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Stereochemistry of substituted isoxazolidines derived from *N*-methyl *C*-diethoxyphosphorylated nitrone

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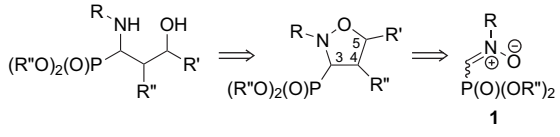
Abstract—Cycloadditions of *N*-methyl-*C*-(diethoxyphosphoryl)nitrone **1a** to cyclic alkenes proceeded regio- and diastereospecifically. Reactions of **1a** with 1,1-disubstituted alkenes led to the regiospecific formation of 5,5-disubstituted isoxazolidines **7/8** in nearly equimolar ratios, whereas additions to *trans*-1,2-disubstituted alkenes gave four isomeric isoxazolidines with up to 80% regioselectivity and moderate (up to 60%) diastereoselectivity. Stereochemistry of the substituted isoxazolidines was established based on the conformational analysis using vicinal H–H, H–P and P–C couplings, and was, in some cases, supported by geminal H–C–P=O coupling and deshielding P=O and C=O effects.

1. Introduction

Isoxazolidines have been found to exhibit antimicrobial activity[1–4] and have been used as enzyme inhibitors.[5–8] Isoxazolidine nucleoside analogues, in which a furanose ring has been replaced by an *N*,*O*-heterocyclic system, are a particularly interesting group of compounds due to their potential antiviral activity.[9–14] Isoxazolidines have also been employed as useful building blocks in the synthesis of various natural and unnatural compounds, including alkaloids, biologically active β-aminoacids, β-lactams, amino sugars, as well as simple 1,3-aminoalcohols owing to the facile cleavage of the N–O bond.[15–17] The 1,3-dipolar cycloaddition of nitrones to alkenes has been the most efficient approach employed for the construction of isoxazolidines, since the stereochemistry of the reaction is predictable, and the mechanism has been established.[15,17,18] A wide range of acyclic and cyclic nitrones have been reacted with substituted alkenes leading to the formation of structurally diverse and highly functionalized nitrogen-containing compounds.[15,16,19] Studies on both inter- and intramolecular nitrone to alkene dipolar cycloadditions have received much interest from a stereochemical point of view, since up to three new stereogenic centres can be created in the isoxazolidines depending on the structural features of the starting materials. Despite the known existence of acyclic nitrones as mixtures of (*E*)- and (*Z*)-isomers, or as single isomer in the case of cyclic analogues, the diastereoselectivity of cycloaddition depends also on the structure of the alkene dipolarophiles. In most cases, cycloadducts were formed in a predictable regio- and stereocontrolled manner due to steric and electronic effects.

Synthesis of functionalized α-aminophosphonates has attracted significant attention, since α-aminophosphonates have been recognized as structural mimetics of natural and unnatural α-aminoacids.[20] Recently, a convenient method for the synthesis of *C*-phosphorylated nitrones **1** has been described and their reactivity in cycloadditions with terminal alkenes has been briefly examined.[21] Substituted 3-phosphorylated isoxazolidines can be employed as key intermediates in the synthesis of functionalized 1-amino-3-hydroxyphosphonates by utilizing the known hydrogenolytic transformation of isoxazolidines into 4-hydroxy-2-aminoacids (Scheme 1).



Scheme 1. Retrosynthesis of substituted α-aminophosphonates from nitrones **1**.

In this paper, a full account of the studies previously communicated[21] is given and the reactivity of nitrone **1a** with di-, tri- and tetrasubstituted alkenes is explored. In particular, 1,2-disubstituted and especially cyclic alkenes were studied in order to obtain particularly interesting, highly functionalized conformationally restricted phosphonate analogues of aminoacids.

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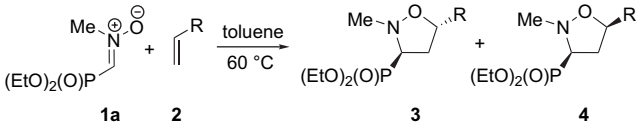
2. Results and discussion

As reported earlier, the 1,3-dipolar cycloadditions of nitrone **1a** to terminal alkenes were carried out in toluene at 60 °C (Scheme 2, Table 1).[21] Reactions were conducted until the starting nitrone disappeared. The ratios of diastereomeric isoxazolidines **3** and **4** were calculated from the ^{31}P and ^{1}H NMR spectra of crude reaction mixtures.



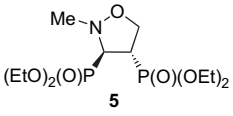
Scheme 2. 1,3-Dipolar cycloadditions of nitrone **1a** and terminal alkenes.

Table 1. Isoxazolidines **3** and **4** produced via Scheme 2

Entry	R	Reaction time (h)	trans/cis ratio (**3**:**4**)	Yield (%)
a	CH_2OH	48	62:38	**3a** (38);[a] **4a** (20)[a]
b	CH_2NHBoc	48	72:28	Inseparable (83)[b]
c	CH_2Br	40	65:35	Inseparable (61)[b]
d	CH_2SiMe_3	40	95:5	**3d** (64)[a]
e	COOMe	24	90:10	**3e** (73)[a]
f	OAc	40	90:10	**3f** (62)[a]
g	Ph	24	90:10	**3g** (60);[a] **4g** (2)[a]
h	$P(O)(OEt)_2$	24	74:19[c]	**3h** (29);[a] **4h** (7)[a]
i	$CH_2P(O)(OEt)_2$	50	74:26	**3i** (23);[a] **4i** (4)[a]

[a] Yield of pure materials obtained after silica gel chromatography.
[b] Yield of pure mixture of two diastereoisomers.
[c] C4-regioisomer **5** (7%) was also produced.

The cycloadditions of nitrone **1a** with terminal alkenes were regiospecific (except for entry h, Table 1) and afforded trans/cis mixtures of *C*5-substituted isoxazolidines **3a–i** and **4a–i** in moderate (65:35) to very good (95:5) diastereoselectivity. When diethyl vinylphosphonate (**2h**) was used, however, the *C*4-regioisomer **5** was also formed, and its presence was detected in the crude product by ^{31}P NMR spectroscopy. Based on the coupling constant value of $^{3}J(P\text{–}C3C4\text{–}P)$=30.5 Hz, which was found to be comparable with a similar coupling observed for **7f** [$^{3}J(P\text{–}C3C3a\text{–}P4)$=25.5 Hz] (vide infra), the trans arrangement of the two phosphonate substituents in **5** was suggested.



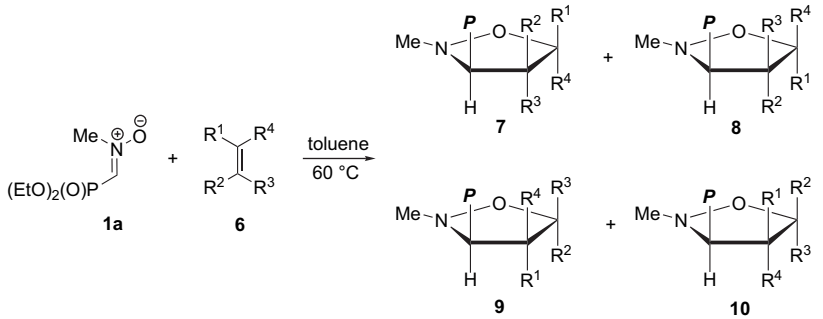
The trans configuration of the major 3,5-substituted isoxazolidines **3** and the cis relationship for minor isomers **4** were already established.[21]

The ratios of isoxazolidines **3** and **4** produced in thermal cycloadditions can be modified by the application of $ZnCl_2$.[19] When nitrone **1a** was reacted with allyl alcohol (**2a**) and allyltrimethylsilane (**2d**) in the presence of an equimolar amount of $ZnCl_2$ at room temperature, mixtures of isoxazolidines **3** and **4** enriched with the cis isomers (20:80 and 55:45, respectively) were produced, as compared to those formed under thermal conditions (Table 1, entries a and d). However, for vinylphosphonate (**2h**) and allylphosphonate (**2i**) no influence of $ZnCl_2$ on the cis/trans ratios of the respective isoxazolidines was noticed.

Having established the stereochemistry of the cycloaddition of **1a** with terminal alkenes, the scope and limitation of this reaction were investigated with di-, tri- and tetrasubstituted alkenes (Scheme 3, Table 2).

Addition of **1a** to cyclic alkenes **6a–6f** was diastereospecific (entries a–f, Table 2), and was also found to be regiospecific for **6c** and **6f** (entries c and f, Table 2). However, a 21:79 mixture of diastereoisomeric products was formed from 3-phospholene **6e**, because a new stereogenic centre at P(6) in the bicyclic system was created (entry e, Table 2). Surprisingly, a single diastereoisomer **7f** was obtained from 2-phospholene **6f**. Cycloadditions with 1,1-disubstituted alkenes **6g**, **6h** and **6i** also occurred regiospecifically (Table 2), however, a negligible diastereoselectivity for **6h** and **6i** was observed (entries h and i). On the other hand, *trans*-1,2-disubstituted alkenes **6j** and **6k** led to mixtures of four isoxazolidines with 54 and 82% regioselectivity and moderate, 20–60% diastereoselectivity (entries j and k, Table 2). Furthermore, treatment of nitrone **1a** with diethyl 2-(propan-2-ylidene)malonate **6l** did not give a cycloaddition product, due to the decomposition of the starting nitrone as was observed after heating the reaction mixture for 20 days.

The mixtures of 3,5,5-trisubstituted isoxazolidines **7h** and **8h** as well as **7i** and **8i** were found to be partially separable, giving fractions enriched with the respective isomers of up to 90% purity. This was sufficient to unambiguously calculate the chemical shifts and coupling constants for each component of the diastereoisomeric pairs of isoxazolidines **7h/8h** and **7i/8i**. Three out of four 3,4,5-trisubstituted isoxazolidines formed from chalcone **6j** and nitrone **1a** were isolated as pure compounds in 12% (**7j**), 50% (**8j**) and 3% (**10j**)



Scheme 3. 1,3-Dipolar cycloadditions of nitrone **1a** and substituted alkenes; **P**=$P(O)(OEt)_2$.

Table 2. Isoxazolidines **7**, **8**, **9** and **10** produced via Scheme 3

Entry	Substituted alkenes **6**				Reaction time	**7**:**8**	**9**:**10**	Yield (%)
	R^1	R^2	R^3	R^4				
a	H	H	$-CH_2CH_2CH_2CH_2-$		18 days	100:0	—	**7a** (100)[a]
b	H	H	$-CH_2CH_2CH_2-$		7 days	100:0	—	**7b** (90)[a]
c	H	H	$-CH_2CH_2O-$		24 h	100:0	—	**7c** (70)[a]
d	H	H	$-CH_2OCH_2-$		24 h	100:0	—	**7d** (71)[a]
e	H	H	$-CH_2P(O)(Ph)CH_2-$		48 h	100:0	—	**7e** (82)[b] (inseparable)[c]
f	H	H	$-P(O)(Ph)CH_2CH_2-$		24 h	100:0	—	**7f** (88)[a]
g	$P(O)(OEt)_2$	H	H	$P(O)(OEt)_2$	24 h	—	—	**7g** (90)[a]
h	$P(O)(OEt)_2$	H	H	COOEt	24 h	46:54	—	Inseparable (90)[b]
i	CH_3	H	H	COOMe	24 h	40:60	—	Inseparable (90)[b]
j	H	C(O)Ph	H	Ph	48 h	20:57	5:18	**7j** (12),[a] **8j** (50),[a] **10j** (3)[a]
k	H	COOEt	H	Ph	48 h	55:36	7:2	**7k** (13),[a] **8k** (7)[a]
l	COOEt	CH_3	CH_3	COOEt	20 days	—	—	Decomposition[d]

[a] Yield of pure materials obtained after silica gel chromatography.
[b] Yield of pure mixture of two diastereoisomers.
[c] A mixture of inseparable *P*(6)-diastereoisomers (21:79) was produced.
[d] Decomposition of the starting nitrone **1a** was observed. The unreacted alkene **6l** was recovered in 80% yield.

yields. On the other hand, only two major diastereoisomers **7k** and **8k**, obtained from ethyl cinnamate **6k**, could be isolated as pure compounds.

