

Highly diastereoselective synthesis of N-substituted 4-(diethoxyphosphoryl)-pyrrolidines-3-carboxylate starting from tetraethyl methylenediphosphonate

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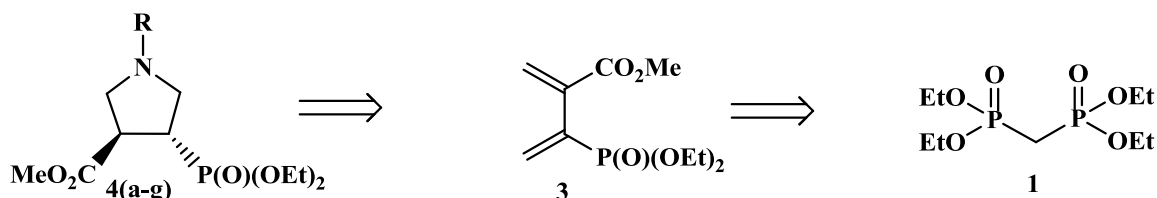
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Abstract: This paper describes a convenient synthesis of novel series of 3,4-disubstituted pyrrolidines based on the aza-Michael addition of primary amines to 3,4-difunctionalized-1,3-diene followed by an intramolecular cyclization.

Keywords: Aza-Michael addition, pyrrolidines, intramolecular-cyclization, 3,4-difunctionalized buta-1,3-diene.

Introduction

Pyrrolidines and structurally related compounds have attracted considerable interest due to their potential pharmacological activities¹ and are considered as subunits of many bioactive molecules²⁻⁶ and natural products⁷⁻⁹. Over the last years, increasing efforts have been developed to provide reliable methods for their preparation. According to the literature, the mainly synthetic methods consist of [3+2] cycloaddition of azomethine ylide,^{7a,c} ring closing metathesis (RCM) reaction,^{7d,9b} metal carbenoid NH insertions¹² on electrophilic carbon-carbon double bond activations,^{10,11,13} and metal-catalyzed hydroamination reactions¹⁴. However, most of these methods suffer from low yields, the use of expensive chemicals and remain insufficient to produce a wide variety of pyrrolidines. This limitation prompted us to develop a new and efficient synthesis of pyrrolidines **4** using available 2,3-difunctionalized buta-1,3-diene **3** as starting material (Scheme 1).



Scheme 1: Retrosynthetic method for access to pyrrolidines **4**

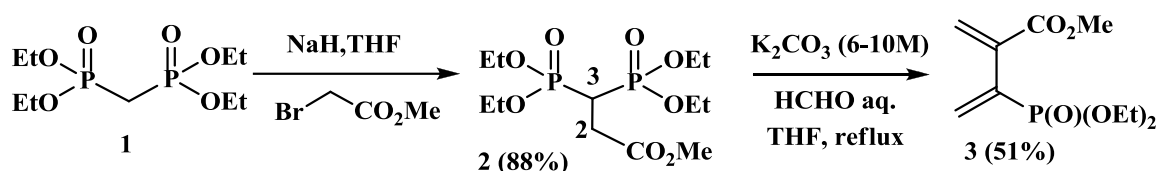
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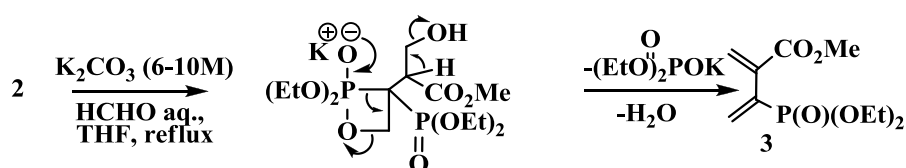
Results and Discussion

