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Regioselective synthesis of 4- and 5-oxazole-phosphine oxides and -phosphonates from 2*H*-azirines and acyl chlorides

Francisco Palacios,* Ana M. Ochoa de Retana, José I. Gil and José M. Alonso

Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco. Apartado 450, 01080 Vitoria, Spain

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Abstract—A simple and efficient regioselective synthesis of 4-oxazole-phosphine oxides **11** and -phosphonates **12** from 2*H*-azirine-phosphine oxides **1** and -phosphonates **6** is described. The key step for the synthesis of oxazoles **11** is a base-mediated ring closure of vinylogous α-aminophosphorus compounds derived from phosphine oxides **4** and from phosphonates **8**. These derivatives **4** and **8** are obtained by reaction of functionalized azirines **1** and **6** with acyl chlorides **2** and subsequent acid-catalyzed ring opening of *N*-acylaziridine-phosphine oxides **3** and -phosphonates **7**. Regioselective thermal ring cleavage of *N*-acylaziridine-phosphine oxides **3** leads α-chloro-β-(*N*-acylamido)-phosphine oxides **13** and their treatment with bases gives 5-oxazole-phosphine oxides **16**.

1. Introduction

2*H*-Azirine ring systems represent an important class of compounds because of their high reactivity[1] in the preparation of acyclic functionalized amino derivatives[2a–c] and heterocycles.[2d–h] In particular, 2*H*-azirines containing a carboxylic ester group are constituents of naturally occurring antibiotics[1a] and are excellent reagents for the preparation of functionalized aziridines[1,3] and α-[3b,4a–e] and β-amino acid derivatives,[3b,4f–h] while molecular modifications involving the introduction of organophosphorus functionalities, replacing the carboxylic ester for an isosteric phosphorus group, could increase the use of these substrates as intermediates not only in organic synthesis but also in medicinal chemistry.[1,5] For this reason, we have previously reported the preparation of 2*H*-azirine-phosphine oxides[6] and -phosphonates by a base-mediated Neber reaction of tosyl oximes.[7]

In this context, we have also described new methods for the preparation of five,[8] and six[9] membered phosphorus substituted nitrogen heterocycles from functionalized phosphine oxides and phosphonates and the synthetic uses of amino phosphorus derivatives as starting materials for the preparation of acyclic compounds[10] and phosphorus-containing heterocycles.[11] Recently, we described the use of phosphorylated 2*H*-azirines for the synthesis of α- and β-amino phosphorus derivatives[12] as well as their dimerization to phosphorylated pyrazines[13] and the ring opening of these azirines **I** with carboxylic acids followed by the cyclization of the corresponding adducts **II** to oxazoles containing phosphorus substituents in position 4 **III** through the azirine-oxozolone methodology[14] (Fig. 1). Furthermore, the reaction of acyl halides with simple azirines to give *N*-acylaziridines,[15] oxazoles,[16] or unsaturated *N*-acylimines[17] has been described. However, the behaviour of phosphorylated azirines with acyl halides has not been reported. For this reason and continuing with our interest in the synthesis of new phosphorus substituted heterocycles, we here report an easy and high yielding synthesis of 4- (**III**, Fig. 1) and

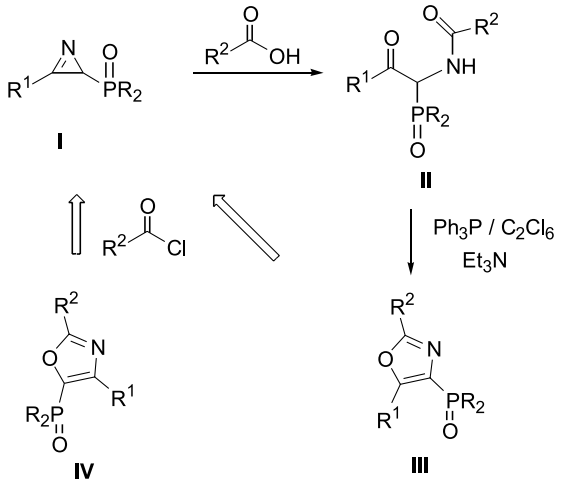

Figure 1.

Keywords: Azirine phosphine oxide and phosphonate; Oxazole; Acyl chloride.

* Corresponding author. Tel.: +34-945-013103; fax: +34-945-013049; e-mail: qoppagaf@vf.ehu.es

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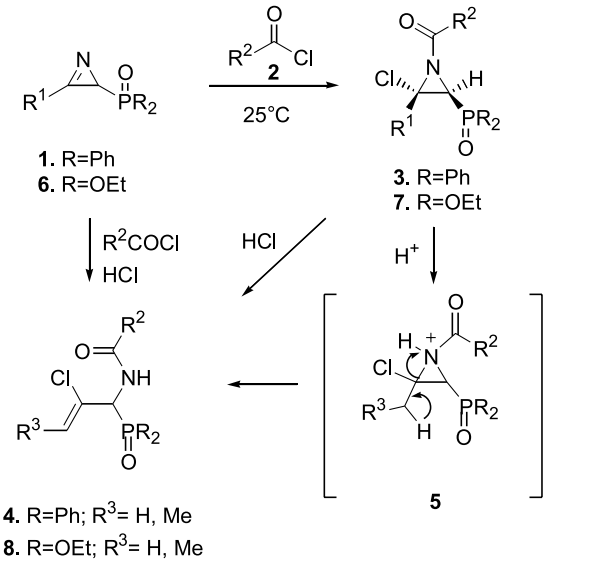
5-(oxazolyl)-phosphorus derivatives (**IV**, Fig. 1) from easily available azirines and acyl chlorides, as well as the formation and isolation of their *N*-acyl-aziridine precursors. Simple oxazoles are common units in a wide variety of polyoxazole marine natural products possessing biological activity,[18] and oxazoles are also widely used intermediates for functional transformations.[19]

2. Results and discussion

2.1. Reaction of azirines 1 and 6 with acyl chlorides

2*H*-Azirines are ambident reagents and are capable of acting in organic reactions not only as nucleophiles (N-1), but also as electrophiles (C-3).[1] Carboxylic acids can ring open these strained three membered heterocycles **I** to give amides **II** by means of acid-catalyzed addition of carboxylate nucleophile and these amides **II** can be used for the preparation of oxazoles **III** (Fig. 1). However, a different behaviour could be expected in the case of other carboxylic derivatives such as acyl chlorides, because in this case the acyl group could act as electrophile. So, we initially explored the reaction of acyl chlorides with phosphorylated azirines. Reaction of azirine-phosphine oxide **1a** (R=Ph, $R^1=CH_3$) with acetyl chloride **2a** ($R^2=CH_3$) at room temperature led exclusively to the formation of *trans*-(*N*-acyl-3-chloro-3-methyl-aziridinyl-phosphine oxide) **3aa** (R=Ph, $R^1=R^2=CH_3$) (Scheme 1, Table 1, entry 1). No trace of the *cis*-aziridine could be observed by ^{31}P NMR. Spectroscopic data were in agreement with the assigned structure of compound **3aa**. In the ^{31}P NMR spectrum the phosphine oxide group of this aziridine **3aa** resonated at $\delta_P=23.2$ ppm, while well resolved doublets at $\delta=3.32$ ppm ($^2J_{PH}=23.0$ Hz) for H-2 in the ^1H NMR spectrum as well as at $\delta_C=44.7$ ppm ($^1J_{PC}=96.2$ Hz) and at $\delta_C=59.8$ ppm ($^2J_{PC}=5.5$ Hz) for C-2 and C-3 in the ^{13}C NMR spectrum were observed. The stereochemical assignment was based on NOE experiments. The exclusive formation of *trans*-aziridine **3aa** suggests that the approach of the chloride to the cyclic compound from the opposite position to the phosphine oxide group is more favourable, due to the high exocyclic dihedral angle of the saturated carbon and to the presence of the bulky phosphorus group. The scope of the reaction was not limited to acetyl chloride **2a** ($R^2=CH_3$), given that not only benzoyl chloride **2b** ($R^2=Ph$), but also functionalized acyl chlorides containing olefine groups **2c** ($R^2=(CH_2)_4CH=CH_2$), and **2d** ($R^2=CH=CH_2$) also reacted with azirine **1a** to give functionalized *trans*-(*N*-acylaziridines) **3ab**-**3ad** (Scheme 1, Table 1, entries 2–4) in a regioselective fashion. Likewise, 3-ethyl- **1b** ($R^1=C_2H_5$) and 3-phenyl-azirines **1c** ($R^1=Ph$) also reacted with acetyl chloride **2a** ($R^2=CH_3$) to afford only *trans*-aziridinyl-phosphine oxides **3ba** and **3ca** (Scheme 1, Table 1, entries 5,6).