The assignment of relative configurations of isoxazolidines has often been difficult due to conformational flexibility of the substituted five-membered ring. The structures of the cycloadducts obtained in this study were established based on conformational analysis. To this end, all vicinal H–H coupling constants and chemical shifts of ring protons were unambiguously extracted from the ^{1}H NMR spectra. In addition, the presence of the diethoxyphosphoryl group at C(3) in the isoxazolidine ring imparted greater stereochemically valuable data over *PCCH*[22,23] and *PCCC*[23–26] vicinal couplings, and appeared to be extremely useful in establishing the stereochemistries of phosphorus-labelled heterocycles.[27,28]

Based on the accepted concerted mechanism of the nitrone to alkene cycloaddition,[15,17,18] the cis-fusion of the rings in the bicyclic isoxazolidines obtained from nitrone **1a** and cyclic alkenes **6a**–**6f** is expected. A set of vicinal couplings found for **7a**: *J*(*H*–C3C3a–*H*)=3.6 Hz, *J*(*H*–C3aC7a–*H*)=4.2 Hz, *J*(*H*–C3aC3–*P*)=16.0 Hz, *J*(*P*–CC–*C*7a)=4.5 Hz and *J*(*P*–CC–*C*4)=11.5 Hz, *J*(*Hax*–C3aC4–*Hax*)=11.0 Hz, *J*(*Hax*–C3aC4–*Heq*)=5.0 Hz, *J*(*Heq*–C7aC7–*Heq*)=4.2 Hz and *J*(*Heq*–C7aC7–*Hax*)=4.2 Hz clearly indicates the stable E_{3a} conformation of the isoxazolidine ring, while the cyclohexane ring exists as a $_{7a}C^5$ chair. In this conformation of the bicyclic **7a**, the diethoxyphosphoryl group is forced to reside in a pseudoaxial position of the isoxazolidine ring. Furthermore, it occupies the same side of the molecule as both bridgehead protons, *H*–C(3a) and *H*–C(7a) (Fig. 1).

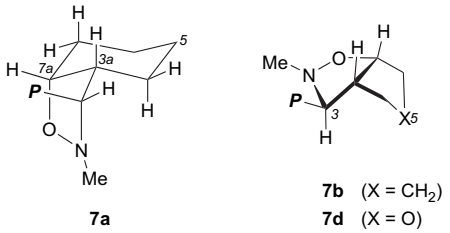


Figure 1. The preferred conformation of **7a**, **7b** and **7d**; **P**=P(O)(OEt)$_2$.

Similar application of the dihedral angle relationships derived from the sets of vicinal couplings found for compounds **7b**–**7f** allowed us to propose stable conformations for these fused isoxazolidines (Table 3, Figs. 1 and 2). This clearly established the cis relationships between the diethoxyphosphoryl group at C(3) and both bridgehead hydrogens at C(3a) and C(6a).

In addition to the various vicinal coupling constants, two other spectral data deserve comments in connection with conformational preferences of **7f** and both isomers of **7e**. Significant deshielding of the *H*–C(3) in **7f** (δ_H=3.79 ppm), as compared to the chemical shifts of the same hydrogen atoms in **7a**–**7e** (2.38–2.99 ppm), undoubtedly results from very close spacial proximity of the P=O group from the phospholane ring and *H*–C(3) (Fig. 2). This observation strongly suggests that the P=O group at P(4) adopts a pseudoaxial position. Less pronounced deshielding of the *H*–C(3) (δ_H=2.99 ppm) and *Hα*–C(4) (δ_H=2.25 ppm) in the major diastereoisomer of **7e** was observed, as compared to the same hydrogens in the minor diastereoisomer (δ_H=2.72 and 1.97 ppm, respectively). On the other hand, the P=O group slightly deshielded the *H*–C(3a) (δ_H=3.65 ppm) and *Hα*–C(6a) (δ_H=4.82 ppm) in the minor diastereoisomer of **7e**.

Moreover, in establishing the conformational features of the isoxazolidine/phospholane fused systems **7e** and **7f** two-bond H–C–P couplings[27] proved very helpful. Thus, the pseudoaxial disposition of phosphoryl oxygen in the phospholane ring of **7f** is further supported by the value of ^2J(PCH)=2.4 Hz found for the H–C_{3a}–P_4=O unit, as illustrated by the respective Newman projection (Fig. 2). For the major and minor diastereoisomers of **7e** two slightly different conformations were assigned based on the analysis of vicinal couplings (Fig. 2). Again, values of the geminal phosphorus–hydrogen couplings [$^2J(PCH_{4\alpha})$=16.8 Hz, $^2J(PCH_{4\beta})$=7.5 Hz for the major **7e** and $^2J(PCH_{4\alpha})$=6.8 Hz, $^2J(PCH_{4\beta})$=15.4 Hz, $^2J(PCH_{6\beta})$=16.4 Hz for the minor **7e**] fully support the already established conformations.

Structures of 3,5,5- and 3,4,5-trisubstituted isoxazolidines (Table 2, entries h–k) were also unequivocally established based on the conformational analysis. The diagnostic vicinal couplings are shown in Table 4.

Table 3. Vicinal couplings for compounds **7b–7f** and their conformations

Vicinal coupling constants (Hz)	Compounds					
	7b	**7c**	**7d**	**7e** (major)	**7e** (minor)	**7f**
J(*P*–C3C4–*C*6*a*)	9.8	10.0	9.5	10.0	6.9	8.8
J(*P*–C3C3a–*C*4)	3.4	3.8	3.4	5.2	8.3	—
J(*P*–C3C3a–*H*)	16.2	17.1	16.0	18.3	20.0	20.1
J(*H*–C3C3a–*H*)	8.0	8.4	7.8	7.0	5.2	5.7
J(*H*–C3aC6a–*H*)	8.0	5.4	7.0	7.0	6.4	5.7
J(*H*–C3aC4–*Hα*)	0	0.9	0	7.0	9.3	—
J(*H*–C3aC4–*Hβ*)	8.0	8.4	6.0	9.2	8.8	—
J(*H*–C6aC6–*Hα*)	0	—	0	5.3	2.0	0
J(*H*–C6aC6–*Hβ*)	3.7	—	3.8	5.3	6.4	4.5
J(*Hβ*–C4C5–*Hα*)	Overlap	11.4	—	—	—	—
J(*Hα*–C4C5–*Hα*)	Overlap	5.4	—	—	—	—
J(*Hβ*–C4C5–*Hβ*)	Overlap	8.4	—	—	—	—
J(*P*5–C4C3a–*H*)	—	—	—	8.7	0	—
J(*P*4–C3aC3–*H*)	—	—	—	—	—	18.9
J(*P*4–C3aC6a–*H*)	—	—	—	—	—	24.0
J(*P*5–C4C3a–*C*3)	—	—	—	6.0	10.6	—
J(*P*5–C4C3a–*C*6*a*)	—	—	—	10.0	9.7	—
J(*P*5–C6C6a–*H*)	—	—	—	18.6	21.2	—
Conformation[a]	E_3/E_5	E_3/E^4	E_3/E_5	$E_3/{}^4T_5$	${}^{6a}E/E_4$	${}^{6a}E/{}^6E$

[a] Isoxazolidine ring/fused ring.

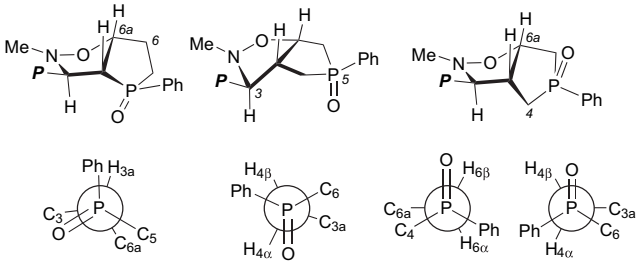
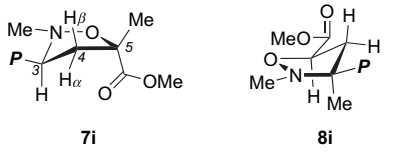


Figure 2. The preferred conformations of **7f** and **7e** (major—left, minor—right); **P**=P(O)(OEt)$_2$.

Furthermore, in some instances the P═O and C═O deshielding effects were observed and they were employed as additional arguments for establishing the relative configurations. For instance, in the E_5 conformation of the isoxazolidine **7i**, the *Hα*–C(4) is shifted downfield (δ_H=3.05 ppm) by the C═O group compared to the same hydrogen atom in diastereoisomer **8i** (δ_H=2.36 ppm). On the other hand, the *Hβ*–C(4) in **8i** (cis-positioned to the COOMe) was shifted downfield (δ_H=3.22 ppm), while in **7i** the respective hydrogen resonated at δ_H=2.49 ppm (Fig. 3).



7i **8i**

Figure 3. The preferred conformations of **7i** and **8i**; **P**=P(O)(OEt)$_2$.

A general tendency of the diethoxyphosphoryl group to occupy pseudoequatorial positions is observed for all isoxazolidines reported herein, except for the compound **7a** in which this substituent is forced to reside in a pseudoaxial position in the chair conformation of the six-membered ring. Moreover, the phenyl group also prefers to be positioned equatorially. In the phospholane rings of compounds **7e** and **7f** this preference is additionally enhanced by pseudoaxial orientation of the P═O group.

3. Conclusions

Cycloadditions of nitrone **1a** to cyclic alkenes led to the formation of single diastereoisomers **7**, in which the diethoxyphosphoryl group is located on the same side of the

Table 4. Vicinal couplings for compounds **7h–k**, **8h–k** and **10j** and their conformations

Vicinal coupling constants (Hz)	Compounds								
	7h	**8h**	**7i**	**8i**	**7j**	**8j**	**10j**	**7k**	**8k**
J(*P*–C3C4–*C*5)	12.0	9.4	8.3	10.6	3.7	5.4	9.2	4.3	5.4
J(*P*–C3C4–*Hα*)	3.3	4.8	4.8	6.6	21.3	—	—	17.4	
J(*P*–C3C4–*Hβ*)	14.4/16.5[a]	16.5	16.8	18.3	—	17.7	17.1	—	13.5
J(*H*–C3C4–*Hα*)	6.6	8.4	7.8	9.3	9.9	—	—	10.2	—
J(*H*–C3C4–*Hβ*)	12.3	9.6	10.5	8.7	—	7.2	8.7	—	7.5
J(*Hα*–C4C5–*Hβ*)	—	—	—	—	9.0	—	—	8.7	—
J(*Hβ*–C4C5–*Hα*)	—	—	—	—	—	7.8	4.2	—	7.0
J(*P*–C5C4–*C*3)	6.0	4.5	—	—	—	—	—	—	—
J(*P*–C5C4–*Hα*)	0.9	17.7	—	—	—	—	—	—	—
J(*P*–C5C4–*Hβ*)	16.5/14.4[a]	11.4	—	—	—	—	—	—	—
J(*P*–C3C4–*C*═O)	—	—	—	—	5.2	4.0	—	6.6	5.4
J(*P*–C3C4–C_{ipso})	—	—	—	—	—	—	0	—	—
Conformation	${}_3E$	E^4	${}_3E$	E^4	E^5	E_5	${}_3T^2$	E^5	${}^1E$

[a] The values cannot be assigned unequivocally.

molecule as both bridgehead hydrogens. Reactions of **1a** with 1,1-disubstituted alkenes appeared to be regiospecific, giving 3,5,5-trisubstituted isoxazolidines **7/8** with low diastereoselectivities. Additions to *trans*-1,2-disubstituted alkenes proceeded with good regio- (up to 80%) and moderate (up to 60%) diastereoselectivity.