1,3-Dienes and their functionalized derivatives showed chemical utility and have been employed as useful intermediates in organic synthesis¹⁵⁻²³ and several studies focused on their preparation.²⁴⁻³³ Hence, they are capable of undergoing synthetic transformations, such as cyclization to various five or six-membered carbo- or heterocycles.^{15,24-34} The synthetic interest of dienes led us to propose a quick route to the 2,3-difunctionalized derivative **3**. The starting material of our synthetic sequence depicted in the scheme 2, was based on the preparation of methyl 3,3-bis(diethoxyphosphoryl)propanoate **2**³⁵ through a simple alkylation reaction of tetraethyl methylenediphosphonate **1**³⁶ with methyl bromoacetate in a basic medium (NaH). The latter was served as a key intermediate for the introduction of two methylene moieties by means of the Wittig-Horner reaction in the presence of aqueous formaldehyde (30%) and using aqueous potassium carbonate (6-10M) as base in THF at reflux. Pure methyl 3-(diethoxyphosphoryl)-2-methylenebut-3-enoate **3** was selectively obtained as yellow oil with moderate yield (scheme 2).



Scheme 2: Synthesis of novel methyl-3-(diethoxyphosphoryl)-2-methylenebut-3-enoate **3**

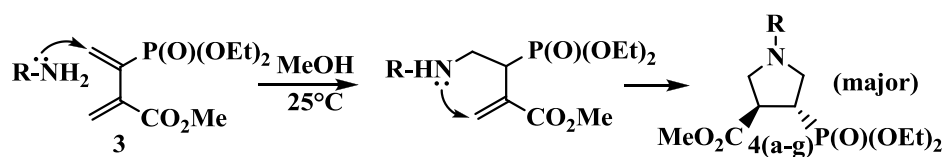
As shown in Scheme 3, the new alkylated phosphonate **2** showed a particular ability to undergo a *bis*-hydroxymethylation process. In fact, the reaction of target **2** with aqueous formaldehyde revealed two possible hydroxymethylations at the C-2 and C-3 carbon atoms followed, first by a deshydration then elimination of diethylphosphate salt. This process provides pure 3,4-difunctionalized-1,3-diene **3**, a useful synthon for the synthesis of several 3,4-functionalized pyrrolidines (Scheme 3).



Scheme 3: Synthesis of 1,3-diene **3** through the *bis*-(hydroxymethylation-elimination) process

As part of aza-Michael reaction^{24,37-40} and in continuation of our interest in the synthesis of multifunctional pyrrolidines, we report herein, an elegant and simple synthesis of methyl *N*-1-alkyl-4-(diethoxyphosphoryl)pyrrolidine-3-carboxylate **4**. In our approach, the construction of the nitrogen-containing heterocycle was based on an efficient coupling of primary amines and methyl 3-(diethoxyphosphoryl)-2-methylenebut-3-enoate **3**. Indeed, the condensation of 1,3-diene **3** with primary amines in methanol as solvent at room temperature, proceeds *via* two-step sequence: nucleophilic conjugate addition of amine to the activated vinylic moiety leading to a β -aminophosphonate intermediate, which undergoes spontaneously intramolecular cyclization through 5-endo-trig process to provide the

corresponding pure pyrrolidines **4a-g** in good yields ranging from 55 to 87% (Scheme 4, Table 1).



Scheme 4: Tandem double conjugated addition-cyclization synthesis of pyrrolidines **4a-g**

Table 1: Preparation of 3,4-difunctionalized pyrrolidines **4a-g**

Pyrrolidine 4	R	Trans/Cis ^a	Time (h)	Yield (%) ^b
4 a	<i>p</i> -FC ₆ H ₄ CH ₂	92:8	48	70
4 b	<i>p</i> -MeOC ₆ H ₄ CH ₂	93:7	22	55
4 c	C ₆ H ₅ CH ₂	93:7	48	56
4 d	^c C ₆ H ₁₁	92:8	22	75
4 e	<i>p</i> -ClC ₆ H ₄ CH ₂	92:8	48	60
4 f		92:8	72	87
4 g	C ₆ H ₅ (CH ₃)CH	52:48	32	70

^aCalculated by integration of the OMe signals of **4a-g**. ^bYields referred to isolated pure product.

As shown in Table 1, 3,4-disubstituted pyrrolidines **4a-g** were obtained as a mixture of *cis* and *trans* diastereoisomers. The stereochemistry of the separated *cis* and *trans* diastereoisomers **4g** was confirmed by nOe experiments in ¹H NMR at 300 MHz. Indeed, several measurements have shown a positive and mutual effect (+10.5%) between H-C3 and the H-C4 for the *cis* diastereoisomer whereas this enhancement was +3.1 % for the *trans* one. The latter result suggested the *trans* configuration for the major isomer **4g** (Figure 1). Although we have not firmly established the configuration of other pyrrolidines, it is possible to assign the *trans* configuration for the major diastereomer of the family of products **4a-g**, reported in this work.