Scheme 1.

Table 1. *N*-Acylaziridine-phosphine oxides **3** obtained

Entry	Compound	R^1	R^2	Yield (%)[a]
1	**3aa**	CH_3	CH_3	76
2	**3ab**	CH_3	Ph	81
3	**3ac**	CH_3	$(CH_2)_4CH=CH_2$	43
4	**3ad**	CH_3	$CH=CH_2$	96
5	**3ba**	C_2H_5	CH_3	85
6	**3ca**	Ph	CH_3	80

[a] Yield of isolated purified compounds **3**.

Ring expansion of *N*-acylaziridines to five membered heterocycles can be achieved by thermal treatment or in the presence of acids,[20] while no ring opening reaction of *N*-acylaziridines containing phosphorus substituents has been reported. We explored the reaction of azirine-phosphine oxides because this reaction can be used as a model of the influence of phosphorus substituents by the ring opening reaction of these substrates and functionalized amides generated could then be used for the preparation of phosphorylated oxazoles. Treatment of functionalized *N*-acylaziridines **3aa**-**ac** with hydrogen chloride in THF at room temperature led to the formation of vinylogous α-amido-phosphine oxides **4aa**-**ac** (Scheme 1, Table 2, entries 1–3). Both conjugative addition of HCl to the acryloyl group of *N*-acylaziridine **3ad** ($R^2=CH=CH_2$) and the ring opening was observed when this aziridine **3ad** was treated with HCl to give α-amido-phosphine oxides **4ad** ($R^2=CH_2$–CH_2Cl) (Scheme 1, Table 2, entry 4). Spectroscopic data were in agreement with the assigned structure of compounds **4**. The formation of α-amido-phosphine oxides **4** could be explained by protonation of the nitrogen atom of the *N*-acylaziridine followed by formation of the carbon–carbon double bond and ring opening of activated aziridinium ion **5**. From a synthetic point of view, it is noteworthy that the preparation of these α-amido-phosphine oxides **4** can also be directly prepared from azirines **1** without the isolation of *N*-acylaziridines **3**, when these heterocycles **1** were treated with acyl chlorides **2** in a THF solution containing hydrogen chloride (Scheme 1, Table 2, entries 1–3). The use of azirines containing an ethyl group at 3-position **1b** ($R^1=C_2H_5$) gave **4ba** ($R^3=CH_3$) (Scheme 1, Table 2, entry 5) and allowed us to assign the *Z*-configuration of the carbon–carbon double bond based on NOE experiments.

These processes can be extended to azirines derived from phosphonates **6**. Treatment of 3-alkyl azirines **6a** (R=OEt, $R^1=Me$) and **6b** (R=OEt, $R^1=C_2H_5$), with acetyl chloride

Table 2. Vinylogous amides **4** and **8** obtained

Entry	Compound	R	R^2	R^3	Yield (%)[a]
1	**4aa**	Ph	CH_3	H	96 (96)[b]
2	**4ab**	Ph	Ph	H	33 (42)[b]
3	**4ac**	Ph	$(CH_2)_4CH{=}CH_2$	H	22 (40)[b]
4	**4ad**	Ph	$CH_2{-}CH_2Cl$	H	48
5	**4ba**	Ph	CH_3	CH_3	58[b]
6	**8aa**	OEt	CH_3	H	91
7	**8ad**	OEt	$CH{=}CH_2$	H	78
8	**8ba**	OEt	CH_3	CH_3	87

[a] Yield of isolated purified compounds **4** and **8**.
[b] Yield of isolated compounds **4** obtained one pot from azirines **1**.

2a ($R^2{=}CH_3$) and acryloyl chloride **2d** ($R^2{=}CH{=}CH_2$) gave vinylogous amides containing a diethoxyphosphoryl group in the α-position **8aa** (R=OEt, $R^2{=}CH_3$, $R^3{=}H$), **8ad** (R=OEt, $R^2{=}CH{=}CH_2$, $R^3{=}H$) and **8ba** (R=OEt, $R^2{=}CH_3$, $R^3{=}CH_3$) (Scheme 1, Table 2, entries 6–8), without the isolation of the *N*-acylaziridine precursors **7**. This strategy describes, as far as we know, the first synthesis of vinylogous α-amido-phosphine oxides and -phosphonates. α-Aminophosphonates[21] can be considered as surrogates for α-aminoacids,[22a] and have been used as haptens for the generation of catalytic antibodies,[10b,c] as antibacterial agents,[22d,e] and as nucleoside,[22f] or as phosphapeptide enzyme inhibitors.[22g–k]

2.2. Formation of oxazoles 11, 12 and 16

Oxazoles are common heterocycles in a wide variety of natural products possessing biological activity and also are widely used intermediates for functional transformations.[18,19] Given that phosphorus substituents regulate important biological functions,[5] we thought that *N*-acylaziridines **3** or α-amido-phosphine oxides **4** could be used for the preparation of oxazoles. Vinylogous amides **4** (R=Ph, $R^3{=}$ H, CH_3) were treated with 2 N aqueous NaOH solution in dichloromethane to give 3-alkyl-oxazole phosphine oxides **11** (R=Ph, $R^1{=}CH_3$, C_2H_5) in good yields and in a regioselective fashion (Scheme 2, Table 3, entries 1–5). Formation of oxazoles **11** could be explained by cyclization of intermediate **9** and subsequent loss of HCl from dihydrooxazol **10**. However, in the case of oxazoles containing an aryl substituent, this 5-phenyl oxazole **11ca** (R=Ph, $R^1{=}$Ph) was directly obtained from 3-phenyl azirine **1c** by ring expansion with acetyl chloride and HCl via an aziridinium cation (Scheme 2, Table 3, entry 6).

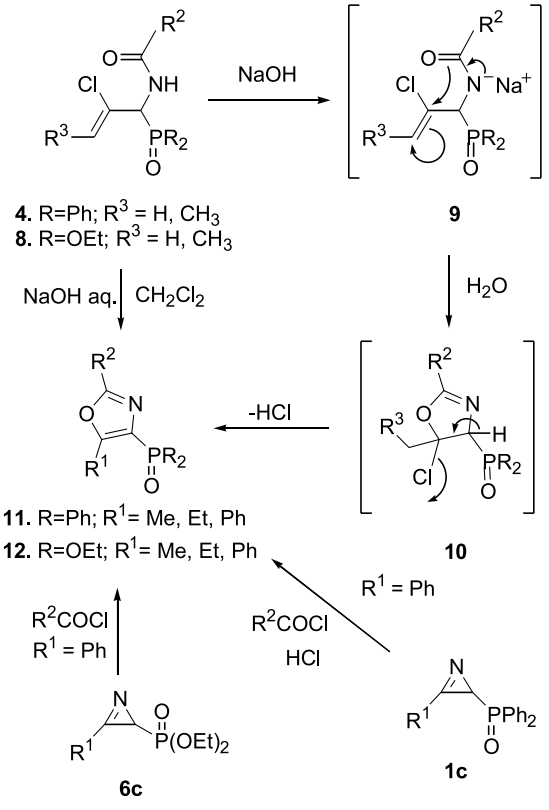
Table 3. 4-Oxazolyl-phosphine oxides **11** and -phosphonates **12** obtained

Entry	Compound	R	R^1	R^2	Yield (%)[a]
1	**11aa**	Ph	CH_3	CH_3	87
2	**11ab**	Ph	CH_3	Ph	82
3	**11ac**	Ph	CH_3	$(CH_2)_4CH{=}CH_2$	71
4	**11ad**	Ph	CH_3	$CH{=}CH_2$	52
5	**11ba**	Ph	C_2H_5	CH_3	67
6	**11ca**	Ph	Ph	CH_3	58
7	**12aa**	OEt	CH_3	CH_3	59
8	**12ad**	OEt	CH_3	$CH{=}CH_2$	63
9	**12ba**	OEt	C_2H_5	CH_3	65
10	**12ca**	OEt	Ph	CH_3	92

[a] Yield of isolated purified compounds **11** and **12**.

Ring closure of α-amido-phosphonates **8** with 2 N aqueous NaOH solution gave oxazole phosphonates **12** (Scheme 1, Table 3, entries 7–9), and ring expansion of 3-phenyl azirine **6c** (R=OEt, $R^1{=}$Ph) with acetyl chloride **2a** ($R^2{=}CH_3$) gave directly 5-phenyl oxazole phosphonate **12ca** (R=OEt, $R^1{=}$Ph, $R^2{=}CH_3$) (Scheme 2, Table 3, entry 10).