Stereochemistry of substituted isoxazolidines has been established based on the conformational analysis using combinations of *H*–CC–*H*, *H*–CC–*P* and *C*–CC–*P* vicinal couplings, H–C–P=O geminal couplings and deshielding effects of the P=O and C=O groups.

As the synthesis of *C*-phosphorylated isoxazolidine cycloadducts is straightforward, and the regio- and stereochemistry of their formation is predictable, they could be used as suitable precursors for the synthesis of various substituted α-aminophosphonates. Studies on the synthesis of enantiomerically pure α-aminophosphonates, including phosphohomoserine, phosphonate analogues of α-hydroxyglutamic acid and proline are currently under investigation in this laboratory, and among others.

4. Experimental

4.1. General

^{1}H NMR spectra were taken in $CDCl_3$ or C_6D_6 on the following spectrometers: Varian Mercury-300 and Bruker DPX (500 MHz) with TMS as an internal standard. ^{13}C and ^{31}P spectra were recorded for $CDCl_3$ or C_6D_6 solution on a Varian Mercury-300 instrument at 75.5 and 121.5 MHz, respectively. ^{1}H{^{31}P} NMR and ^{1}H–^{1}H COSY experiments were applied, when necessary to support spectral assignments. IR spectra were measured on an Infinity MI-60 FT-IR spectrometer. Melting points were determined on a Boetius apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory of this Faculty on a Perkin–Elmer PE 2400 CHNS analyser.

The following adsorbents were used: column chromatography, Merck silica gel 60 (70–230 mesh); analytical TLC, Merck TLC plastic sheets silica gel 60 F_{254}. TLC plates were developed in various ethyl acetate–hexanes, toluene–isopropanol, toluene–hexanes or chloroform–methanol solvent system. Visualization of spots was effected with iodine vapours.

4.2. General procedure for the cycloaddition of nitrone 1a to alkenes

Nitrone **1a** (1.0 mmol) and an alkene (1.0–10.0 mmol) were stirred in toluene (1–5 mL) at 60 °C and the disappearance of the starting nitrone was monitored by TLC. All volatiles were removed in vacuo and the crude products were purified by chromatography on a silica gel column.

4.3. Diethyl 5-(hydroxymethyl)-2-methylisoxazolidin-3-yl-3-phosphonates (3a and 4a)

From nitrone **1a** (0.914 g, 4.68 mmol) and allyl alcohol (0.64 mL, 9.4 mmol), a mixture of isoxazolidines **3a** and **4a** (1.237 g) was obtained and purified on silica gel with chloroform–MeOH (100:1).

*Compound **3a***: yield 0.45 g, 38%. Colourless oil. IR (film): ν=3400, 2983, 2910, 1444, 1226, 1051, 1023, 970 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.27–4.12 (m, 5H, *H*–C5 and 2×CH_2–O–P), 3.82 (ddAB, J_{AB}=12.0 Hz, J_{3-4}=2.7 Hz, J=0.9 Hz, 1H, C*H*$_2$OH), 3.59 (dAB, J_{AB}=12.0 Hz, J_{3-4}=4.5 Hz, 1H, C*H*$_2$OH), 2.96 (very br s, 1H, CH–P), 2.89 (d, J=0.9 Hz, 3H, C*H*$_3$–N), 2.63–2.34 (m, 2H, P–CH–C*H*$_2$), 2.09 (br s, 1H, OH), 1.36 (t, J=6.9 Hz, 3H, C*H*$_3$–CH_2–O–P), 1.35 (t, J=6.9 Hz, 3H, C*H*$_3$–CH_2–O–P). ^{1}H NMR (C_6D_6, 300 MHz): 4.15–3.97 (m, 3H, CH_2–O–P, *H*–C5), 3.97–3.87 (m, 2H, CH_2–O–P), 3.44 (dAB, J_{AB}=12.0 Hz, J=3.3 Hz, 1H, C*H*$_2$OH), 3.25 (dAB, J_{AB}=12.0 Hz, J=4.5 Hz, 1H, C*H*$_2$OH), 2.93 (s, 3H, C*H*$_3$–N), 2.82 (bdd, $J_{3-4\alpha}$=9.6 Hz, $J_{3-4\beta}$=7.8 Hz, 1H, *H*–C3) 2.47 (dddAB, $J_{P-4\beta}$=18.1 Hz, J_{AB}=12.2 Hz, $J_{3-4\beta}$=7.8 Hz, $J_{5-4\beta}$=7.8 Hz, 1H, *Hβ*–C4), 2.22 (dddAB, J_{AB}=12.2 Hz, $J_{P-4\alpha}$=9.6 Hz, $J_{3-4\alpha}$=9.6 Hz, $J_{5-4\alpha}$=7.8 Hz, 1H, *Hα*–C4), 1.20 (br s, 1H, OH), 1.07 (t, J=7.2 Hz, 3H), 1.02 (t, J=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 77.60 (d, $^3J_{PCCC}$=8.3 Hz, C5), 64.41 (d, $^1J_{PC}$=166.8 Hz, C3), 63.29 (d, J=6.8 Hz, C–O–P), 62.62 (d, J=6.8 Hz, C–O–P), 62.84 (s, C1′), 46.22 (very br d, *C*–N–C–P), 34.09 (br d, $^2J_{PCC}$=2.3 Hz, C4), 16.75 (d, J=5.3 Hz), 16.70 (d, J=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 22.98. Anal. Calcd for $C_9H_{20}NO_5P$: C, 42.69; H, 7.96; N, 5.53. Found: C, 42.59; H, 8.07; N, 5.35.

*Compound **4a***: yield 0.236 g, 20%. Colourless oil. IR (film): ν=3399, 2983, 2911, 1444, 1231, 1047, 1028, 970 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.34 (dddd, $J_{5-4\alpha}$=8.1 Hz, $J_{5-4\beta}$=6.0 Hz, $J_{5-1'a}$=4.8 Hz, $J_{5-1'b}$=2.7 Hz, 1H, *H*–C5), 4.28–4.12 (m, 4H, CH_2–O–P), 3.75 (dAB, J_{AB}=12.0 Hz, $J_{5-1'a}$=2.7 Hz, 1H, *Ha*–C1′), 3.65 (dAB, J_{AB}=12.0 Hz, $J_{5-1'b}$=4.8 Hz, 1H, *Hb*–C1′), 3.07 (ddd, $J_{3-4\alpha}$=9.0 Hz, $J_{3-4\beta}$=7.2 Hz, J_{3-P}=6.3 Hz, 1H, *H*–C3), 2.81 (d, J=0.3 Hz, 3H, C*H*$_3$–N), 2.63 (dddAB, J_{AB}=12.6 Hz, $J_{4\alpha-P}$=12.6 Hz, $J_{4\alpha-3}$=9.0 Hz, $J_{4\alpha-5}$=8.1 Hz, 1H, *Hα*–C4), 2.47 (dddAB, J_{AB}=12.6 Hz, $J_{4\beta-P}$=18.9 Hz, $J_{4\beta-3}$=7.2 Hz, $J_{4\beta-5}$=6.0 Hz, 1H, *Hβ*–C4), 2.46 (br s, 1H, OH), 1.34 (t, J=6.9 Hz, 6H, 2×C*H*$_3$–CH_2–O–P). ^{1}H NMR (C_6D_6, 300 MHz): 4.10–3.84 (m, 5H, CH_2–O–P, *H*-5), 3.69 (dAB, J_{AB}=12.0 Hz, $J_{5-1'a}$=2.7 Hz, 1H, *Ha*–C1′), 3.52 (dAB, J_{AB}=12.0 Hz, $J_{5-1'b}$=4.5 Hz, 1H, *Hb*–C1′), 2.72 (ddd, $J_{3-4\alpha}$=9.0 Hz, $J_{3-4\beta}$=6.9 Hz, J_{3-P}=6.6 Hz, 1H, *H*–C3), 2.57 (s, 3H, CH_3–N), 2.47 (dddAB, J_{AB}=12.9 Hz, $J_{4\beta-P}$=18.6 Hz, $J_{4\beta-3}$=6.9 Hz, $J_{4\beta-5}$=5.7 Hz, 1H, *Hβ*–C4), 2.05 (dddAB, J_{AB}=12.9 Hz, $J_{4\alpha-P}$=13.8 Hz, $J_{4\alpha-3}$=9.0 Hz, $J_{4\alpha-5}$=8.4 Hz, 1H, *Hα*–C4), 1.04 (t, J=7.2 Hz, 6H, 2×C*H*$_3$–CH_2–O–P). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 76.77 (d, $^3J_{PCCC}$=5.3 Hz, C5), 64.30 (d, $^1J_{PC}$=170.5 Hz, C3), 63.24 (s, C1′), 63.13 (d, J=6.8 Hz, C–O–P), 63.00 (d, J=6.8 Hz, C–O–P), 46.04 (d, J=9.8 Hz, *C*–N–C–P), 32.54 (s, C4), 16.70 (d, J=5.3 Hz), 16.68 (d, J=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 23.77. Anal. Calcd for $C_9H_{20}NO_5P$: C, 42.69; H, 7.96; N, 5.53. Found: C, 42.52; H, 8.16; N, 5.86.

4.3.1. Diethyl 5-(*tert*-butoxycarbonylaminomethyl)-2-methylisoxazolidin-3-yl-3-phosphonate (3b and 4b). From nitrone **1a** (0.287 g, 1.47 mmol) and *N*-Boc-allylamine (0.254 g, 1.62 mmol), an inseparable mixture of **3b**

and **4b** (0.43 g, 83%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

*Compounds **3b** and **4b***: colourless oil. IR (film): ν=3316, 2979, 2932, 1711, 1526, 1366, 1250, 1171, 1040, 1027, 970 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 5.11 (br s, 1H×0.28), 4.79 (very br t, 1H×0.72), 4.30–4.05 (m, 5H), 3.51–3.40 (m, 1H×0.72), 3.40–3.30 (m, 1H×0.28), 3.30–3.15 (m, 1H×0.72), 2.98 (ddd, J=8.7, 8.7, 4.2 Hz, 1H×0.28), 2.86 (d, J=1.2 Hz, 3H×0.72), 2.81 (d, J=0.9 Hz, 3H×0.28), 2.70–2.44 (m, 1H), 2.31–2.13 (m, 1H), 1.44 (s, 9H), 1.36 (t, J=6.9 Hz, 3H×0.28), 1.35 (t, J=6.9 Hz, 3H×0.28), 1.34 (t, J=6.9 Hz, 3H×0.72), 1.33 (t, J=6.9 Hz, 3H×0.72). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 155.91 (C═O, **6b**), 155.90 (C═O, **5b**), 79.44 (s, $C(CH_3)_3$, **5b**), 79.21 (s, $C(CH_3)_3$, **6b**), 76.13 (d, $^{3}J_{PCCC}$=8.3 Hz, C5, **5b**), 74.91 (d, $^{3}J_{PCCC}$=6.8 Hz, C5, **6b**), 64.25 (d, $^{1}J_{PC}$=169.8 Hz, C3, **5b**), 64.22 (d, $^{1}J_{PC}$=170.5 Hz, C3, **6b**), 63.14 (d, J=6.8 Hz, C–O–P, **5b**), 63.00 (d, J=6.8 Hz, C–O–P, **6b**), 62.53 (d, J=6.8 Hz, C–O–P, **6b**), 62.40 (d, J=7.5 Hz, C–O–P, **5b**), 46.20 (d, J=7.5 Hz, *C*–N–C–P, **5b**), 46.13 (d, J=3.8 Hz, *C*–N–C–P, **6b**), 43.03 (s, C1′, **6b**), 42.55 (s, C1′, **5b**), 35.03 (d, $^{2}J_{PCC}$=2.3 Hz, C4, **5b**), 34.71 (d, $^{2}J_{PCC}$=1.5 Hz, C4, **6b**), 28.43 (s, C(CH_3)$_3$, **5b**), 28.46 (s, C(CH_3)$_3$, **6b**), 16.61 (d, J=6.0 Hz, **5b** and **6b**), 16.56 (d, J=5.3 Hz, **5b** and **6b**). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 22.30 (**6b**) and 22.00 (**5b**). Anal. Calcd for $C_{14}H_{29}N_2O_6P$: C, 47.72; H, 8.30; N, 7.95. Found: C, 47.96; H, 8.16; N, 7.84.

