 1595(m) **C=N**, 1500(m), 1480(m), 1455(s), 1445(s), 1395(s), 1370(s), 1255(s, b) **P=O**, 1165(s), 1100(s), 1030(s, b) **P-O-C**, 975(s, b), 890(m), 730(m), 700(s), 670(s, b), 580(s) cm^{-1}. Anal. Calcd for $C_{13}H_{22}NO_4P$: C, 53.14; H, 6.69; N, 5.16; P, 11.42. Found: C, 53.03; H 6.76; N, 5.03; P, 11.25.-

***Preparation of diethyl benzyloxyaminomethylphosphonate* (9)**

To a solution of *O*-benzylformaldoxime (**10**)(1.35 g, 10mmol) in 0.5M ethanolic HCl (50 ml) was added triethylphosphite(1.66 g, 10 mmol). The mixture was stirred for 2 h at 65°C. The solvent was removed under reduced pressure. Then ether (50 ml) and water (50 ml) were added together with Na_2CO_3 (6 g). After 3 h stirring, the organic phase was separated and dried over anhydrous Na_2SO_4. Evaporation of all volatile compounds under reduced pressure (40°C/ 0.01 torr) left a colorless oil, which was subjected to column chromatography (silica gel, ether). Yield 1.4 g (51%), colorless oil. ^{1}H-Nmr ($CDCl_3$) δ= 1.30 (virt. t, J= 8 Hz, 6H, O-CH_2-$\mathbf{C}H_3$), 3.32 (d, $^2J_{PC}$= 12 Hz, 2H, **H-1**,), 4.11 (m, 4H, O-$\mathbf{C}H_2$-CH_3), 4.72 (s, 2H, O-$\mathbf{C}H_2$-Ph, 5.79 (br. s, 1H, **NH**, H/D exchange), 7.28 - 7.42 (m, 5H, $\mathbf{H}_{Ar}$). ^{13}C-Nmr ($CDCl_3$, {^{1}H}) δ= 16.2 (d, $^3J_{PC}$= 6.1 Hz, O-CH_2-$\mathbf{C}H_3$), 47.9 (d, $^1J_{PC}$= 146 Hz, **C-1**), 61.9 (d, $^2J_{PC}$= 6.7 Hz, O-$\mathbf{C}H_2$-CH_3), 75.9 (s, O-$\mathbf{C}H_2$-Ph), 127.7, 128.2, 128.3, (s, $\mathbf{C}_{Ar}$), 137.3 (s, $\mathbf{C}_i$). Ir (film) ν= 3235(m) **NH**, 370(w), 3040(m), 2990(s), 2940(m), 2920(m), 1500(w), 1480(w), 1455(m), 1395(m), 1370(m), 1245(s) **P=O**, 1165(m), 1100(m, sh), 1030(vs), **P-O-C**, 750(m), 700(s) cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO_4P$: C,52.75; H, 7.37; N, 5.13; P, 11.34. Found: C, 52.57; H 7.42; N, 4.93; P, 11.56.

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