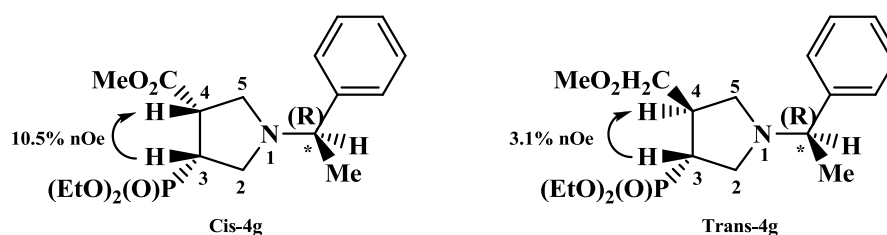


Figure 1: Assignment of the configuration of product **4g** through the study of the nOe spectra.

Conclusion

In summary, we have developed a new and highly stereoselective synthesis of 3,4-difunctionalized pyrrolidines **4a-g** by an effective coupling reaction between new 2,3-disubstituted-1,3-diene **3** and primary amines. The proposed strategy is considered as a reliable and positive contribution among the different routes of access to new 3,4-difunctionalized pyrrolidines reported in the literature.

Experimental Section

General. All commercially available chemicals and reagents were used without further purification. All the reactions were monitored by TLC on silica gel plates (Fluka Kieselgel 60 F₂₅₄). Flash column chromatography was performed with 70-230 mesh silica gel. The ¹H and ¹³C spectra were recorded in CDCl₃ at ambient temperature on a Bruker AMX 300 spectrometer. Some products secured by DEPT 135, HMQC and HMBC experiments. Chemical shifts are given in δ (ppm) and coupling constants J (Hz) relative to TMS as internal standard; multiplicities were recorded as s (singlet), d (doublet), dd (double doublet), t (triplet), dt (double triplet), q (quartet) or m (multiplet). Reactions involving anhydrous conditions were conducted in dry glassware under a nitrogen atmosphere.

Synthesis of methyl 3,3-bis(diethoxyphosphoryl)propanoate (2)

To cooled (0°C) and stirred suspension of NaH (65 mmol) in THF (400 mL) was added dropwise a solution of *bis*-(diethoxyphosphoryl)methane (50 mmol) in THF (100 mL). After the formation of H₂ had decreased, methyl bromoacetate (65 mmol) was added dropwise and the mixture was refluxed overnight. The resulting mixture was hydrolyzed with saturated ammonium chloride solution then extracted with ethyl acetate. The combined organic layers were washed with H₂O, dried on MgSO₄ and the solvent was evaporated under reduced pressure.

(2) Yield: 88%; colorless oil.

¹H-NMR (300 MHz, CDCl₃): 4.18 (dq, 8H, $J = 7.5$ Hz, $J = 7.5$ Hz, 4OCH₂) ; 3.73 (s, 3H, OCH₃) ; 3.1 (tt, 1H, $^2J_{H-P} = 24$ Hz, $^3J_{H-H} = 6$ Hz, CH) ; 2.8 (dt, 2H, $^3J_{H-P} = 18$ Hz, $^3J_{H-H} = 6$ Hz, CH₂) ; 1.33 (t, 12H, $J = 7.5$ Hz, 4CH₃) ; ¹³C-NMR (75 MHz, CDCl₃): 171.4 (C=O) ; 62.7 (d, 4 OCH₂, $^2J_{C-P} = 6.75$ Hz) ; 52.2 (s, OCH₃) ; 33.0 (t, CH, $^1J_{C-P} = 135$ Hz) ; 30.5 (d, CH₂, $^2J_{C-P} = 8.25$ Hz) ; 16.3 (d, 4CH₃, $^3J_{C-P} = 6$ Hz) ; ³¹P-NMR (121 MHz, CDCl₃): 21.94.