4.3.2. Diethyl 5-(bromomethyl)-2-methylisoxazolidin-3-yl-3-phosphonate (3c and 4c). From nitrone **1a** (0.195 g, 1.00 mmol) and allyl bromide (0.173 mL, 2.00 mmol), an inseparable mixture of **3c** and **4c** (0.193 g, 61%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

*Compounds **3c** and **4c***: colourless oil. IR (film): ν=3472, 2981, 2909, 1442, 1239, 1040, 1028, 969 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.42–4.12 (m, 5H, 2×CH_2OP and *H*–C5), 3.54 (dAB, J_{AB}=9.9 Hz, J=5.7 Hz, 1H×0.35), 3.45 (ddAB, J_{AB}=10.8 Hz, J=4.8, 0.6 Hz, 1H×0.65), 3.39 (dAB, J_{AB}=10.8 Hz, J=6.0 Hz, 1H×0.65), 3.38 (dAB, J_{AB}=9.9 Hz, J=7.8 Hz, 1H×0.35), 3.05–2.93 (m, 1H), 2.89 (d, J=1.2 Hz, 3H×0.65), 2.85 (d, J=0.9 Hz, 3H×0.35), 2.83–2.60 (m, 1H), 2.50–2.34 (m, 1H), 1.36 (t, J=7.0 Hz, 3H), 1.35 (t, J=7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 75.99 (d, J=3.0 Hz, C5 in **6c**), 75.89 (d, J=9.1 Hz, C5 in **5c**), 64.46 (d, J=170.0 Hz, C3 in **5c**), 64.21 (d, J=168.3 Hz, C3 in **6c**), 63.36 (d, J=6.0 Hz, **5c**), 63.25 (d, J=6.8 Hz, **6c**), 62.72 (d, J=6.0 Hz, **6c**), 62.64 (d, J=6.8 Hz, **5c**), 46.49 (d, J=3.8 Hz, **6c**), 46.30 (d, J=5.3 Hz, **5c**), 37.47 (d, J=2.3 Hz, **6c**), 37.28 (d, J=2.3 Hz, **5c**), 34.00 (s, C3 in **6c**), 32.89 (s, C3 in **5c**), 16.77 (d, J=5.3 Hz, **5c** and **6c**), 16.72 (d, J=6.0 Hz, **5c** and **6c**). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 23.05 (**6c**) and 22.68 (**5c**). Anal. Calcd for $C_9H_{19}BrNO_4P$: C, 34.19; H, 6.06; N, 4.43. Found: C, 34.10; H, 6.24; N, 4.46.

4.3.3. Diethyl 2-methyl-5-[(trimethylsilyl)methyl]isoxazolidin-3-yl-3-phosphonate (3d and 4d). From nitrone **1a** (0.524 g, 2.69 mmol) and allyltrimethylsilane (0.428 mL, 2.69 mmol), pure **3d** (0.536 g, 64%) and fractions containing mixtures of **3d** and **4d** (0.075 g, 9%) were obtained after chromatography on a silica gel column with chloroform–MeOH (100:1).

*Compound **3d***: colourless oil. IR (film): ν=2955, 2881, 1248, 1054, 1027, 965, 841 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.27–4.13 (m, 4H, CH_2–O–P), 4.08 (dddd, $J_{5-1'b}$=9.1 Hz, $J_{5-4\alpha}$=8.7 Hz, $J_{5-4\beta}$=6.6 Hz, $J_{5-1'a}$=5.7 Hz, 1H, *H*–C5), 2.94 (ddd, $J_{3-4\alpha}$=10.5 Hz, $J_{3-4\beta}$=6.0 Hz, $J_{3\text{-}P}$=1.2 Hz, 1H, *H*–C3), 2.85 (d, J=1.2 Hz, 3H, CH_3–N), 2.53 (dddAB, J_{AB}=12.3 Hz, $J_{4\beta\text{-}P}$=18.9 Hz, $J_{4\beta-5}$=6.6 Hz, $J_{4\beta-3}$=6.0 Hz, 1H, *Hβ*–C4), 2.02 (dddAB, J_{AB}=12.3 Hz, $J_{4\alpha\text{-}P}$=13.5 Hz, $J_{4\alpha-3}$=10.5 Hz, $J_{4\alpha-5}$=8.7 Hz, 1H, *Hα*–C4), 1.35 (t, J=6.9 Hz, 6H, 2×CH_3–CH_2–O–P), 1.07 (dAB, J_{AB}=14.1 Hz, $J_{5-1'a}$=5.7 Hz, 1H, *Ha*–C1′), 0.81 (dAB, J_{AB}=14.1 Hz, $J_{5-1'b}$=9.1 Hz, 1H, *Hb*–C1′), 0.05 (s, 9H, C(CH_3)$_3$). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 75.33 (d, $^{3}J_{PCCC}$=6.9 Hz, C5), 64.57 (d, $^{1}J_{PC}$=168.6 Hz, C3), 62.95 (d, J=6.6 Hz, C–O–P), 62.38 (d, J=6.9 Hz, C–O–P), 46.17 (d, J=4.0 Hz, H_3C–N–C–P), 40.21 (d, $^{2}J_{PCC}$=2.9 Hz, C4), 21.87 (s, C1′), 16.63 (d, J=5.7 Hz), −0.81 (s, C(CH_3)$_3$). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 24.12. Anal. Calcd for $C_{12}H_{28}NO_4PSi$: C, 46.58; H, 9.12; N, 4.53. Found: C, 46.49; H, 9.35; N, 4.52.

4.3.4. Methyl 3-(diethoxyphosphoryl)-2-methylisoxazolidin-5-yl-5-carboxylate (3e and 4e). From nitrone **1a** (0.448 g, 2.30 mmol) and methyl acrylate (0.311 mL, 3.45 mmol) pure **3e** (0.473 g, 73%) was obtained by column chromatography (chloroform–MeOH, 100:1), followed by fractions containing mixture of **3e** and **4e** (0.080 g, 12%).

*Compound **3e***: colourless oil. IR (film): ν=3473, 2983, 2913, 1744, 1441, 1222, 1052, 1025, 970 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.56 (dd, $J_{5-4\beta}$=8.4 Hz, $J_{5-4\alpha}$=5.7 Hz, 1H, *H*–C5), 4.26–4.13 (m, 4H, CH_2–O–P), 3.78 (s, 3H, CH_3O(O)C), 3.13 (ddd, $J_{3-4\alpha}$=8.4 Hz, $J_{3-4\beta}$=8.4 Hz, $J_{3\text{-}P}$=3.3 Hz, 1H, *H*–C3), 2.96 (d, J=1.0 Hz, 3H, CH_3–N), 2.88 (dddAB, J_{AB}=12.6 Hz, $J_{4\beta\text{-}P}$=16.8 Hz, $J_{4\beta-3}$=8.4 Hz, $J_{4\beta-5}$=8.4 Hz, 1H, *Hβ*–C4), 2.70 (dddAB, J_{AB}=12.6 Hz, $J_{4\alpha\text{-}P}$=9.6 Hz, $J_{4\alpha-3}$=8.4 Hz, $J_{4\alpha-5}$=5.7 Hz, 1H, *Hα*–C4), 1.36 (t, J=6.9 Hz, 3H, CH_3–CH_2–O–P), 1.35 (t, J=7.0 Hz, 3H, CH_3–CH_2–O–P). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 171.1 (s, C═O), 74.98 (d, $^{3}J_{PCCC}$=8.3 Hz, C5), 63.38 (d, J=6.8 Hz, C–O–P), 63.35 (d, $^{1}J_{PC}$=169.8 Hz, C3), 62.68 (d, J=7.5 Hz, C–O–P), 52.58 (s, *C*H$_3$O(O)C), 46.71 (d, J=5.3 Hz, *C*–N–C–P), 36.53 (d, $^{2}J_{PCC}$=2.3 Hz, C4), 16.66 (d, J=5.3 Hz), 16.60 (d, J=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 21.39. Anal. Calcd for $C_{10}H_{20}NO_6P$: C, 42.71; H, 7.17; N, 4.98. Found: C, 42.76; H, 7.09; N, 4.91.

4.3.5. Diethyl 5-acetoxy-2-methylisoxazolidin-3-yl-3-phosphonate (3f and 4f). From nitrone **1a** (0.510 g, 2.49 mmol) and vinyl acetate (1.00 mL, 10.8 mmol), pure **3f** (0.434 g, 62%) and fractions containing mixture of **3f** and **4f** (0.223 g, 32%) were obtained after column chromatography (chloroform–MeOH, 100:1).