Next, we also explored the behaviour of *N*-acylaziridines **3** when they were heated in the presence of a base, in order to test whether these substrates could be opened in a different regioselective fashion than before, with presence of acid. Thermal treatment of *N*-acylaziridines **3aa** (R=Ph, $R^1{=}R^2{=}CH_3$), **3ab** (R=Ph, $R^1{=}CH_3$, $R^2{=}$Ph), **3ad** (R=Ph, $R^1{=}CH_3$, $R^2{=}CH{=}CH_2$), **3ba** (R=Ph, $R^1{=}C_2H_5$, $R^2{=}CH_3$), in refluxing chlorobenzene and in the presence of tributylamine led to the formation of vinylamides **13aa**, **13ab**, **13ad** and **13ba** in moderate yields (Scheme 3, Table 4, entries 1–4) and a small proportion of oxazoles **11**. The formation of oxazoles **11** (minor components) can be explained as before (Scheme 2) by regioselective ring opening of the N–C2 bond followed by cyclization to the five membered ring, while formation of major compounds **13** could be explained by regioselective ring opening of the

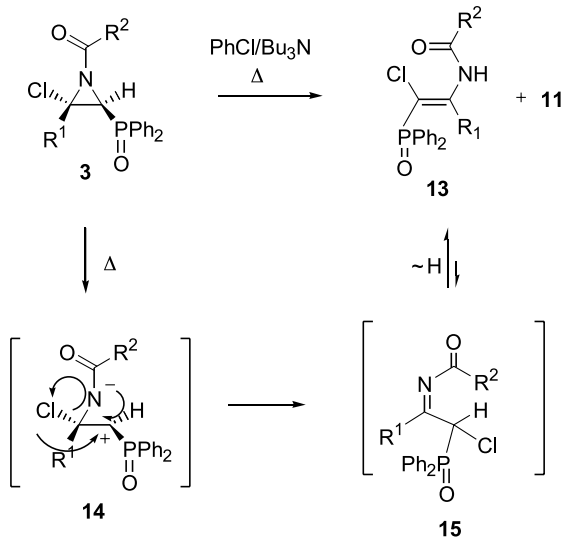


Scheme 2.

Table 4. Enamides **13** and 5-oxazolyl-phosphine oxides **16**

Entry	Compound	R^1	R^2	Yield (%)[a]
1	**13aa**	CH_3	CH_3	41
2	**13ab**	CH_3	Ph	60
3	**13ad**	CH_3	$CH{=}CH_2$	15
4	**13ba**	C_2H_5	CH_3	54
5	**16aa**	CH_3	CH_3	65
6	**16ab**	CH_3	Ph	72
7	**16ba**	C_2H_5	CH_3	57

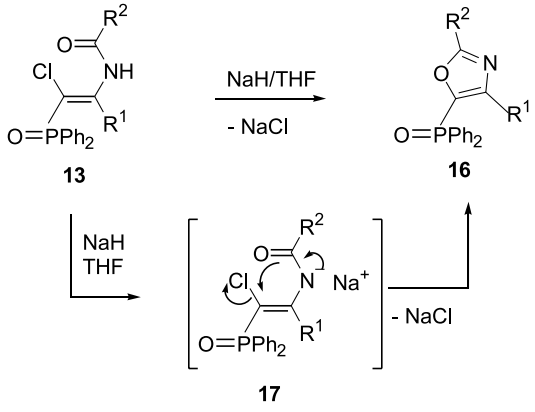
[a] Yield of isolated purified compounds **13** and **16**.



Scheme 3.

N–C1 single bond of the ring through an intermediate **14**, chloride rearrangement and formation of functionalized acylimine **15** containing chloro and phosphine oxide groups in the α position, followed by tautomerization.

Finally, base-mediated (NaH) ring closure of enamides **13** in THF reflux gave only 5-oxazolyl-phosphine oxides **16** (Scheme 4, Table 4, entries 5–7) in good yields and in a regioselective fashion. The formation of oxazoles **16** can be explained by deprotonation, sodium amidure salt formation and intramolecular nucleophilic cyclization of intermediate **17** with the loss of NaCl. As far as we know, this process describes the first synthesis of oxazole derivatives containing phosphorus substituent in position 5.



Scheme 4.

3. Conclusion

In conclusion, this account describes a simple, mild, and convenient strategy for the preparation of oxazoles containing phosphorus substituents in position 4 and 5 from easily available azirine-phosphine oxides **1** and -phosphonates **6** and acyl chlorides. *N*-Acylaziridines **3** can be isolated and these strained heterocycles can be used for the preparation of vinylogous α-amido-phosphine oxides **3** and phosphonates **8** when azirines were treated with acyl chlorides in the presence of HCl, while functionalised enamides **13** were obtained by thermal treatment of *N*-acylaziridines **3**. Ring closure of vinylogous α-amides **4**, **8** gives 4-oxazolyl-phosphine oxides **11** and -phosphonates **12** while intramolecular cyclization of enamides **13** affords 5-oxazolyl-phosphine oxides **16**. Oxazoles[18] are common compounds in a wide variety of natural products possessing biological activity and both oxazoles and α-aminophosphonates[21] are widely used intermediates in organic and medicinal chemistry.[18,19,21,22]

4. Experimental

4.1. General

Chemicals were purchased from Aldrich Chemical Company. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with Merck silica gel 60 F_{254} plates. Visualization was accomplished by UV light. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM). Melting points were determined with an Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^{1}H (400, 300, 250 MHz), ^{13}C (100, 75 MHz) and ^{31}P NMR (120 MHz) spectra were recorded on a Bruker Avance 400 MHZ and a Varian Unity 300 MHz Plus spectrometer using $CDCl_3$ or CD_3OD solutions with TMS as an internal reference (δ= 0.00 ppm) for ^{1}H and ^{13}C NMR spectra and phosphoric acid (85%) (δ=0.0 ppm) for ^{31}P NMR spectra. Chemical shifts (δ) are reported in ppm. Coupling constants (J) are reported in Hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EIMS) on a Hewlett Packard 5971 spectrometer or by chemical ionization (CI) on a Hewlett Packard 1100 MSD spectrometer. Data are reported in the form m/z (intensity relative to base=100). Infrared spectra (IR) were taken on a Nicolet IRFT Magna 550 spectrometer, and were obtained as solids in KBr or as neat oils. Peaks are reported in cm^{-1}. Elemental analyses were performed in a LECO CHNS-932 apparatus. Azirines **1** and **6** were prepared according to literature procedures.[6,7]

4.2. General procedure for the preparation of *N*-acylaziridine-phosphine oxides 3

The corresponding acyl chloride **2** (5 mmol) was added to a solution of 2*H*-azirine-2-diphenylphosphine oxide **1** (5 mmol) in benzene (10 mL) under a nitrogen atmosphere. The mixture was stirred at room temperature until TLC indicated the disappearance of azirine (1–38 h). Evaporation of solvent under reduced pressure and chromatographic purification by flash column chromatography with hexane/ethyl acetate or crystallization afforded the corresponding derivatives **3**.

4.2.1. *trans*-*N*-Acetyl-3-chloro-3-methyl-aziridin-2-yl diphenyl phosphine oxide (3aa). The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) and acetyl chloride **2a** (0.38 mL, 5 mmol). Chromatographic purification and crystallization

from hexane/ethyl acetate gave 1.27 g (76%) of compound **3aa**; mp 197–198 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.06 (s, 3H), 2.23 (s, 3H), 3.32 (d, $^2J_{PH}$=23.0 Hz, 1H), 7.39–7.54 (m, 6H), 7.73–7.81 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.9, 25.0, 44.7 (d, $^1J_{PC}$=96.2 Hz), 59.8 (d, $^2J_{PC}$=5.5 Hz), 128.6–132.6 (m), 178.2 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 23.2 ppm; IR (KBr) ν_{max} 3065, 1720, 1388, 1366, 1210 cm^{-1}; *MS* (EI): *m/z* 335 (M^++2, 21), 333 (M^+, 62). Anal. Calcd for $C_{17}H_{17}ClNO_2P$: C, 61.18; H, 5.13; N, 4.20. Found: C, 61.35; H, 5.11; N, 4.21.