Synthesis of methyl 3-(diethoxyphosphoryl)-2-methylenebut-3-enoate (3)

In 25 mL Erlenmeyer fitted with a condenser, were introduced successively 5 mL of tetrahydrofuran (THF), 0.5g of alkylated phosphonate **2** then 0.6g of aqueous potassium carbonate (6-10M) and 2 mL (28 mmol) of 30% aqueous formaldehyde. The obtained solution was stirred at reflux during 48 hours. The mixture was diluted with H₂O and extracted with ethyl acetate. The combined organic layers were washed with brine and dried over MgSO₄. The solvent was removed to leave an oil which was purified by chromatography on silica gel (AcOEt: ethyl acetate).

(3) Yield: 51 %; colorless oil.

¹H-NMR (300 MHz, CDCl₃): 6.3 (t, 2H, $^3J_{H-P} = ^2J_{H-H} = 19$ Hz, CH₂_{ethylenic}) ; 6.10 (s, 1H, CH_{ethylenic}) ; 5.88 (s, 1H, CH_{ethylenic}) ; 4.3 (dq, 4H, $J = 9$ Hz, $J = 9$ Hz, 2OCH₂) ; 3.71 (s, 3H, OCH₃) ; 1.24 (t, 6H, $J = 7.5$ Hz, 2CH₃) ; ¹³C-NMR (75 MHz, CDCl₃): 165.1 (d, C=O, $^3J_{C-P} =$

8.25 Hz) ; 135.9 (d, =C, $^2J_{C-P}$ = 11.25 Hz) ; 134.4 (d, =C, $^1J_{C-P}$ = 178.5 Hz) ; 127.3 (d, =CH₂, $^3J_{C-P}$ = 5.25 Hz) ; 133.5 (d, =CH₂, $^2J_{C-P}$ = 30Hz) ; 61.2 (d, 2OCH₂, $^2J_{C-P}$ = 9 Hz) ; 51.2 (s, OCH₃) ; 15.2 (d, 2CH₃, $^3J_{C-P}$ = 6 Hz) ; $^{31}\text{P-NMR}$ (121 MHz, CDCl₃): 15.51.

Synthesis of 3,4-disubstituted pyrrolidines 4a-g

At room temperature, to a stirred solution of buta-1,3-diene (0.81 mmol) diluted in 5 mL of absolute methanol was added dropwise primary amine (0.81 mmol). After stirring during the time indicated in table (1), the mixture was concentrated and the obtained residue was purified by chromatography on silica gel (neat ethyl acetate).

Methyl 4-(diethoxyphosphoryl)-N-1-(4-fluorobenzyl)pyrrolidine-3-carboxylate (4a):

Yield: 70 % ; yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl₃): 7.26 (dd, 2H, $^3J_{H-H}$ = 9 Hz, $^4J_{H-F}$ = 6 Hz, , 2CH_{aromatic}) ; 6.98 (t, 2H, $^3J_{H-F}$ = $^3J_{H-H}$ = 9 Hz, 2CH_{aromatic}) ; 4.09 (dq, 4H, J = 7.5 Hz, J = 7.5 Hz, 2OCH₂) ; 3.71 (s, 3H, OCH₃) ; 3.58 (d, 2H, J = 3 Hz, CH₂N) ; 3.25-3.23 (m, 2H, CH₂N) ; 3.15-3.10 (m, 2H, CH₂N) ; 2.90-2.83 (m, 1H, CHC=O) ; 2.7-2.64 (m, 1H, CHP(O)) ; 1.30 (2t, 6H, J = 7.5Hz, J = 7.5Hz, 2CH₃) ; $^{13}\text{C-NMR}$ (75 MHz, CDCl₃): 173.7 (d, C=O, $^3J_{C-P}$ = 6Hz) ; 162.0 (d, =C, $^1J_{C-F}$ = 243 Hz) ; 134.1 (d, =C, $^4J_{C-F}$ = 3 Hz) ; 130.0 (d, =CH, $^3J_{C-F}$ = 6 Hz) ; 115.0 (d, =CH, $^2J_{C-F}$ = 21.75 Hz) ; 62.1 (d, 2OCH₂, $^2J_{C-P}$ = 9 Hz) ; 58.4 (s, OCH₃) ; 57.1 (d, CH₂N, $^3J_{C-P}$ = 6 Hz) ; 53.9 (d, CH₂N, $^2J_{C-P}$ = 9 Hz) ; 52.3 (s, CH₂N) ; 44.0 (d, CHC=O, $^2J_{C-P}$ = 9 Hz) ; 36.8 (d, CHP=O, $^1J_{C-P}$ = 148.5 Hz) ; 16.4 (d, 2CH₃, $^3J_{C-P}$ = 6 Hz) ; $^{31}\text{P-NMR}$ (121 MHz, CDCl₃): 30.16.