*Compound **3f***: colourless oil. IR (film): ν=2986, 2913, 1752, 1441, 1260, 1235, 1054, 1024, 971 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 6.28 (dd, $J_{5-4\beta}$=4.2 Hz, $J_{5-4\alpha}$=0.9 Hz, 1H, *H*–C5), 4.28–4.14 (m, 4H, 2×CH_2–O–P), 3.27 (ddd, $J_{3-4\beta}$=11.4 Hz, $J_{3-4\alpha}$=6.9 Hz, $J_{3\text{-}P}$=1.8 Hz, 1H, *H*–C3), 2.99 (d, J=0.8 Hz, 3H, CH_3–N), 2.70 (dddAB, J_{AB}=12.9 Hz, $J_{4\beta\text{-}P}$=17.1 Hz, $J_{4\beta-3}$=11.1 Hz, $J_{4\beta-5}$=4.2 Hz, 1H, *Hβ*–C4),

2.65 (dddAB, J_{AB}=12.9 Hz, $J_{4\alpha-3}$=6.9 Hz, $J_{4\alpha\text{-}P}$=3.0 Hz, $J_{5-4\alpha}$=0.9 Hz, 1H, *Hα*–C4), 2.08 (s, 3H, C*H*$_3$C(O)O), 1.35 (t, *J*=6.9 Hz, 6H, C*H*$_3$–CH$_2$–O–P). ^{1}H NMR (C_6D_6, 300 MHz): 6.28 (d, $J_{5-4\beta}$=4.5 Hz, 1H, *H*–C5), 4.16–4.04 (m, 2H, CH$_2$–O–P), 3.98–3.88 (m, 2H, CH$_2$–O–P), 3.19 (ddd, $J_{3-4\beta}$=12.0 Hz, $J_{3-4\alpha}$=6.6 Hz, $J_{3\text{-}P}$=1.5 Hz, 1H, *H*–C3), 2.98 (s, 3H, CH$_3$–N), 2.54 (dddAB, J_{AB}=12.9 Hz, $J_{4\beta\text{-}P}$=17.4 Hz, $J_{4\beta-3}$=12.0 Hz, $J_{4\beta-5}$=4.5 Hz, 1H, *Hβ*–C4), 2.32 (ddAB, J_{AB}=12.9 Hz, $J_{4\alpha\text{-}P}$=3.0 Hz, $J_{4\alpha-3}$= 6.6 Hz, 1H, *Hα*–C4), 1.55 (s, 3H, C*H*$_3$C(O)O), 1.07 (t, *J*=7.0 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.01 (t, *J*=7.3 Hz, 3H, C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 169.77 (s, C=O), 95.69 (d, $^3J_{PCCC}$=9.5 Hz, C5), 63.66 (d, *J*=6.0 Hz, C–O–P), 62.88 (d, *J*=6.8 Hz, C–O–P), 61.79 (d, $^1J_{PC}$=175.8 Hz, C3), 49.91 (br d, *J*=7.5 Hz, *C*–N–C–P), 39.91 (d, $^2J_{PCC}$=2.3 Hz, C4), 21.58 (s, *C*H$_3$C(O)O), 16.68 (d, *J*=5.3 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 21.84. Anal. Calcd for $C_{10}H_{20}NO_6P$: C, 42.71; H, 7.17; N, 4.98. Found: C, 42.52; H, 7.09; N, 4.97.

4.3.6. Diethyl 2-methyl-5-phenylisoxazolidin-3-yl-3-phosphonate (3g and 4g). From nitrone **1a** (0.635 g, 3.25 mmol) and styrene (0.559 mL, 4.88 mmol), pure **3g** (0.584 g, 60%) and pure **4g** (0.021 g, 2%) were obtained after purification on a silica gel column with chloroform–MeOH (100:1) and toluene–isopropanol (100:1).

Compound ***3g***: colourless oil. IR (film): *ν*=2982, 2908, 1453, 1239, 1053, 1027, 966 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 7.38–7.25 (m, 5H), 5.02 (dd, $J_{5-4\alpha}$=8.4 Hz, $J_{5-4\beta}$=6.9 Hz, 1H, *H*–C5), 4.30–4.14 (m, 4H, 2×CH$_2$–O–P), 3.12 (ddd, $J_{3-4\alpha}$=10.5 Hz, $J_{3-4\beta}$=6.9 Hz, $J_{3\text{-}P}$=1.8 Hz, 1H, *H*–C3), 2.97 (d, *J*=0.8 Hz, 3H, C*H*$_3$–N), 2.88 (dddAB, J_{AB}=12.9 Hz, $J_{4\beta\text{-}P}$=18.6 Hz, $J_{4\beta-3}$=6.9 Hz, $J_{4\beta-5}$= 6.9 Hz, 1H, *Hβ*–C4), 2.48 (dddAB, J_{AB}=12.9 Hz, $J_{4\alpha-3}$= 10.5 Hz, $J_{4\alpha\text{-}P}$=12.9 Hz, $J_{5-4\alpha}$=8.4 Hz, 1H, *Hα*–C4), 1.38 (t, *J*=7.2 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.36 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 138.81 (C$_{ipso}$), 128.44, 128.04, 126.45, 78.81 (d, $^3J_{PCCC}$=7.2 Hz, C5), 64.60 (d, $^1J_{PC}$=168.6 Hz, C3), 63.15 (d, *J*=6.3 Hz, C–O–P), 62.49 (d, *J*=7.2 Hz, C–O–P), 46.24 (br d, *J*=4.0 Hz, H$_3$*C*–N–C–P), 40.32 (d, $^2J_{PCC}$=3.1 Hz, C4), 16.69 (d, *J*=5.7 Hz), 16.62 (d, *J*=5.7 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 23.45. Anal. Calcd for $C_{14}H_{22}NO_4P$: C, 56.18; H, 7.41; N, 4.68. Found: C, 56.16; H, 7.41; N, 4.84.

Compound ***4g***: colourless oil. IR (film): *ν*=2983, 2910, 1672, 1452, 1249, 1053, 1027, 967 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 7.44–7.25 (m, 5H), 5.14 (dd, $J_{5-4\beta}$= 8.7 Hz, $J_{5-4\alpha}$=6.6 Hz, 1H, *H*–C5), 4.25–4.13 (m, 4H, 2×CH$_2$–O–P), 3.23 (ddd, $J_{3-4\beta}$=9.3 Hz, $J_{3-4\alpha}$=8.1 Hz, $J_{3\text{-}P}$=4.2 Hz, 1H, *H*–C3), 2.95 (dddAB, J_{AB}=12.3 Hz, $J_{4\alpha-3}$=8.1 Hz, $J_{4\alpha\text{-}P}$=6.6 Hz, $J_{5-4\alpha}$=6.6 Hz, 1H, *Hα*–C4), 2.93 (d, *J*=0.9 Hz, 3H, C*H*$_3$–N), 2.55 (dddAB, J_{AB}= 12.3 Hz, $J_{4\beta\text{-}P}$=18.6 Hz, $J_{4\beta-3}$=9.3 Hz, $J_{4\beta-5}$=8.7 Hz, 1H, *Hβ*–C4), 1.32 (t, *J*=7.2 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.31 (t, *J*=7.2 Hz, 3H, C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 139.40 (C$_{ipso}$), 128.20, 127.70, 77.31 (d, $^3J_{PCCC}$=8.3 Hz, C5), 65.10 (d, $^1J_{PC}$=172.8 Hz, C3), 63.10 (d, *J*=6.8 Hz, C–O–P), 62.43 (d, *J*=5.3 Hz, C–O–P), 47.07 (d, *J*=9.1 Hz, H$_3$*C*–N–C–P), 41.10 (d, $^2J_{PCC}$=1.5 Hz, C4), 16.49 (d, *J*=6.0 Hz), 16.47 (d, *J*=5.3 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 23.52. Anal. Calcd for $C_{14}H_{22}NO_4P$: C, 56.18; H, 7.41; N, 4.68. Found: C, 56.42; H, 7.67; N, 4.78.

4.3.7. Tetraethyl 2-methylisoxazolidine-3,5-diyl-3,5-bis(phosphonate) (3h and 4h). From nitrone **1a** (0.927 g, 4.75 mmol) and vinylphosphonate (0.741 mL, 4.75 mmol) a mixture of **3h**, **4h** and **5** (1.557 g, 91%) was obtained and subjected to purification on silica gel with chloroform–MeOH (100:1).

Compound ***3h***: yield 0.50 g, 29%. Colourless oil. IR (film): *ν*=3529, 3486, 2983, 2911, 1246, 1047, 1026, 969 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 4.30–4.13 (m, 9H, 4×CH$_2$–O–P and *H*–C5), 3.12 (very br, 1H, *H*–C3), 2.94 (s, 3H, CH$_3$–N), 2.88–2.72 (m, 2H, *Hα*–C4 and *Hβ*–C4), 1.35 (t, *J*=6.9 Hz, 12H, 4×C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 71.80 (d, $^1J_{PC}$=169.0 Hz, $^3J_{PCCC}$=8.3 Hz, C5), 63.89 (d, $^1J_{PC}$=169.0 Hz, $^3J_{PCCC}$=5.3 Hz, C3), 63.38 (d, *J*=6.0 Hz, C–O–P), 63.33 (d, *J*=6.8 Hz, C–O–P), 62.85 (d, *J*=6.8 Hz, C–O–P), 62.72 (d, *J*=6.8 Hz, C–O–P), 46.49 (d, *J*=4.5 Hz, H$_3$*C*–N–C–P), 34.63 (d, $^2J_{PCC}$=0.8 Hz, C4), 16.72 (d, *J*=5.3 Hz), 16.69 (d, *J*=5.3 Hz), 16.67 (d, *J*=5.3 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 21.38 and 20.58. Anal. Calcd for $C_{12}H_{27}NO_7P_2$: C, 40.11; H, 7.57; N, 3.90. Found: C, 39.92; H, 7.79; N, 3.92.

Compound ***4h***: yield 0.113 g, 7%. Colourless oil. IR (film): *ν*=3478, 2985, 2912, 1247, 1047, 1025, 971 cm^{-1}. ^{1}H NMR (C_6D_6, 300 MHz): 4.29–3.90 (m, 9H, 4×CH$_2$–O–P and *H*–C5), 3.02 (dddAB, J_{AB}=12.0 Hz, $J_{4\beta-P3}$=18.0 Hz, $J_{4\beta-P5}$=16.5 Hz, $J_{4\beta-3}$=10.3 Hz, $J_{4\beta-5}$=10.3 Hz, 1H, *Hβ*–C4), 2.79 (s, 3H, C*H*$_3$–N), 2.67 (ddd, $J_{3-4\beta}$=10.3 Hz, $J_{3-4\alpha}$=7.0 Hz, $J_{3\text{-}P}$=3.8 Hz, 1H, *H*–C3), 2.51 (dddAB, J_{AB}=12.0 Hz, $J_{4\alpha-3}$=7.0 Hz, $J_{4\alpha-P3}$=7.0 Hz, $J_{4\alpha-P5}$= 3.3 Hz, $J_{5-4\alpha}$=6.6 Hz, 1H, *Hα*–C4), 1.13 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.07 (t, *J*=7.2 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.05 (t, *J*=7.2 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.03 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 70.56 (d, $^1J_{PC}$=169.8 Hz, $^3J_{PCCC}$=9.8 Hz, C5), 64.52 (d, $^1J_{PC}$= 169.8 Hz, $^3J_{PCCC}$=7.5 Hz, C3), 63.55 (d, *J*=6.8 Hz, C–O–P), 63.22 (d, *J*=6.8 Hz, C–O–P), 63.01 (d, *J*=6.8 Hz, C–O–P), 62.73 (d, *J*=6.8 Hz, C–O–P), 46.80 (d, *J*=6.8 Hz, H$_3$*C*–N–C–P), 35.42 (s, C4), 16.63 (d, *J*=6.0 Hz). ^{31}P NMR (C_6D_6, 121.5 MHz): 21.85 and 21.42. Anal. Calcd for $C_{12}H_{27}NO_7P_2$: C, 40.11; H, 7.57; N, 3.90. Found: C, 39.93; H, 7.62; N, 3.85.

4.3.8. Diethyl 5-[(diethoxyphosphoryl)methyl]-2-methylisoxazolidin-3-yl-3-phosphonate (3i and 4i). From nitrone **1a** (0.713 g, 3.65 mmol) and allylphosphonate (0.640 mL, 3.65 mmol), a mixture of **3i** and **4i** (1.24, 91%) was obtained and purified on silica gel with chloroform–MeOH (100:1).