4.2.2. *trans*-*N*-Benzoyl-3-chloro-3-methyl-aziridin-2-yl diphenyl phosphine oxide (3ab). The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) and benzoyl chloride **2b** (0.58 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.60 g (81%) of compound **3ab**; mp 144–145 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.20 (s, 3H), 3.57 (d, $^2J_{PH}$= 22.7 Hz, 1H), 7.40–7.58 (m, 9H), 7.79–7.97 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 44.2 (d, $^1J_{PC}$= 96.7 Hz), 61.6 (d, $^2J_{PC}$=5.0 Hz), 128.1–134.0 (m), 175.0 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 23.5 ppm; IR (KBr) ν_{max} 3065, 1697, 1384, 1201 cm^{-1}; *MS* (EI): *m/z* 397 (M^++2, 18), 395 (M^+, 55). Anal. Calcd for $C_{22}H_{19}ClNO_2P$: C, 66.76; H, 4.84; N, 3.54. Found: C, 66.56; H, 4.81; N, 3.54.

4.2.3. *trans*-3-Chloro-3-methyl-*N*-(6-heptenoyl)-aziridin-2-yl diphenyl phosphine oxide (3ac). The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) and 6-heptenoyl chloride **2c** (0.73 g, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 0.85 g (43%) of compound **3ac**; mp 153–154 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (m, 2H), 1.69 (m, 2H), 2.06 (m, 2H), 2.11 (m, 3H), 2.58 (m, 2H), 3.40 (d, $^3J_{PH}$= 24.0 Hz, 1H), 4.97 (m, 2H), 5.78 (m, 1H), 7.45–7.63 (m, 6H), 7.81–7.88 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7, 25.1, 28.1, 33.3, 37.8, 44.2 (d, $^1J_{PC}$=97.0 Hz), 60.1 (d, $^2J_{PC}$=5.6 Hz), 114.7, 128.5–132.5 (m), 138.2, 181.1 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 23.3 ppm; IR (KBr) ν_{max} 3060, 1700, 1200 cm^{-1}; *MS* (EI): *m/z* 403 (M^++2, 21), 401 (M^+, 68). Anal. Calcd for $C_{22}H_{25}ClNO_2P$: C, 65.75; H, 6.27; N, 3.49. Found: C, 65.60; H, 6.29; N, 3.48.

4.2.4. *trans*-*N*-Acryloyl-3-chloro-3-methyl-aziridin-2-yl diphenyl phosphine oxide (3ad). The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) and acryloyl chloride **2d** (0.41 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.66 g (96%) of compound **3ad**; mp 113–114 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.10 (m, 3H), 3.40 (d, $^2J_{PH}$= 22.6 Hz, 1H), 5.89 (dd, $^3J_{HHcis}$=9.5 Hz, $^2J_{HHgem}$=3.8 Hz, 1H), 6.35 (m, $^3J_{HHcis}$=9.5 Hz, $^2J_{HHgem}$=3.8 Hz, $^3J_{HHtrans}$= 1.7 Hz, 2H), 7.40–7.56 (m, 6H), 7.76–7.83 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.1, 44.3 (d, $^1J_{PC}$=96.2 Hz), 60.5 (d, $^2J_{PC}$=5.5 Hz), 128.6–132.6 (m), 131.1, 131.4, 173.3 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 23.4 ppm; IR (KBr) ν_{max} 3060, 1705, 1187 cm^{-1}; *MS* (EI): *m/z* 347 (M^++2, 11), 345 (M^+, 33). Anal. Calcd for $C_{18}H_{17}ClNO_2P$: C, 62.53; H, 4.96; N, 4.05. Found: C, 62.44; H, 4.98; N, 4.07.

4.2.5. *trans*-*N*-Acetyl-3-chloro-3-ethyl-aziridin-2-yl diphenyl phosphine oxide (3ba). The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **1b** (1.34 g, 5 mmol) and acetyl chloride **2a** (0.38 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.47 g (85%) of compound **3ba**; mp 120–121 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.17 (t, $^3J_{HH}$=7.3 Hz, 3H), 2.22 (m, $^3J_{HH}$=7.2 Hz, $^3J_{HHgem}$=7.2 Hz, 1H), 2.29 (d, $^5J_{PH}$= 1.4 Hz, 3H), 2.47 (m, $^3J_{HH}$=7.2 Hz, $^3J_{HHgem}$=7.2 Hz, 1H), 3.43 (d, $^2J_{PH}$=23.2 Hz, 1H), 7.25–7.61 (m, 6H), 7.81–7.89 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.2, 25.0, 30.8, 45.4 (d, $^1J_{PC}$=96,7 Hz), 65.4 (d, $^2J_{PC}$= 4.5 Hz), 127.3–132.5 (m), 178.5 (d, $^3J_{PC}$=2.5 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 22.7 ppm; IR (KBr) ν_{max} 3058, 1666, 1434, 1374, 1199 cm^{-1}; *MS* (CI): *m/z* 348 (M^++1, 90). Anal. Calcd for $C_{18}H_{19}ClNO_2P$: C, 62.16; H, 5.51; N, 4.03. Found: C, 62.28; H, 5.50; N, 4.01.

4.2.6. *trans*-*N*-Acetyl-3-chloro-3-phenyl-aziridin-2-yl diphenyl phosphine oxide (3ca). The general procedure was followed using 2*H*-azirine-2-diphenylphosphine oxide **1c** (1.59 g, 5 mmol) and acetyl chloride **2a** (0.38 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.58 g (80%) of compound **3ca**; mp 97–98 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 3.86 (d, $^2J_{PH}$= 18.5 Hz, 1H), 7.12–7.58 (m, 13H), 7.79–7.86 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.1, 47.6 (d, $^1J_{PC}$=98.2 Hz), 61.3 (d, $^2J_{PC}$=5.5 Hz), 127.8–134.3 (m), 179.3 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 22.6 ppm; IR (KBr) ν_{max} 3065, 1699, 1434, 1381, 1242 cm^{-1}; *MS* (CI): *m/z* 335 (M^++1, 40). Anal. Calcd for $C_{22}H_{19}ClNO_2P$: C, 66.76; H, 4.84; N, 3.54. Found: C, 66.62; H, 4.85; N, 3.55.

4.3. General procedure for the preparation of α-amidophosphine oxides 4

A solution of the corresponding *N*-acylaziridine-phosphine oxide **3** (5 mmol) in THF (10 mL) was saturated with hydrogen chloride and the mixture was stirred at room temperature under a nitrogen atmosphere until the formation of a precipitate (4 h). Evaporation of solvent under reduced pressure and crystallization from ethyl acetate afforded compounds **4**.

4.3.1. *N*-[2-Chloro-1-(diphenylphosphinyl)-allyl]-acetamide (4aa). The general procedure was followed using *N*-acylaziridinephosphine oxide **3aa** (1.67 g, 5 mmol). Crystallization from ethyl acetate gave 1.60 g (96%) of compound **4aa**; mp 228–229 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.96 (s, 3H), 5.29 (d, $^2J_{HHgem}$= 2.1 Hz, 1H), 5.48 (dd, $^2J_{HHgem}$=2.1 Hz, $^4J_{PH}$=2.2 Hz, 1H), 5.77 (dd, $^2J_{PH}$=7.4 Hz, $^3J_{HH}$=9.8 Hz, 1H), 7.47–7.56 (m, 6H), 7.65 (d, $^3J_{HH}$=9.8 Hz, 1H), 7.74–7.86 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.8, 53.9 (d, $^1J_{PC}$= 76.0 Hz), 118.1 (d, $^3J_{PC}$=6.5 Hz), 128.5–132.5 (m), 135.5, 169.7 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 31.7 ppm; IR (KBr) ν_{max} 3227, 3180, 3060, 1670, 1205 cm^{-1}; *MS* (EI): *m/z* 335 (M^++2, 15), 333 (M^+, 42). Anal. Calcd for

$C_{17}H_{17}ClNO_2P$: C, 61.18; H, 5.13; N, 4.20. Found: C, 61.39; H, 5.12; N, 4.21.

The compound **4aa** was obtained directly (1.60 g, 96%) when 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) was added to a solution of acetyl chloride **2a** (0.38 mL, 5 mmol) in benzene (10 mL) saturated of hydrogen chloride and the mixture was stirred at room temperature for 2 h.