Methyl 4-(diethoxyphosphoryl)-N-1-(4-methoxybenzyl)pyrrolidine-3-carboxylate (4b):

Yield: 55 % ; yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl₃): 7.20 (d, 2H, J = 9 Hz, 2CH_{aromatic}) ; 6.83 (d, 2H, J = 9 Hz, 2CH_{aromatic}) ; 4.11 (dq, 4H, J = 7.5 Hz, J = 7.5 Hz, 2OCH₂) ; 3.78 (s, 3H, OCH₃) ; 3.70 (s, 3H, OCH₃) ; 3.55 (d, 2H, J = 3 Hz, CH₂N) ; 3.23-3.20 (m, 2H, CH₂N) ; 3.10-3.95 (m, 2H, CH₂N) ; 2.85-2.79 (m, 1H, CHC=O) ; 2.60-2.56 (m, 1H, CHP=O) ; 1.29 (2t, 6H, J = 7.5Hz, J = 7.5Hz, 2CH₃) ; $^{13}\text{C-NMR}$ (75 MHz, CDCl₃): 173.7 (d, C=O, $^3J_{C-P}$ = 6 Hz) ; 158.7 (s, =C) ; 130.3 (s, =C) ; 129.7 (s, =CH) ; 113.6 (s, =CH) ; 62.0 (d, 2OCH₂, $^2J_{C-P}$ = 9 Hz) ; 58.53 (s, CH₂N) ; 57.1 (d, CH₂N, $^3J_{C-P}$ = 6 Hz) ; 55.2 (s, OCH₃) ; 53.8 (s, OCH₃) ; 52.2 (d, CH₂N, $^2J_{C-P}$ = 9 Hz) ; 44.0 (d, CHC=O, $^2J_{C-P}$ = 9 Hz) ; 36.7 (d, CHP=O, $^1J_{C-P}$ = 148.5 Hz) ; 16.4 (d, 2CH₃, $^3J_{C-P}$ = 6 Hz) ; $^{31}\text{P-NMR}$ (121 MHz, CDCl₃): 30.29.

Methyl N-1-benzyl-4-(diethoxyphosphoryl)pyrrolidine-3-carboxylate (4c):

Yield: 56 % ; yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl₃): 7.3 (m, 5H, CH_{aromatic}) ; 4.09 (dq, 4H, J = 7.5 Hz, J = 7.5 Hz, 2OCH₂) ; 3.71 (s, 3H, OCH₃) ; 3.62 (d, 2H, J = 3 Hz, CH₂N) ; 3.21-3.18 (m, 2H, CH₂N) ; 3.02-2.97 (m, 2H, CH₂N) ; 2.92-2.88 (m, 1H, CHC=O) ; 2.77-2.73 (m, 1H, CHP=O) ; 1.29 (2t, 6H, J = 7.5 Hz, J = 7.5 Hz, 2CH₃) ; $^{13}\text{C-NMR}$ (75 MHz, CDCl₃): 173.7 (d, C=O, $^3J_{C-P}$ = 7.5 Hz) ; 138.2 (s, =C) ; 128.6 (s, =CH) ; 128.2 (s, =CH) ; 127.1 (s, =CH) ; 125.5, (s, =CH) ; 62.0 (d, 2OCH₂, $^2J_{C-P}$ = 9 Hz) ; 59.1(d, CH₂N, $^3J_{C-P}$ = 7.5 Hz) ; 57.2 (d, CHC=O, $^2J_{C-P}$ = 9 Hz) ; 53.9 (s, OCH₃) ; 52.2 (d, CH₂N, $^2J_{C-P}$ = 9 Hz) ; 44.0 (s, CH₂N) ; 36.7 (d, CHP=O, $^1J_{C-P}$ = 148.5 Hz) ; 16.4 (d, 2CH₃, $^3J_{C-P}$ = 7.5Hz) ; $^{31}\text{P-NMR}$ (121 MHz, CDCl₃): 30.26.