Compound ***3i***: yield 0.312 g, 23%. Colourless oil. IR (film): *ν*=3471, 2984, 2910, 1237, 1029, 967 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 4.23–3.94 (m, 9H, 4×CH$_2$–O–P and *H*–C5), 2.86 (ddd, $J_{3-4\alpha}$=10.5 Hz, $J_{3-4\beta}$=6.9 Hz, $J_{3\text{-}P}$= 2.1 Hz, 1H, *H*–C3), 2.76 (d, *J*=1.0 Hz, 3H, CH$_3$–N), 2.60 (dddAB, J_{AB}=12.6 Hz, $J_{4\beta\text{-}P}$=19.5 Hz, $J_{4\beta-3}$=6.9 Hz, $J_{4\beta-5}$=6.9 Hz, 1H, *Hβ*–C4), 2.19 (dddAB, J_{AB}=12.6 Hz, $J_{4\alpha\text{-}P}$=12.6 Hz, $J_{4\alpha-3}$=10.5 Hz, $J_{4\alpha-5}$=8.1 Hz, 1H, *Hα*–C4), 2.12 (ddAB, J_{AB}=15.0 Hz, $J_{P\text{-}1'a}$=20.1 Hz, $J_{5-1'a}$=5.1 Hz, 1H, *Ha*–C1′), 1.86 (ddAB, J_{AB}=15.0 Hz, $J_{P\text{-}1'b}$=18.3 Hz,

$J_{5-1'b}$=8.4 Hz, 1H, *Hb*–C1′), 1.25 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.24 (t, *J*=7.2 Hz, 6H, 2×C*H*$_3$–CH$_2$–O–P), 1.23 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 72.08 (d, $^3J_{PCCC}$=7.4 Hz, C5), 64.25 (d, $^1J_{PC}$=168.6 Hz, C3), 63.28 (d, *J*=6.3 Hz, C–O–P), 62.49 (d, *J*=7.2 Hz, C–O–P), 62.04 (d, *J*=6.9 Hz, C–O–P), 61.96 (d, *J*=6.6 Hz, C–O–P), 46.26 (br s, *C*–N–C–P), 38.71 (br s, C4), 30.68 (d, $^1J_{PC}$=140.6 Hz, C1′), 16.73 (d, *J*=5.7 Hz), 16.68 (d, *J*=5.4 Hz), 16.62 (d, *J*=6.0 Hz), 16.60 (d, *J*=6.0 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 26.47 and 22.23. Anal. Calcd for $C_{13}H_{29}NO_7P_2$: C, 41.82; H, 7.83; N, 3.75. Found: C, 41.92; H, 8.03; N, 3.70.

Compound ***4i***: yield 0.061 g, 4%. Colourless oil. IR (film): ν=3471, 2984, 2910, 1237, 1029, 967 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 4.23–3.94 (m, 9H, 4×CH$_2$–O–P and *H*–C5), 2.86 (ddd, $J_{3-4\alpha}$=10.5 Hz, $J_{3-4\beta}$=6.9 Hz, $J_{3\text{-}P}$=2.1 Hz, 1H, *H*–C3), 2.76 (d, *J*=1.0 Hz, 3H, C*H*$_3$–N), 2.60 (dddAB, J_{AB}=12.6 Hz, $J_{4\beta-P}$=19.5 Hz, $J_{4\beta-3}$=6.9 Hz, $J_{4\beta-5}$=6.9 Hz, 1H, *Hβ*–C4), 2.19 (dddAB, J_{AB}=12.6 Hz, $J_{4\alpha-P}$=12.6 Hz, $J_{4\alpha-3}$=10.5 Hz, $J_{4\alpha-5}$=8.1 Hz, 1H, *Hα*–C4), 2.12 (ddAB, J_{AB}=15.0 Hz, $J_{P\text{-}1'a}$=20.1 Hz, $J_{5-1'a}$=5.1 Hz, 1H, *Ha*–C1′), 1.86 (ddAB, J_{AB}=15.0 Hz, $J_{P\text{-}1'b}$=18.3 Hz, $J_{5-1'b}$=8.4 Hz, 1H, *Hb*–C1′), 1.25 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P), 1.24 (t, *J*=7.2 Hz, 6H, 2×C*H*$_3$–CH$_2$–O–P), 1.23 (t, *J*=6.9 Hz, 3H, C*H*$_3$–CH$_2$–O–P). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 72.08 (d, $^3J_{PCCC}$=7.4 Hz, C5), 64.25 (d, $^1J_{PC}$=168.6 Hz, C3), 63.28 (d, *J*=6.3 Hz, C–O–P), 62.49 (d, *J*=7.2 Hz, C–O–P), 62.04 (d, *J*=6.9 Hz, C–O–P), 61.96 (d, *J*=6.6 Hz, C–O–P), 46.26 (br s, *C*–N–C–P), 38.71 (br s, C4), 30.68 (d, $^1J_{PC}$=140.6 Hz, C1′), 16.73 (d, *J*=5.7 Hz, *C*–C–O–P), 16.68 (d, *J*=5.4 Hz), 16.62 (d, *J*=6.0 Hz), 16.60 (d, *J*=6.0 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 26.47 and 22.23. Anal. Calcd for $C_{13}H_{29}NO_7P_2$: C, 41.82; H, 7.83; N, 3.75. Found: C, 42.04; H, 7.62; N, 3.67.

4.3.9. Diethyl octahydro-2-methylbenzo[*d*]isoxazol-3-yl-3-phosphonate (7a). From nitrone **1a** (0.121 g, 0.671 mmol) and cyclohexene (0.68 mL, 6.7 mmol), pure **7a** (0.186 g, 100%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

Compound ***7a***: colourless oil. IR (film): ν=2981, 2934, 2864, 1445, 1248, 1056, 1023, 963 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 4.24–4.10 (m, 4H), 4.08 (q, *J*=4.2 Hz, 1H, *H*–C7a), 2.91 (d, *J*=1.2 Hz, 3H, C*H*$_3$N), 2.70 (dd, J_{3-3a}=3.6 Hz, $J_{3\text{-}P}$=1.5 Hz, 1H, *H*–C3), 2.60 (ddddd, $J_{3a\text{-}P}$=16.0 Hz, *J*=11.0, 5.0, 4.2, 3.6 Hz, 1H, *H*–C3a), 2.02–1.90 (m, 1H), 1.86–1.75 (m, 1H), 1.72–1.59 (m, 2H), 1.52–1.10 (m, 3H), 1.30–1.20 (m, 1H), 1.34 (t, *J*=7.2 Hz, 6H). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 75.48 (d, $^3J_{PCCC}$=4.5 Hz, C7a), 71.45 (d, $^1J_{PC}$=172.0 Hz, C3), 62.78 (d, *J*=6.9 Hz, C–O–P), 62.60 (d, *J*=6.9 Hz, C–O–P), 47.68 (d, *J*=6.9 Hz, H$_3$*C*–N–C–P), 44.22 (d, $^2J_{PCC}$=2.0 Hz, C3a), 30.17 (d, $^3J_{PCCC}$=11.5 Hz, C4), 26.05, 24.00 (d, *J*=1.4 Hz), 20.77, 16.71 (d, *J*=5.7 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 24.26. Anal. Calcd for $C_{12}H_{24}NO_4P$: C, 51.98; H, 8.72; N, 5.05. Found: C, 51.95; H, 8.65; N, 4.89.

4.3.10. Diethyl hexahydro-2-methyl-2*H*-cyclopenta[*d*]-isoxazol-3-yl-3-phosphonate (7b). From nitrone **1a** (0.162 g, 0.830 mmol) and cyclopentene (0.110 mL, 1.24 mmol), pure **7b** (0.190 g, 90%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

Compound ***7b***: colourless oil. IR (film): ν=2950, 2935, 2871, 1442, 1251, 1220, 1054, 1025, 964 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 4.47 (dd, J_{6a-3a}=8.0 Hz, J_{6a-6}=3.7 Hz, 1H, *H*–C6a), 4.25–4.13 (m, 4H), 3.23 (dq, $J_{3a\text{-}P}$=16.2 Hz, J_{3a-3}=8.0 Hz, 1H, *H*–C3a), 2.82 (d, *J*=1.2 Hz, 3H, C*H*$_3$N), 2.38 (br d, J_{3-3a}=8.0 Hz, 1H, *H*–C3), 1.89–1.80 (m, 1H), 1.75–1.60 (m, 4H), 1.50–1.40 (m, 1H), 1.36 (t, *J*=6.9 Hz, 6H). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 83.00 (d, $^3J_{PCCC}$=9.8 Hz, C6a), 72.21 (d, $^1J_{PC}$=162.6 Hz, C3), 63.13 (d, *J*=6.6 Hz, C–O–P), 62.36 (d, *J*=6.9 Hz, C–O–P), 51.68, 45.32, 31.90, 31.57 (d, $^3J_{PCCC}$=3.4 Hz, C4), 23.35, 16.73 (d, *J*=6.0 Hz), 16.69 (d, *J*=6.0 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 23.30. Anal. Calcd for $C_{11}H_{22}NO_4P$: C, 50.18; H, 8.42; N, 5.32. Found: C, 50.01; H, 8.48; N, 5.11.

4.3.11. Diethyl hexahydro-2-methylfuro[3,2-*d*]isoxazol-3-yl-3-phosphonate (7c). From nitrone **1a** (0.327 g, 1.68 mmol) and 2,3-dihydrofuran (0.253 mL, 3.36 mmol), pure **7c** (0.311 g, 70%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

Compound ***7c***: colourless oil. IR (film): ν=2981, 2912, 2879, 1444, 1252, 1226, 1053, 1023, 968 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 5.71 (d, J_{6a-3a}=5.4 Hz, 1H, *H*–C6a), 4.27–4.13 (m, 4H), 4.04 (dd, ^2J=9.0 Hz, *J*=8.4 Hz, 1H, *Hβ*–C5), 3.97 (ddd, *J*=11.4 Hz, ^2J=9.0 Hz, *J*=5.4 Hz, 1H, *Hα*–C5), 3.42 (ddddd, $J_{3a\text{-}P}$=17.1 Hz, J_{3a-3}=8.4 Hz, $J_{3a-4\beta}$=8.4 Hz, J_{3a-6a}=5.4 Hz, $J_{3a-4\alpha}$=0.9 Hz, 1H, *H*–C3a), 2.89 (d, *J*=0.9 Hz, 3H, C*H*$_3$N), 2.66 (br dd, J_{3-3a}=8.4 Hz, $^2J_{3\text{-}P}$=3.0 Hz, 1H, *H*–C3), 2.02 (dddAB, J_{AB}=13.2 Hz, J_{4-5}=11.4 Hz, J_{4-3a}=8.4 Hz, J_{4-5}=8.4 Hz, 1H, *Hβ*–C4), 1.89 (ddAB, J_{AB}=13.2 Hz, J_{4-5}=5.4 Hz, J_{4-3a}=0.9 Hz, 1H, *Hα*–C4), 1.36 (t, *J*=7.0 Hz, 6H). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 106.20 (d, $^3J_{PCCC}$=10.0 Hz, C6a), 68.90 (d, $^1J_{PC}$=164.5 Hz, C3), 66.39 (s, C5), 63.27 (d, *J*=6.8 Hz, C–O–P), 62.49 (d, *J*=7.5 Hz, C–O–P), 51.10 (d, *J*=1.5 Hz, C3a), 45.97 (br s, *C*H$_3$N), 30.77 (d, $^3J_{PCCC}$=3.8 Hz, C4), 16.59 (d, *J*=6.0 Hz), 16.56 (d, *J*=5.3 Hz). ^{31}P NMR (CDCl$_3$, 121.5 MHz): 21.37. Anal. Calcd for $C_{10}H_{20}NO_5P$: C, 45.28; H, 7.60; N, 5.28. Found: C, 45.24; H, 7.63; N, 5.27.