4.3.2. *N*-[2-Chloro-1-(diphenylphosphinyl)-allyl]-benzamide (4ab). The general procedure was followed using *N*-acylaziridinephosphine oxide **3ab** (1.98 g, 5 mmol). Crystallization from ethyl acetate gave 0.65 g (33%) of compound **4ab**; mp 223–224 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.36 (d, $^2J_{HHgem}$=2.1 Hz, 1H), 5.50 (d, $^2J_{HHgem}$=2.1 Hz, 1H), 5.91 (dd, $^2J_{PH}$=9.3 Hz, $^3J_{HH}$=8.1 Hz, 1H), 7.37–7.57 (m, 11H), 7.69 (d, $^3J_{HH}$=7.5 Hz, 1H), 7.81–7.90 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.4 (d, $^1J_{PC}$=75.0 Hz), 118.2 (d, $^3J_{PC}$=6.6 Hz), 127.2–133.3 (m), 135.5, 166.8 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 31.8 ppm; IR (KBr) ν_{max} 3204, 3065, 1646, 1200 cm^{-1}; *MS* (EI): *m/z* 398 (M^++3, 15), 396 (M^++1, 73). Anal. Calcd for $C_{22}H_{19}ClNO_2P$: C, 66.76; H, 4.84; N, 3.54. Found: C, 66.98; H, 4.78; N, 3.55.

The compound **4ab** was obtained directly (1.60 g, 96%) when 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) was added to a solution of benzoyl chloride **2b** (0.58 mL, 5 mmol) in benzene (10 mL) saturated of hydrogen chloride and the mixture was stirred at room temperature for 2 h.

4.3.3. *N*-[2-Chloro-1-(diphenylphosphinyl)-allyl]-heptenamide (4ac). The general procedure was followed using *N*-acylaziridinephosphine oxide **3ac** (2.01 g, 5 mmol). Crystallization from ethyl acetate gave 0.44 g (22%) of compound **4ac**; mp 187–188 °C (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16–1.26 (m, 2H), 1.31–1.51 (m, 2H), 1.91–1.98 (m, 2H), 2.09–2.29 (m, 2H), 4.90–4.98 (m, 2H), 5.30 (d, $^4J_{PH}$=0.5 Hz, 1H), 5.45 (d, $^4J_{PH}$=0.5 Hz, 1H), 5.68 (m, 1H), 5.77 (dd, $^2J_{PH}$=9.9 Hz, $^3J_{HH}$=7.5 Hz, 1H), 7.35 (d, $^3J_{HH}$=7.5 Hz, 1H), 7.44–7.58 (m, 6H), 7.75–7.87 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.0, 28.1, 33.3, 36.1, 53.6 (d, $^1J_{PC}$=76.0 Hz), 114.6, 118.1 (d, $^3J_{PC}$=6.6 Hz), 128.5–132.5 (m), 135.5, 138.3, 172.6 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 31.7 ppm; IR (KBr) ν_{max} 3220, 3065, 1660, 1195 cm^{-1}; *MS* (EI): *m/z* 404 (M^++3, 1), 402 (M^++1, 3). Anal. Calcd for $C_{22}H_{25}ClNO_2P$: C, 65.75; H, 6.27; N, 3.49. Found: C, 65.82; H, 6.23; N, 3.46.

The compound **4ac** was obtained directly (0.80 g, 40%) when 2*H*-azirine-2-diphenylphosphine oxide **1a** (1.28 g, 5 mmol) was added to a solution of 6-heptenoyl chloride **2c** (0.73 g, 5 mmol) in benzene (10 mL) saturated of hydrogen chloride and the mixture was stirred at room temperature for 2 h.

4.3.4. 3-Chloro-*N*-[2-chloro-1-(diphenylphosphinyl)-allyl]-propionamide (4ad). The general procedure was followed using *N*-acylaziridinephosphine oxide **3ad** (1.75 g, 5 mmol). Crystallization from ethyl acetate gave 0.92 g (48%) of compound **4ad**; mp 236–237 °C (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.68 (t, $^3J_{HH}$=6.6 Hz, 2H), 3.62 (t, $^3J_{HH}$=6.6 Hz, 2H), 5.29 (d, $^2J_{HHgem}$=2.1 Hz, 1H), 5.47 (d, $^2J_{HHgem}$=2.1 Hz, 1H), 5.74 (dd, $^2J_{PH}$=9.5 Hz, $^3J_{HH}$=7.1 Hz, 1H), 7.46–7.53 (m, 6H), 7.73–7.83 (m, 4H), 7.91 (d, $^3J_{HH}$=7.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.2, 39.0, 54.3 (d, $^1J_{PC}$=76.0 Hz), 119.7 (d, $^3J_{PC}$=7.5 Hz), 129.0–133.7 (m), 131.4 (d, $^2J_{PC}$=10.0 Hz), 172.3 (d, $^3J_{PC}$=5.5 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 31.7 ppm; IR (KBr) ν_{max} 3231, 3065, 1672, 1189 cm^{-1}; *MS* (EI): *m/z* 384 (M^++3, 16), 382 (M^++1, 18). Anal. Calcd for $C_{18}H_{18}Cl_2NO_2P$: C, 56.56; H, 4.75; N, 3.66. Found: C, 56.76; H, 4.76; N, 3.67.

4.3.5. *N*-[2-Chloro-1-(diphenylphosphinyl)-buten-2-enyl]-acetamide (4ba). This compound **4ba** was obtained directly when 2*H*-azirine-2-diphenylphosphine oxide **1b** (1.34 g, 5 mmol) was added to a solution of acetyl chloride **2a** (0.38 mL, 5 mmol) in benzene (10 mL) saturated of hydrogen chloride and the mixture was stirred at room temperature for 5 h. Crystallization from ethyl acetate gave 1.01 g (58%) of compound **4ba**; mp 231–232 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (m, $^5J_{PH}$=6.4 Hz, $^3J_{HH}$=3.0 Hz, 3H), 1.92 (s, 3H), 5.71 (dd, $^2J_{PH}$=9.9 Hz, $^3J_{HH}$=7.0 Hz, 1H), 5.82 (m, $^4J_{PH}$=6.6 Hz, $^3J_{HH}$=3.2 Hz, 1H), 7.21–7.80 (m, 10H), 8.00 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.6 (d, $^4J_{PC}$=3.0 Hz), 54.0 (d, $^1J_{PC}$=78.1 Hz), 127.3–132.6 (m), 170.0 (d, $^3J_{PC}$=6.4 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 32.6 ppm; IR (KBr) ν_{max} 3230, 3184, 3051, 1660, 1182 cm^{-1}; *MS* (CI): *m/z* 348 (M^++1, 100). Anal. Calcd for $C_{18}H_{19}ClNO_2P$: C, 62.16; H, 5.51; N, 4.03. Found: C, 62.30; H, 5.52; N, 4.02.

4.4. General procedure for the preparation of diethyl α-amidophosphonate 8

The corresponding acyl chloride **2** (5 mmol) was added to a solution of the corresponding 2*H*-azirine-phosphonate **6** (5 mmol) in benzene (10 mL) under a nitrogen atmosphere. The mixture was stirred at room temperature until TLC indicated the disappearance of azirine (1–36 h). Evaporation of solvent under reduced pressure and chromatographic purification by flash column chromatography with hexane/ethyl acetate afforded the corresponding derivatives **8**.

4.4.1. Diethyl (1-acetylamino-2-chloro-allyl)-phosphonate (8aa). The general procedure was followed 2*H*-azirine-phosphonate **6a** (0.96 g, 5 mmol) and acetyl chloride **2a** (0.38 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.35 g (91%) of compound **8aa** as an oil; R_f 0.65 (ethyl acetate/methanol 5%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27 (m, 6H), 2.01 (s, 3H), 4.15 (m, 4H), 5.15 (dd, $^2J_{PH}$=21.4 Hz, $^3J_{HH}$=9.3 Hz, 1H), 5.41 (m, 1H), 5.53 (m, 1H), 6.70 (d, $^3J_{HH}$=9.3 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.1, 22.5, 51.8 (d, $^1J_{PC}$=159.3 Hz), 63.3, 63.6, 117.1 (d, $^3J_{PC}$=9.1 Hz), 135.3 (d, $^2J_{PC}$=4.0 Hz), 169.7 (d, $^3J_{PC}$=7.5 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 19.1 ppm; IR (NaCl) ν_{max} 3258, 1666, 1186, 1097 cm^{-1}; *MS* (EI): *m/z* 271 (M^++2, 27), 269 (M^+, 42). Anal. Calcd for $C_9H_{17}ClNO_4P$: C, 40.09; H, 6.35; N, 5.19. Found: C, 40.28; H, 6.33; N, 5.20.