Methyl N-1-cyclohexyl-4-(diethoxyphosphoryl)pyrrolidine-3-carboxylate (4d):

Yield: 75 % ; yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl₃): 4.10 (dq, 4H, J = 6.75 Hz, J = 6.75 Hz, 2OCH₂) ; 3.72 (s, 3H, OCH₃) ; 3.20-3.16 (m, 2H, CH₂N) ; 3.00-2.95 (m, 2H, CH₂N) ; 2.80-2.76 (m, 1H, CHC=O) ; 2.70-2.64 (m, 1H, CHP=O) ; 2.06-2.00 (m, 1H, CHN) ; 1.85-1.81 (m, 4H, CH₂CHcycl) ; 1.59-

1.52 (m, 4H, CH₂cycl) ; 1.46-1.41 (m, 2H, CH₂cycl) ; 1.31 (2t, 6H, $J = 7.5$ Hz, $J = 7.5$ Hz, 2CH₃) ; ¹³C-NMR (75 MHz, CDCl₃): 173.8 (d, C=O, ³J_{C-P} = 6 Hz) ; 62.1 (d, 2OCH₂, ²J_{C-P} = 9.75 Hz) ; 61.9 (s, CHN) ; 54.9 (d, CH₂N, ²J_{C-P} = 9.75 Hz) ; 52.3 (d, CH₂N, ³J_{C-P} = 6 Hz) ; 51.7 (s, OCH₃) ; 43.6 (s, CH₂CHcycl) ; 43.3 (s, CH₂CHcycl) ; 36.4 (d, CHP=O, ¹J_{C-P} = 148.5 Hz) ; 31.4 (d, CHC=O, ²J_{C-P} = 9.75Hz) ; 25.9 (s, CH₂cycl) ; 24.8 (s, 2CH₂cycl) ; 16.4 (d, 2CH₃, ³J_{C-P} = 6 Hz) ; ³¹P-NMR (121 MHz, CDCl₃): 30.32.

Methyl N-1-(4-Chlorobenzyl)-4-(diethoxyphosphoryl)pyrrolidine-3-carboxylate (4e):

Yield: 60 % yellow oil.

¹H-NMR (300 MHz, CDCl₃): 7.25 (d, 4H, $J = 3$ Hz, CH_{aromatic}) ; 4.11 (dq, 4H, $J = 6.25$ Hz, 6.25 Hz, 2OCH₂) ; 3.71 (s, 3H, OCH₃) ; 3.58 (d, 2H, $J = 3$ Hz, CH₂N) ; 3.22-3.19 (m, 2H, CH₂N) ; 3.02-2.98 (m, 1H, CHC=O) ; 2.71-2.68 (m, 2H, CH₂N) ; 2.60 (m, 1H, CHP=O) ; 1.33 (dt, 6H, $J = 6$ Hz, $J = 6$ Hz, 2CH₃) ; ¹³C-NMR (75 MHz, CDCl₃): 173.6 (d, C=O, ³J_{C-P} = 7.5 Hz) ; 136.9 (=C) ; 132.8 (=C) ; 129.8 (=CH) ; 128.4 (=CH) ; 62.0 (d, 2OCH₂, ²J_{C-P} = 9.75 Hz) ; 58.4 (s, OCH₃) ; 57.1 (d, CH₂N, ²J_{C-P} = 9.75Hz) ; 53.9 (d, CH₂N, ³J_{C-P} = 7.5 Hz) ; 52.3 (d, CHC=O, ²J_{C-P} = 9.75Hz) ; 44.0(s, CH₂N) ; 36.7 (d, CHP=O, ¹J_{C-P} = 148.5 Hz) ; 16.4 (d, 2CH₃, ³J_{C-P} = 7.5 Hz) ; ³¹P-NMR (121 MHz, CDCl₃): 30.13.