4.3.12. Diethyl hexahydro-2-methylfuro[3,4-*d*]isoxazol-3-yl-3-phosphonate (7d). From nitrone **1a** (0.130 g, 0.670 mmol) and 2,5-dihydrofuran (0.100 mL, 1.34 mmol), pure **7d** (0.126 g, 71%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

Compound ***7d***: colourless oil. IR (film): ν=2979, 2929, 2857, 1250, 1223, 1092, 1052, 1024, 971 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): 4.65 (dd, J_{6a-3a}=7.0 Hz, $J_{6a-6\beta}$=3.8 Hz, 1H, *H*–C6a), 4.25–4.12 (m, 4H), 4.01 (AB, J_{AB}=10.8 Hz, 1H, *Hα*–C6), 3.97 (dAB, J_{AB}=9.9 Hz, 1H, *Hα*–C4), 3.58 (dAB, J_{AB}=9.9 Hz, $J_{3a-4\beta}$=6.0 Hz, 1H, *Hβ*–C4), 3.55–3.40 (dddd, $J_{3a\text{-}P}$=16.0 Hz, J_{3a-3}=7.8 Hz, J_{3a-6a}=7.0 Hz, $J_{3a-4\beta}$=6.0 Hz, 1H, *H*–C3a), 3.42 (dAB, J_{AB}=10.8 Hz, $J_{6a-6\beta}$=3.8 Hz, 1H, *Hβ*–C6), 2.86 (d, *J*=1.0 Hz, 3H, C*H*$_3$N), 2.65 (d, J_{3-3a}=7.8 Hz, 1H, *H*–C3), 1.36 (t, *J*=7.1 Hz, 3H), 1.35 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (CDCl$_3$, 75.5 MHz): 82.02 (d, $^3J_{PCCC}$=9.5 Hz, C6a), 72.45 (s, C6), 71.84 (s, $^3J_{PCCC}$=3.4 Hz, C4), 70.86 (d,

$^{1}J_{PC}$=157.7 Hz, C3), 63.32 (d, J=6.3 Hz, C–O–P), 62.55 (d, J=6.9 Hz, C–O–P), 53.63, 45.27, 16.76 (d, J=5.7 Hz), 16.72 (d, J=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 22.26. Anal. Calcd for $C_{10}H_{20}NO_5P$: C, 45.28; H, 7.60; N, 5.28. Found: C, 45.33; H, 7.66; N, 5.13.

4.3.13. Diethyl hexahydro-2-methyl-5-oxo-5-phenyl-2*H*-phospholo[3,4-*d*]isoxazol-3-yl-3-phosphonate (7e). From nitrone **1a** (0.530 g, 2.72 mmol) and 3-phospholene **6e** (0.484 g, 2.72 mmol), pure **7e** (0.608 g, 82%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

*Compound **7e***: colourless oil. IR (film): ν=3447, 2981, 2927, 1657, 1439, 1392, 1250, 1232, 1162, 1025, 970 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): 7.9–7.8 (m, 1H), 7.75–7.65 (m, 2H), 7.6–7.48 (m, 2H), 4.82 (dddd, $J_{6a–P5}$=21.6 Hz, $J_{6a–3a}$=6.4 Hz, $J_{6a–6\beta}$=6.4 Hz, $J_{6a–6\alpha}$=2.0 Hz, 1H×0.21, *H*–C6a), 4.68 (dddd, $J_{6a–P5}$=18.9 Hz, $J_{6a–3a}$=7.0 Hz, $J_{6a–6\beta}$=5.4 Hz, $J_{6a–6\alpha}$=5.4 Hz, 1H×0.79, *H*–C6a), 4.28–4.13 (m, 4H), 3.65 (ddddd, $J_{3a–P3}$=20.1 Hz, $J_{3a–4\alpha}$=9.3 Hz, $J_{3a–4\beta}$=8.8 Hz, $J_{3a–6a}$=6.4 Hz, $J_{3a–3}$=5.2 Hz, 1H×0.21, *H*–C3a), 3.35 (dddddd, $J_{3a–P3}$=18.3 Hz, $J_{3a–P5}$=8.7 Hz, $J_{3a–4\beta}$=9.2 Hz, $J_{3a–4\alpha}$=7.0 Hz, $J_{3a–6a}$=7.0 Hz, $J_{3a–3}$=7.0 Hz, 1H×0.79, *H*–C3a), 2.99 (dd, $J_{3–3a}$=7.0 Hz, $^{2}J_{3–P3}$=2.5 Hz, 1H×0.79, *H*–C3), 2.94 (d, J=1.2 Hz, 3H×0.79, CH_3N), 2.90 (d, J=1.0 Hz, 3H×0.21, CH_3N), 2.72 (dd, $J_{3–3a}$=5.2 Hz, $^{2}J_{3–P3}$=3.1 Hz, 1H×0.21, *H*–C3), 2.55 (dddd, $^{2}J_{4\beta–P5}$=15.4 Hz, $J_{4\beta–4\alpha}$=15.4 Hz, $J_{4\beta–3a}$=8.8 Hz, $^{4}J_{HH}$=1.0 Hz, 1H×0.21, *Hβ*–C4), 2.45 (dddd, $^{2}J_{6\beta–P5}$=16.4 Hz, $^{2}J_{6\beta–6\alpha}$=16.4 Hz, $J_{6\beta–6a}$=6.4 Hz, $^{4}J_{HH}$=1.0 Hz, 1H×0.21, *Hβ*–C6), 2.40–2.30 (m, 2H×0.79 from *H*–C6 and 1H×0.21 from *Hα*–C6), 2.36 (ddd, $^{2}J_{4\beta–4\alpha}$=15.9 Hz, $J_{4\beta–3a}$=9.2 Hz, $^{2}J_{4\beta–P5}$=7.5 Hz, 1H×0.79, *Hβ*–C4), 2.25 (ddd, $^{2}J_{4\alpha–P5}$=16.8 Hz, $^{2}J_{4\alpha–4\beta}$=15.9 Hz, $J_{4\alpha–3a}$=7.0 Hz, 1H×0.79, *Hα*–C4), 1.97 (ddd, $J_{4\alpha–4\beta}$=15.4 Hz, $J_{4\alpha–3a}$=9.3 Hz, $^{2}J_{4\alpha–P5}$=6.8 Hz, 1H×0.21, *Hα*–C4), 1.35 (t, J=6.9 Hz, 3H), 1.34 (t, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 131.97 (d, J=2.9 Hz), 131.60 (d, J=92.5 Hz, C_{ipso}×0.79), 131.30 (d, J=92.8 Hz, C_{ipso}×0.21), 130.14 (d, J=10.3 Hz, C×0.21), 129.58 (d, J=10.0 Hz, C×0.79), 128.64 (d, J=11.7 Hz, C×0.79), 128.43 (d, J=12.0 Hz, C×0.21), 79.13 (dd, J=9.7, 6.9 Hz, C6a×0.21), 78.05 (dd, J=10.0, 10.0 Hz, C6a×0.79), 72.67 (dd, $^{1}J_{PC}$=169.0 Hz, J=10.6 Hz, C3×0.21), 72.44 (dd, $^{1}J_{PC}$=164.0 Hz, J=6.0 Hz, C3×0.79), 63.20 (d, J=6.6 Hz, C×0.21), 62.92 (d, J=6.3 Hz, C×0.79), 62.45 (d, J=6.9 Hz, C×0.79), 62.28 (d, J=6.9 Hz, C×0.21), 48.33 (d, J=9.7, 1.6 Hz, C3a×0.21), 47.73 (d, J=10.3 Hz, C3a×0.79), 45.90 (d, J=3.4 Hz, CH_3N×0.21), 45.49 (s, CH_3N×0.79), 35.09 (dd, $^{1}J_{PC}$=64.4 Hz, J=8.3 Hz, C4×0.21), 32.70 (dd, $^{1}J_{PC}$=65.0 Hz, J=5.2 Hz, C4×0.79), 32.38 (d, $^{1}J_{PC}$=64.7 Hz, C6×0.21), 32.04 (d, $^{1}J_{PC}$=65.3 Hz, C6×0.79), 16.35 (d, J=5.3 Hz), 16.29 (d, J=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 63.68 (d, J=5.8 Hz, 1P×0.21), 61.69 (d, J=4.3 Hz, 1P×0.79), 21.28 (d, J=4.3 Hz, 1P×0.79), 20.93 (d, J=5.8 Hz, 1P×0.21). Anal. Calcd for $C_{16}H_{25}NO_5P_2$: C, 51.48; H, 6.75; N, 3.75. Found: C, 51.55; H, 6.72; N, 3.67.

4.3.14. Diethyl hexahydro-2-methyl-4-oxo-4-phenyl-2*H*-phospholo[2,3-*d*]isoxazol-3-yl-3-phosphonate (7f). From nitrone **1a** (0.195 g, 1.00 mmol) and 2-phospholene **6f** (0.178 g, 1.00 mmol), pure **7f** (0.329 g, 88%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

*Compound **7f***: colourless oil. IR (film): ν=3467, 2981, 2931, 1650, 1440, 1241, 1183, 1113, 1055, 1023, 971 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.75–7.65 (m, 2H), 7.6–7.45 (m, 3H), 4.74 (ddd, $J_{6a–P4}$=24.0 Hz, $J_{3a–6a}$=5.7 Hz, $J_{6a–6\beta}$=4.5 Hz, 1H, *H*–C6a), 4.30–4.10 (m, 4H), 3.79 (ddd, $J_{3–P4}$=18.9 Hz, $J_{3–3a}$=5.7 Hz, $^{2}J_{3-P}$=1.8 Hz, 1H, *H*–C3), 3.12 (dddd, $J_{3a–P3}$=20.1 Hz, $J_{3a–3}$=5.7 Hz, $J_{3a–6a}$=5.7 Hz, $^{2}J_{3–P4}$=2.4 Hz, 1H, *H*–C3a), 2.98 (d, J=1.2 Hz, 3H, CH_3N), 2.55–2.40 (m, 1H, *H*–C5), 2.40–2.25 (m, 2H, *H*–C5 and *H*–C6), 1.95–1.80 (m, 1H, *H*–C6), 1.29 (t, J=7.2 Hz, 3H), 1.26 (t, J=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 132.97 (d, $^{1}J_{PC}$=92.8 Hz, C_{ipso}), 132.20 (d, J=2.6 Hz), 129.58 (d, J=9.4 Hz), 128.99 (d, J=11.7 Hz), 81.56 (dd, $J_{C6a–P3}$=8.8 Hz, $J_{C6a–P4}$=5.0 Hz, C6a), 64.31 (d, $^{1}J_{PC}$=168.6 Hz, C3), 63.32 (d, J=6.3 Hz), 62.91 (d, J=6.6 Hz), 48.69 (dd, $^{1}J_{P4–C3a}$=66.5 Hz, $^{2}J_{C3a–P3}$=2.5 Hz, C3a), 45.79 (d, J=4.0 Hz, CH_3N), 24.64 (d, $^{1}J_{P4–C5}$=66.4 Hz, C5), 24.88 (d, $J_{P4–C6}$=7.7 Hz, C6), 16.61 (d, J=5.4 Hz), 16.53 (d, J=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 56.04 (d, J=25.6 Hz) and 22.02 (d, J=25.6 Hz). Anal. Calcd for $C_{16}H_{25}NO_5P_2$: C, 51.48; H, 6.75; N, 3.75. Found: C, 51.41; H, 7.03; N, 3.57.

4.3.15. Hexaethyl 2-methylisoxazolidin-3-yl-3,5,5-tris(phosphonate) (7g). From nitrone **1a** (0.104 g, 0.335 mmol) and **6g** (0.065 g, 0.335 mmol), pure **7g** (0.152 g, 90%) was obtained after purification on silica gel with chloroform–MeOH (100:1).