4.4.2. Diethyl (1-acryloylamino-2-chloro-allyl)-phosphonate (8ad). The general procedure was followed

2*H*-azirine-phosphonate **6a** (0.96 g, 5 mmol) and acryloyl chloride **2d** (0.41 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.10 g (78%) of compound **8ad** as an oil; R_f 0.51 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (m, $^3J_{HH}$= 7.3 Hz, 6H), 4.11 (m, 4H), 5.25 (dd, $^2J_{PH}$=21.5 Hz, $^3J_{HH}$= 9.5 Hz, 1H), 5.41 (m, 1H), 5.59 (m, 1H), 5.65 (dd, $^5J_{PH}$= 2.4 Hz, $^3J_{HHcis}$=9.3 Hz), 6.27 (m, 2H), 7.28 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.2 (d, $^3J_{PC}$=5.5 Hz), 16.3 (d, $^3J_{PC}$=3.5 Hz), 51.9 (d, $^1J_{PC}$=159.1 Hz), 63.5 (d, $^2J_{PC}$= 7.0 Hz), 63.7 (d, $^2J_{PC}$=7.0 Hz), 117.4 (d, $^3J_{PC}$=8.6 Hz), 127.8, 129.9, 135.2, 165.0 (d, $^3J_{PC}$=8.1 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 18.3 ppm; IR (NaCl) ν_{max} 3257, 1679, 1533, 1241, 1029 cm^{-1}; *MS* (EI): *m/z* 281 (M^+, 70). Anal. Calcd for $C_{10}H_{17}ClNO_4P$: C, 42.64; H, 6.08; N, 4.97. Found: C, 42.50; H, 6.10; N, 4.95.

4.4.3. Diethyl (1-acetylamino-2-chloro-but-2-enyl)-phosphonate (8ba). The general procedure was followed 2*H*-azirine-phosphonate **6b** (1.03 g, 5 mmol) and acetyl chloride **2a** (0.38 mL, 5 mmol). Chromatographic purification and crystallization from hexane/ethyl acetate gave 1.23 g (87%) of compound **8ba** as an oil; R_f 0.45 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (m, 6H), 1.72 (dd, $^5J_{PH}$=6.7 Hz, $^3J_{HH}$=4.4 Hz, 3H), 2.01 (s, 3H), 4.09 (m, 4H), 5.17 (dd, $^2J_{PH}$=21.7 Hz, $^3J_{HH}$=9.5 Hz, 1H), 5.97 (m, $^4J_{PH}$=6.7 Hz, $^3J_{HH}$=3.5 Hz, 1H), 6.94 (d, $^3J_{HH}$=9.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 16.3 (d, $^3J_{PC}$=5.0 Hz), 23.0, 52.3 (d, $^1J_{PC}$=160.6 Hz), 63.3 (d, $^2J_{PC}$=7.0 Hz), 126.7 (d, $^3J_{PC}$=10.1 Hz), 128.2 (d, $^2J_{PC}$=1.5 Hz), 169.3 (d, $^3J_{PC}$=7.5 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 19.8 ppm; IR (NaCl) ν_{max} 3482, 2979, 1712, 1454, 1261, 1016 cm^{-1}; *MS* (CI): *m/z* 284 (M^++1, 40). Anal. Calcd for $C_{10}H_{19}ClNO_4P$: C, 42.34; H, 6.75; N, 4.94. Found: C, 42.48; H, 6.77; N, 4.93.

4.5. General procedure for the preparation of 4-oxazolyl-phosphine oxides 11 and -phosphonates 12

To a solution of the corresponding vinylogous amide **4** (5 mmol) in dichloromethane (20 mL) a 2 N aqueous NaOH solution (0.95 mL, 25 mmol) was added and the heterogeneous mixture was stirred at room temperature for 2 days. The crude was extracted with dichloromethane and the organic layer was dried with anhidrous magnesium sulfate. Evaporation of solvent under reduced pressure afforded a mixture that was chromatographied on silica gel to give compounds **11** and **12**.

4.5.1. 2,5-Dimethyl-oxazol-4-yl diphenylphosphine oxide (11aa). The general procedure was followed using α-amidophosphine oxide **4aa** (1.67 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 1.29 g (87%) of compound **11aa** as a white solid; mp 117–118 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.42 (s, 3H), 2.59 (d, $^4J_{PH}$=1.8 Hz, 3H), 7.41–7.88 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.6, 13.8, 126.5 (d, $^1J_{PC}$=145.0 Hz), 128.3–133.8 (m), 158.9 (d, $^2J_{PC}$= 26.1 Hz), 160.4 (d, $^3J_{PC}$=19.2 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 18.8 ppm; IR (KBr) ν_{max} 3070, 1590, 1447, 1195 cm^{-1}; *MS* (EI): *m/z* 297 (M^+, 89). Anal. Calcd for $C_{17}H_{16}NO_2P$: C, 68.68; H, 5.42; N, 4.71. Found: C, 68.88; H, 5.40; N, 4.69.

4.5.2. 5-Methyl-2-phenyl-oxazol-4-yl diphenylphosphine oxide (11ab). The general procedure was followed using α-amidophosphine oxide **4ab** (1.98 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 1.47 g (82%) of compound **11ab** as a white solid; mp 134–135 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.65 (d, $^4J_{PH}$=1.9 Hz, 3H), 7.35–7.96 (m, 15H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.9, 126.5–133.8 (m), 159.0 (d, $^2J_{PC}$=27.0 Hz), 160.7 (d, $^3J_{PC}$=18.29 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 18.9 ppm; IR (KBr) ν_{max} 3070, 1780, 1585, 1442, 1187 cm^{-1}; *MS* (EI): *m/z* 359 (M^+, 56). Anal. Calcd for $C_{22}H_{18}NO_2P$: C, 73.53; H, 5.05; N, 3.90. Found: C, 73.43; H, 5.06; N, 3.91.

4.5.3. 2-(Hex-5-enyl)-5-methyl-oxazol-4-yl diphenylphosphine oxide (11ac). The general procedure was followed using α-amidophosphine oxide **4ac** (2.01 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 1.30 g (71%) of compound **11ac** as a white solid; mp 77–78 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.44 (tt, $^3J_{HH}$=7.5 Hz, $^3J_{HH}$=7.5 Hz, 2H), 1.75 (tt, $^3J_{HH}$=7.5 Hz, $^3J_{HH}$=7.5 Hz, 2H), 2.12 (dt, $^3J_{HH}$=7.5 Hz, $^3J_{HH}$=7.5 Hz, 2H), 2.58 (d, $^4J_{PH}$=2.1 Hz, 3H), 2.73 (t, $^3J_{HH}$=7.5 Hz, 2H), 4.98 (m, 2H), 5.78 (m, 1H), 7.41–7.89 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.6, 26.3, 27.7, 28.2, 29.6, 114.7, 126.0 (d, $^1J_{PC}$=145.0 Hz), 128.2–133.9 (m), 138.3, 158.6 (d, $^2J_{PC}$=26.7 Hz), 163.8 (d, $^3J_{PC}$= 17.6 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 18.3 ppm; IR (KBr) ν_{max} 3070, 1686, 1600, 1434, 1195 cm^{-1}; *MS* (EI): *m/z* 365 (M^+, 100). Anal. Calcd for $C_{22}H_{24}NO_2P$: C, 72.31; H, 6.62; N, 3.83. Found: C, 72.41; H, 6.60; N, 3.83.

4.5.4. 5-Methyl-2-vinyl-oxazol-4-yl diphenylphosphine oxide (11ad). The general procedure was followed using α-amidophosphine oxide **4ad** (1.91 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.80 g (52%) of compound **11ad** as a white solid; mp 100–101 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.61 (d, $^4J_{PH}$=2.1 Hz, 3H), 5.58 (dd, $^2J_{HHgem}$=0.9 Hz, $^3J_{HHcis}$=11.1 Hz, 1H), 6.10 (dd, $^2J_{HHgem}$=0.9 Hz, $^3J_{HHtrans}$=17.7 Hz, 1H), 6.50 (dd, $^3J_{HHcis}$=11.1 Hz, $^3J_{HHtrans}$=17.7 Hz, 1H), 7.38–7.86 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11,7, 122.4, 123.0, 126.4 (d, $^1J_{PC}$=145.0 Hz), 128.3–133.4 (m), 158.9 (d, $^2J_{PC}$= 26.7 Hz), 159.9 (d, $^3J_{PC}$=18.2 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 18.9 ppm; IR (KBr) ν_{max} 3065, 1750, 1600, 1180 cm^{-1}; *MS* (EI): *m/z* 310(M^++1, 26). Anal. Calcd for $C_{18}H_{16}NO_2P$: C, 69.90; H, 5.21; N, 4.53. Found: C, 69.75; H, 5.19; N, 4.55.