Methyl 4-(diethoxyphosphoryl)-N-1-(furan-2-ylmethyl)pyrrolidine-3-carboxylate (4f):

Yield: 87 % ; yellow oil.

¹H-NMR (300 MHz, CDCl₃): 7.36 (s, 1H, CH_{ethylenic}) ; 6.3(d, 1H, $J = 3$ Hz, CH_{ethylenic}) ; 6.19 (d, 1H, $J = 3$ Hz, CH_{ethylenic}) ; 4.1 (2dq, 4H, $J = 6.75$ Hz, $J = 6.75$ Hz, 2OCH₂) ; 3.71 (s, 3H, OCH₃) ; 3.66 (d, 2H, $J = 6$ Hz, CH₂N) ; 3.23-3.19 (m, 2H, CH₂N) ; 3.02-2.96 (m, 1H, CHC=O) ; 2.90-2.84 (m, 2H, CH₂N) ; 2.75-2.71 (m, 1H, CHP=O) ; 1.29 (dt, 6H, $J = 7.5$ Hz, $J = 7.5$ Hz, 2CH₃) ; ¹³C-NMR (75 MHz, CDCl₃): 173.5 (d, C=O, ³J_{C-P} = 6.75 Hz) ; 151.6 (=C) ; 142.1 (=CH) ; 110.1 (=CH) ; 108.3 (=CH) ; 62.1 (d, 2OCH₂, ²J_{C-P} = 9.5 Hz) ; 56.7 (d, CH₂N, ³J_{C-P} = 6.75Hz) ; 53.6 (s, OCH₃) ; 52.3 (d, CHC=O, ²J_{C-P} = 9.5 Hz) ; 50.7 (d, CH₂N, ²J_{C-P} = 9.5 Hz) ; 44.0 (s, CH₂N) ; 36.7 (d, CHP=O, ¹J_{C-P} = 148.5 Hz) ; 16.4 (d, 2CH₃, ³J_{C-P} = 6.75 Hz) ; ³¹P-NMR (121 MHz, CDCl₃): 30.13.

Methyl 4-(diethoxyphosphoryl)-N-1-(1-phenylethyl)pyrrolidine-3-carboxylate (4g):

Yield: 70 % yellow oil.

¹H-NMR (300 MHz, CDCl₃): 7.24 (m, 5H, CH_{aromatic}) ; 4.1 (dq, 4H, $J = 7.5$ Hz, $J = 7.5$ Hz, 2OCH₂) ; 3.68 (s, 3H, OCH₃) ; 3.62 (d, 2H, $J = 3$ Hz, CH₂N) ; 3.21-3.18 (m, 2H, CH₂N) ; 2.92-2.89 (m, 1H, CHC=O) ; 2.80-2.76 (m, 2H, CH₂N) ; 2.70-2.66 (m, 1H, CHP=O) ; 2.75 (d, 1H, $J = 6$ Hz, CHN) ; 1.29 (d, 3H, $J = 12$ Hz, CH₃) ; 1.27 (t, 6H, $J = 9$ Hz, 2CH₃) ; ¹³C-NMR (75 MHz, CDCl₃): 174.3 (d, C=O, ³J_{C-P} = 6.75Hz) ; 142.5 (s,=C) ; 129.2 (s,=CH) ; 128.7 (s,=CH) ; 128.2 (s,=CH) ; 127.8 (s,=CH) ; 125.7 (=CH) ; 60.8 (d, 2OCH₂, ²J_{C-P} = 9.5 Hz) ; 59.1 (s, CHN) ; 58.7 (s, OCH₃) ; 58.1 (d, CH₂N, ²J_{C-P} = 9.5Hz) ; 57.9 (d, CH₂N, ³J_{C-P} = 6.75 Hz) ; 43.1 (d, CHC=O, ²J_{C-P} = 9.5Hz) ; 38.4 (d, CHP=O, ¹J_{C-P} = 148.5 Hz) ; 22.6 (s, CH₃) ; 16.9 (d, 2CH₃, ³J_{C-P} = 6.75 Hz) ; ³¹P-NMR (121 MHz, CDCl₃): 30.2.

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