4.5.5. 5-Ethyl-2-methyl- oxazol-4-yl diphenylphosphine oxide (11ba). The general procedure was followed using α-amidophosphine oxide **4ba** (1.73 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 1.04 g (67%) of compound **11ba** as a white solid; mp 78–79 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (t, $^3J_{HH}$=7.5 Hz, 3H), 2.43 (s, 3H), 3.04 (q, $^4J_{PH}$=1.2 Hz, $^3J_{HH}$=7.5 Hz, 2H), 7.41–7.87 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.8, 13.8, 19.2, 125.4 (d, $^1J_{PC}$= 142.5 Hz), 128.2–133.8 (m), 160.4 (d, $^3J_{PC}$=18.1 Hz); 163.7 (d, $^2J_{PC}$=27.2 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 19.0 ppm; IR (KBr) ν_{max} 3059, 1586, 1440, 1196 cm^{-1}; *MS* (EI): *m/z* 311 (M^+, 100). Anal. Calcd for

$C_{18}H_{18}NO_2P$: C, 69.45; H, 5.83; N, 4.50. Found: C, 69.48; H, 5.84; N, 4.48.

4.5.6. 2-Methyl-5-phenyl-oxazol-4-yl diphenylphosphine oxide (11ca). The compound **11ca** was obtained directly when 2*H*-azirine-2-diphenylphosphine oxide **1c** (1.58 g, 5 mmol) was added to a solution of acetyl chloride **2a** (0.38 mL, 5 mmol) in benzene (10 mL) saturated of hydrogen chloride and the mixture was stirred at room temperature for 24 h. Chromatographic separation (hexane/ethyl acetate) gave 1.04 g (58%)of compound **11ca** as a white solid; mp 134–135 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.51 (t, $^3J_{HH}$=7.5 Hz, 3H), 7.32–8.09 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 128.3–132.2 (m), 159.0 (d, $^2J_{PC}$=25.2 Hz), 160.5 (d, $^3J_{PC}$=20.0 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 19.6 ppm; IR (KBr) ν_{max} 3051, 1580, 1481, 1202 cm^{-1}; *MS* (CI): *m*/*z* 360 (M^++1, 100). Anal. Calcd for $C_{22}H_{18}NO_2P$: C, 73.53; H, 5.05; N, 3.90. Found: C, 73.68; H, 5.04; N, 3.91.

4.5.7. Diethyl 2,5-(dimethyl-oxazol-4-yl) phosphonate (12aa). The general procedure was followed using diethyl α-amidophosphonate **8aa** (1.35 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.69 g (59%) of compound **12aa** as a colorless oil; R_f 0.34 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, $^3J_{HH}$=7.1 Hz, 6H), 2.44 (s, 3H), 2.54 (d, $^4J_{PH}$=2.4 Hz, 3H), 4.16 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 16.4 (d, $^3J_{PC}$=6.6 Hz), 62.5 (d, $^2J_{PC}$=5.5 Hz), 127.0 (d, $^1J_{PC}$=243.7 Hz), 158.5 (d, $^2J_{PC}$=39.8 Hz), 160.9 (d, $^3J_{PC}$=22.2 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 10.0 ppm; IR (NaCl) ν_{max} 2985, 1730, 1600, 1440, 1029 cm^{-1}; *MS* (EI): *m*/*z* 233 (M^+, 28). Anal. Calcd for $C_9H_{16}NO_4P$: C, 46.35; H, 6.92; N, 6.01. Found: C, 46.50; H, 6.94; N, 5.99.

4.5.8. Diethyl (5-methyl-2-vinyl-oxazol-4-yl)-phosphonate (12ad). The general procedure was followed using diethyl α-amidophosphonate **8ad**, (1.40 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.77 g (63%) of compound **12ad** as a colorless oil; R_f 0.51 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (t, $^3J_{HH}$=6.4 Hz, 6H), 2.53 (d, $^4J_{PH}$=2.3 Hz, 3H), 4.10 (m, 4H), 5.59 (d, $^3J_{HHcis}$=11.1 Hz, 1H), 6.04 (t, $^2J_{HHgem}$=0.8 Hz, $^3J_{HHtrans}$=17.6 Hz, 1H), 6.50 (dd, $^3J_{HHcis}$=11.3 Hz, $^3J_{HHtrans}$=17.7 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 16.3 (d, $^3J_{PC}$=6.6 Hz), 62.6 (d, $^2J_{PC}$=5.5 Hz), 122.6, 122.9, 158.5 (d, $^2J_{PC}$=39.8 Hz), 160.2 (d, $^3J_{PC}$=22.2 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 9.6 ppm; IR (NaCl) ν_{max} 2979, 1739, 1593, 1023 cm^{-1}; *MS* (EI): *m*/*z* 245 (M^+, 42). Anal. Calcd for $C_{10}H_{16}NO_4P$: C, 48.98; H, 6.58; N, 5.71. Found: C, 49.10; H, 6.56; N, 5.72.

4.5.9. Diethyl (5-ethyl-2-methyl-oxazol-4-yl)-phosphonate (12ba). The general procedure was followed diethyl α-amidophosphonate **8ba**, (1.41 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.76 g (65%) of compound **12ba** as a colorless oil; R_f 0.44 (ethyl acetate); ^{1}H NMR (300 MHz, CD_3OD): δ 1.08 (m, $^3J_{HH}$=7.0 Hz, 9H) Hz, 2.24 (s, 3H), 2.78 (dq, $^4J_{PH}$=1.5 Hz, $^3J_{HH}$=7.5 Hz, 2H), 3.71 (m, $^3J_{HH}$=7.8 Hz, 4H) ppm; ^{13}C NMR (75 MHz, CD_3OD): δ 13.3 (d, $^3J_{PC}$=4.1 Hz), 17.0 (d, $^4J_{PC}$=7.0 Hz), 20.0, 61.5, 129.8 (d, $^1J_{PC}$=221.1 Hz), 160.4 (d, $^2J_{PC}$=33.2 Hz), 161.7 (d, $^3J_{PC}$=19.1 Hz) ppm; ^{31}P NMR (120 MHz, CD_3OD): δ 5.0 ppm; IR (NaCl) ν_{max} 2985, 2925, 1666, 1586, 1434, 1049 cm^{-1}; *MS* (EI): *m*/*z* 247 (M^+, 34). Anal. Calcd for $C_{10}H_{18}NO_4P$: C, 48.58; H, 7.34; N, 5.67. Found: C, 48.71; H, 7.32; N, 5.69.

4.5.10. Diethyl (2-methyl-5-phenyl-oxazol-4-yl)-phosphonate (12ca). The compound **12ca** was obtained directly when 2*H*-azirinephosphonate **6c** (1.27 g, 5 mmol) was added to a solution of acetyl chloride **2a** (0.38 mL, 5 mmol) in benzene (10 mL) and the mixture was stirred at room temperature for 24 h. Chromatographic separation (hexane/ethyl acetate) gave 1.36 g (92%) of compound **12ca** as a colorless oil; R_f 0.51 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (t, $^3J_{HH}$=7.1 Hz, 6H), 2.55 (d, $^5J_{PH}$=0.5 Hz, 3H), 4.18 (m, 4H), 7.43 (m, 3H), 8.0 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 15.9 (d, $^4J_{PC}$=6.6 Hz), 62.4 (d, $^2J_{PC}$=5.5 Hz), 123.9 (d, $^1J_{PC}$=226.8 Hz), 126.0–129.5 (m), 157.1 (d, $^2J_{PC}$=37.8 Hz), 160.4 (d, $^3J_{PC}$=22.7 Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 10.0 ppm; IR (NaCl) ν_{max} 3065, 2979, 1580, 1487, 1023 cm^{-1}; *MS* (EI): *m*/*z* 295 (M^+, 24). Anal. Calcd for $C_{14}H_{18}NO_4P$: C, 56.95; H, 6.14; N, 4.74. Found: C, 57.10; H, 6.16; N, 4.73.

4.6. General procedure for the preparation of *N*-vinylamides 13

A solution of the corresponding *N*-acylaziridine-phosphine oxide **3** (5 mmol) and tributylamine (1.15 mL, 5 mmol) in chlorobenzene (10 mL) was refluxing in an atmosphere of nitrogen until TLC indicated the disappearance of *N*-acylaziridine. The crude was washed with HCl 2 N watery solution. The organic layer was dried with anhidrous magnesium sulfate. Evaporation of solvent under reduced pressure afforded a mixture that was chromatographied on silica gel to give compounds **13**.

4.6.1. *cis*-*N*-[2-Chloro-1-methyl-2-(diphenylphosphinyl)-vinyl)-acetamide (13aa). The general procedure was followed using *N*-acylaziridinephosphine oxide **3aa** (1.67 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.68 g (41%) of compound **13aa** as a white solid; mp 130–131 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (d, $^4J_{PH}$=2.4 Hz, 3H), 2.63 (d, $^6J_{PH}$=0.9 Hz, 3H), 7.49–7.85 (m, 10H), 11.64 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.5 (d, $^3J_{PC}$=6.0 Hz), 25.3, 100.4 (d, $^1J_{PC}$=114.0 Hz), 125.0–132.9 (m), 155.0 (d, $^2J_{PC}$=7.5 Hz), 168.7 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 35.6 ppm; IR (KBr) ν_{max} 3158, 3065, 1706, 1630, 1328, 1175 cm^{-1}; *MS* (EI): *m*/*z* 335 (M^++2, 10), 333 (M^+, 30). Anal. Calcd for $C_{17}H_{17}ClNO_2P$: C, 61.18; H, 5.13; N, 4.20. Found: C, 61.39; H, 5.10; N, 4.25.

4.6.2. *cis*-*N*-[2-Chloro-1-methyl-2-(diphenylphosphinyl)-vinyl]-benzamide (13ab). The general procedure was followed using *N*-acylaziridinephosphine oxide **3ab** (1.98 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 1.19 g (60%) of compound **13ab** as a white solid; mp 136–137 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.27 (d, $^4J_{PH}$=1.5 Hz, 3H), 7.38–8.04 (m, 15H), 12.53 (s, 1H) ppm; ^{13}C NMR (75 MHz,

$CDCl_3$): δ 19.0 (d, $^3J_{PC}=6.5$ Hz), 101.1 (d, $^1J_{PC}=115.0$ Hz), 127.0–134.1 (m), 155.0 (d, $^2J_{PC}=7.5$ Hz), 165.1 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 35.8 ppm; IR (KBr) ν_{max} 3120, 1689, 1310, 1154 cm^{-1}; *MS* (EI): *m/z* 397 ($M^+ +2$, 7), 395 (M^+, 17). Anal. Calcd for $C_{22}H_{19}ClNO_2P$: C, 66.76; H, 4.84; N, 3.54. Found: C, 66.80; H, 4.85; N, 3.50.

4.6.3. *cis*-*N*-[2-Chloro-1-methyl-2-(diphenylphosphinyl)-vinyl]-acrylamide (13ad). The general procedure was followed using *N*-acylaziridinephosphine oxide **3ad** (1.75 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.26 g (15%) of compound **13ad** as a white solid; mp 97–98 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (d, $^4J_{PH}=1.8$ Hz, 3H), 5.75 (dd, $^3J_{HHcis}=10.2$ Hz, $^2J_{HHgem}=1.2$ Hz, 1H), 6.20 (dd, $^3J_{HHcis}=10.2$ Hz, $^3J_{HHtrans}=17.1$ Hz, 1H), 6.39 (dd, $^3J_{HHtrans}=17.1$ Hz, $^2J_{HHgem}=1.2$ Hz, 1H), 7.49–7.83 (m, 10H), 11.96 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.6 (d, $^3J_{PC}=6.0$ Hz), 101.1 (d, $^1J_{PC}=114.0$ Hz), 127.8, 128.5–132.7 (m), 155.0 (d, $^2J_{PC}=8.0$ Hz), 163.6 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 35.6 ppm; IR (KBr) ν_{max} 3140, 1700, 1515, 1333, 1192 cm^{-1}; *MS* (EI): *m/z* 347 ($M^+ +2$, 17), 345 (M^+, 54). Anal. Calcd for $C_{18}H_{17}ClNO_2P$: C, 62.53; H, 4.96; N, 4.05. Found: C, 62.36; H, 5.00; N, 4.06.

4.6.4. *cis*-*N*-[2-Chloro-2-(diphenylphosphinyl)-1-ethyl-vinyl)-acetamide (13ba). The general procedure was followed using *N*-acylaziridinephosphine oxide **3ba** (1.73 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.94 g (54%) of compound **13ba** as a white solid; mp 73–74 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.72 (m, 3H), 1.97 (s, 3H), 3.02 (q, $^3J_{HH}=7.32$ Hz, 2H), 7.33–7.65 (m, 10H), 11.42 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.8, 24.1 (d, $^3J_{PC}=5.5$ Hz), 25.4, 100.2 (d, $^1J_{PC}=113.8$ Hz), 128.2–132.9 (m), 160.4 (d, $^2J_{PC}=6.6$ Hz), 168.1 ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 35.7 ppm; IR (KBr) ν_{max} 3124, 3032, 1706, 1606, 1374, 1248 cm^{-1}; *MS* (CI): *m/z* 348 ($M^+ +1$, 53). Anal. Calcd for $C_{18}H_{19}ClNO_2P$: C, 62.16; H, 5.51; N, 4.03. Found: C, 62.30; H, 5.52; N, 4.04.

4.7. General procedure for the preparation of 5-oxazolyl-phosphine oxides 16

A solution of the corresponding *N*-vinylamide **13** (5 mmol) in THF (20 mL) was added to a 0 °C suspension of NaH (0.24 g, 6 mmol) in THF (15 mL). The mixture was refluxed in nitrogen atmosphere until TLC indicated the disappearance of *N*-vinylamide. Ice was added and the mixture was extracted with dichlorometane. The organic layer was dried with anhidrous magnesium sulfate. Evaporation of solvent under reduced pressure afforded a mixture that was chromatographied on silica gel to give compounds **16**.

4.7.1. 2,4-Dimethyloxazol-5-yl diphenylphosphine oxide (16aa). The general procedure was followed using *N*-vinylamide **13aa** (1.67 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 0.97 g (65%) of compound **16aa** as a white solid; mp 111–112 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.23 (d, $^4J_{PH}=1.8$ Hz, 3H), 2.45 (s, 3H), 7.46–7.77 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.7, 14.0, 128.3–133.8, 137.9 (d, $^1J_{PC}=134.4$ Hz), 149.5 (d, $^2J_{PC}=18.1$ Hz), 164.9 (d, $^3J_{PC}=10.1$ Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 16.6 ppm; IR (KBr) ν_{max} 3065, 1593, 1441, 1315, 1202 cm^{-1}; *MS* (EI): *m/z* 297 (M^+, 100). Anal. Calcd for $C_{17}H_{16}NO_2P$: C, 68.68; H, 5.42; N, 4.71. Found: C, 68.88; H, 5.40; N, 4.73.

4.7.2. 4-Methyl-2-phenyl-oxazol-5-yl diphenylphosphine oxide (16ab). The general procedure was followed using *N*-vinylamide **13ab** (1.98 g, 5 mmol). Chromatographic separation (hexane/ethyl acetate) gave 1.29 g (72%) of compound **16ab** as a white solid; mp 158–159 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.44 (d, $^4J_{PH}=1.8$ Hz, 3H), 7.48–8.04 (m, 15H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.9, 126.5–132.5, 138.1 (d, $^1J_{PC}=133.0$ Hz), 150.7 (d, $^2J_{PC}=18.0$ Hz), 164.2 (d, $^3J_{PC}=10.1$ Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 16.6 ppm; IR (KBr) ν_{max} 3070, 3020, 1699, 1205 cm^{-1}; *MS* (EI): *m/z* 359 (M^+, 60). Anal. Calcd for $C_{22}H_{18}NO_2P$: C, 73.53; H, 5.05; N, 3.90. Found: C, 73.36; H, 5.03; N, 3.91.

4.7.3. 4-Ethyl-2-methyl-oxazol-5-yl diphenylphosphine oxide (16ba). The general procedure was followed using *N*-vinylamide **13ba**. Chromatographic separation (hexane/ethyl acetate) gave 0.89 g (57%) of compound **16ba** as a white solid; mp 75–76 °C (hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09 (t, $^3J_{HH}=7.5$ Hz, 3H), 2.39 (d, $^5J_{PH}=0.8$ Hz, 3H), 2.55 (q, $^3J_{HH}=7.6$ Hz, 2H), 7.40–7.70 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 14.1, 19.9, 128.5–132.4, 137.2 (d, $^1J_{PC}=134.5$ Hz), 155.0 (d, $^2J_{PC}=18.1$ Hz), 165.1 (d, $^3J_{PC}=10.6$ Hz) ppm; ^{31}P NMR (120 MHz, $CDCl_3$): δ 16.3 ppm; IR (KBr) ν_{max} 3058, 1719, 1585, 1427, 1202 cm^{-1}; *MS* (EI): *m/z* 311 (M^+, 100). Anal. Calcd for $C_{18}H_{18}NO_2P$: C, 69.45; H, 5.83; N, 4.50. Found: C, 69.57; H, 5.84; N, 4.51.

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