*Compound **7g***: colourless oil. IR (film): ν=3492, 2984, 2913, 1256, 1019, 973 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.40–4.12 (m, 12H), 3.4–3.0 (m, 3H, *H*–C3 and *H*–C4), 2.98 (d, J=1.0 Hz, 3H, CH_3N), 1.36 (t, J=6.9 Hz, 6H), 1.35 (t, J=3 Hz, 3H), 1.34 (t, J=6.9 Hz, 9H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 78.66 (ddd, $^{1}J_{PC}$=160.0, 160.0 Hz, $^{3}J_{PCCC}$=11.8 Hz, C5), 64.55 (br d, $^{1}J_{PC}$=162.6 Hz, C3), 64.26 (d, J=6.9 Hz), 64.17 (d, J=6.9 Hz), 64.03 (d, J=6.6 Hz), 63.87 (d, J=6.6 Hz), 63.71 (d, J=6.4 Hz), 62.61 (d, J=6.9 Hz), 46.50 (s, CH_3N), 40.03 (s, C4), 16.76 (d, J=4.0 Hz), 16.70 (d, J=5.4 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 20.69, 18.12 (AB, J_{AB}=56.7 Hz) and 17.40 (AB, J_{AB}=56.7 Hz). Anal. Calcd for $C_{16}H_{36}NO_{10}P_3$: C, 38.79; H, 7.32; N, 2.83. Found: C, 38.95; H, 7.40; N, 2.83.

4.3.16. Ethyl 3,5-bis(diethoxyphosphoryl)-2-methylisoxazolidine-5-carboxylate (7h and 8h). From nitrone **1a** (0.195 g, 1.00 mmol) and **6h** (0.237 g, 1.00 mmol), a mixture of **7h** and **8h** (0.39 g, 90%) was obtained after purification on silica gel (chloroform–MeOH, 100:1). Further purification on silica gel with hexane–isopropanol (50:1) gave fractions enriched with **7h** (0.074 g, **7h**/**8h**=90:10) and **8h** (0.053 g, **8h**/**7h**=85:15).

*Compound **7h***: colourless oil. IR (film): ν=3490, 2984, 2912, 1733, 1260, 1040, 1023, 973 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.40–4.10 (m, 10H), 3.25–2.95 (m, 3H), 3.01 (d, J=1.2 Hz, 3H), 1.39–1.30 (m, 15H). ^{1}H NMR (C_6D_6, 300 MHz): 4.30–3.80 (m, 10H), 3.55 (dddAB, J_{AB}=12.3 Hz, $J_{P5–4}$=16.5 Hz, $J_{P3–4}$=14.4 Hz, $J_{4–3}$=12.3 Hz, 1H, *Hβ*–C4), 3.39 (dddAB, J_{AB}=12.3 Hz, $J_{4–3}$=6.6 Hz, $J_{P3–4}$=

3.3 Hz, J_{P5-4}=0.9 Hz, 1H, *Hα*–C4), 3.15 (ddd, $J_{3-4\beta}$=12.3 Hz, $J_{3-4\alpha}$=6.6 Hz, $^2J_{P3-3}$=0.9 Hz, 1H, *H*–C3), 3.16 (s, 3H), 1.11 (t, *J*=7.1 Hz, 3H), 1.10 (t, *J*=7.1 Hz, 3H), 1.07 (t, *J*=7.1 Hz, 3H), 0.96 (t, *J*=0.97 Hz, 3H), 0.92 (t, *J*=7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 169.54 (d, ^2J=11.5 Hz, C=O), 82.12 (dd, $^1J_{PC}$=165.5 Hz, $^3J_{P3-C5}$=12.0 Hz, C5), 64.40 (d, *J*=6.8 Hz), 64.24 (d, *J*=6.8 Hz), 63.87 (d, *J*=6.8 Hz), 63.67 (dd, $^1J_{PC}$=168.3 Hz, $^3J_{P5-C3}$=6.0 Hz, C3), 62.70 (d, *J*=6.8 Hz), 62.64, 47.60 (d, *J*=2.9 Hz), 41.18 (d, *J*=1.5 Hz), 16.63 (d, *J*=6.0 Hz), 14.28. ^{31}P NMR ($CDCl_3$, 121.5 MHz): 20.45 and 16.10. Anal. Calcd for $C_{15}H_{31}NO_9P_2$: C, 41.77; H, 7.24; N, 3.25. Found: C, 41.97; H, 7.32; N, 3.25.

Compound ***8h***: colourless oil. IR (film): *ν*=3491, 2984, 2912, 1734, 1260, 1040, 1024, 973 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.40–4.10 (m, 10H), 3.35–3.30 (m, 3H), 2.98 (s, 3H), 1.39–1.26 (m, 15H). ^{1}H NMR (C_6D_6, 300 MHz): 4.25–3.85 (m, 10H), 3.77 (dddAB, J_{AB}=13.2 Hz, J_{P3-4}=16.5 Hz, J_{P5-4}=11.4 Hz, J_{4-3}=9.6 Hz, 1H, *Hβ*–C4), 3.45 (dddAB, J_{AB}=12.3 Hz, J_{P5-4}=17.7 Hz, J_{4-3}=8.4 Hz, J_{P3-4}=4.8 Hz, 1H, *Hα*–C4), 3.25 (br dd, $J_{3-4\beta}$=9.6 Hz, $J_{3-4\alpha}$=8.4 Hz, 1H, *H*–C3), 3.10 (d, *J*=0.6 Hz, 3H), 1.08 (t, *J*=7.1 Hz, 3H), 1.07 (t, *J*=7.1 Hz, 3H), 1.00 (t, *J*=7.1 Hz, 3H), 0.99 (t, *J*=7.1 Hz, 3H), 0.97 (t, *J*=7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 169.44 (d, ^2J=8.0 Hz, C=O), 82.01 (dd, $^1J_{PC}$=160.0 Hz, $^3J_{P3-C5}$=9.4 Hz, C5), 64.77 (dd, $^1J_{PC}$=163.0 Hz, $^3J_{P5-C3}$=4.5 Hz, C3), 64.49 (d, *J*=6.8 Hz), 64.19 (d, *J*=6.8 Hz), 63.65 (d, *J*=6.0 Hz), 62.58 (d, *J*=6.8 Hz), 62.38, 46.01, 39.89, 16.67 (d, *J*=5.3 Hz), 16.60 (d, *J*=5.3 Hz), 14.33. ^{31}P NMR ($CDCl_3$, 121.5 MHz): 20.98 and 16.29. Anal. Calcd for $C_{15}H_{31}NO_9P_2$: C, 41.77; H, 7.24; N, 3.25. Found: C, 41.91; H, 7.08; N, 3.18.

4.3.17. Methyl 3-diethoxyphosphoryl-2,5-dimethylisoxazolidine-5-carboxylate (7i and 8i). From nitrone **1a** (0.39 g, 2.00 mmol) and **6i** (1.0 mL, 10.0 mmol), a mixture of **7i** and **8i** (0.529 g, 90%) was obtained after purification on silica gel (chloroform–MeOH, 100:1). Further purification on silica gel with toluene–isopropanol (100:1) gave fractions enriched with **8i** (0.033 g, **8i/7i**=95:5) and **7i** (0.10 g, **7i/8i**=50:50).

Compound ***7i***: colourless oil. IR (film): *ν*=2473, 2984, 1737, 1444, 1238, 1203, 1053, 1024, 969 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.27–4.07 (m, 4H), 3.77 (s, 3H), 3.15 (ddd, $J_{3-4\beta}$=10.5 Hz, $J_{3-4\alpha}$=7.8 Hz, $^2J_{3-P}$=3.0 Hz, 1H, *H*–C3), 3.05 (ddd, ^2J=12.6 Hz, J_{4-3}=7.8 Hz, J_{4-P}=4.8 Hz, 1H, *Hα*–C4), 2.92 (d, *J*=1.2 Hz, 3H), 2.49 (ddd, J_{4-P}=16.8 Hz, ^2J=12.6 Hz, J_{4-3}=10.5 Hz, 1H, *Hβ*–C4), 1.56 (s, 3H), 1.36 (t, *J*=7.2 Hz, 3H), 1.33 (t, *J*=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 173.7 (C=O), 81.59 (d, *J*=10.6 Hz, C5), 64.53 (d, $^1J_{PC}$=169.0 Hz, C3), 63.35 (d, *J*=6.0 Hz), 62.63 (d, *J*=6.8 Hz), 52.76 (s, *C*H$_3$), 46.94 (d, *J*=4.5 Hz, *C*H$_3$N), 43.21 (d, *J*=2.3 Hz, C4), 23.77, 16.67 (d, *J*=6.0 Hz), 16.63 (d, *J*=5.3 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 22.33. Anal. Calcd for $C_{11}H_{22}NO_6P$: C, 44.74; H, 7.51; N, 4.74. Found: C, 44.63; H, 7.81; N, 4.61.

Compound ***8i***: colourless oil. IR (film): *ν*=2473, 2984, 1737, 1444, 1238, 1203, 1053, 1024, 969 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.27–4.07 (m, 4H), 3.77 (s, 3H,), 3.22 (ddd, J_{P-4}=18.3 Hz, ^2J=12.9 Hz, J_{4-3}=9.3 Hz, 1H, *Hβ*–C4), 3.00 (ddd, $J_{4\beta-3}$=9.3 Hz, $J_{4\alpha-3}$=9.3 Hz, *J*=1.5 Hz, 1H, *H*–C3), 2.92 (d, *J*=1.2 Hz, 3H), 2.36 (ddd, ^2J=12.9 Hz, J_{4-3}=9.3 Hz, J_{P-4}=6.6 Hz, 1H, *Hα*–C4), 1.50 (s, 3H), 1.35 (t, *J*=7.2 Hz, 3H), 1.32 (t, *J*=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 174.40 (C=O), 81.03 (d, *J*=8.3 Hz), 64.76 (d, $^1J_{PC}$=165.3 Hz, C3), 63.35 (d, *J*=6.0 Hz), 62.41 (d, *J*=6.8 Hz), 52.64 (s, *C*H$_3$), 45.85 (d, *J*=2.3 Hz, *C*H$_3$N), 42.18 (d, *J*=2.3 Hz, C4), 23.55, 16.60 (d, *J*=5.3 Hz), 16.53 (d, *J*=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 22.12. Anal. Calcd for $C_{11}H_{22}NO_6P$: C, 44.74; H, 7.51; N, 4.74. Found: C, 44.84; H, 7.73; N, 4.73.

4.3.18. Phosphonates obtained from 1a and chalcone (7j–10j). From nitrone **1a** (0.781 g, 4.00 mmol) and **6j** (0.833 g, 4.00 mmol), pure **7j** (0.201 g, 12%), **8j** (0.825 g, 50%) and **10j** (0.044 g, 3%) were obtained after purification on silica gel with ethyl acetate–hexane (2:1).

4.3.18.1. Diethyl 5-benzyl-2-methyl-4-phenylisoxazolidin-3-yl-3-phosphonate 7j. Mp 79–80 °C, colourless needles. IR (KBr): *ν*=2975, 2919, 1681, 1446, 1246, 1224, 1048, 1026 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.9–7.83 (m, 2H), 7.6–7.5 (m, 1H), 7.4–7.38 (m, 4H), 7.35–7.2 (m, 3H), 5.69 (d, J_{4-5}=9.0 Hz, 1H, *H*–C5), 4.45 (ddd, J_{4-P}=21.3 Hz, J_{4-3}=9.9 Hz, J_{4-5}=9.0 Hz, 1H, *H*–C4), 4.19–4.08 (m, 2H), 4.05–3.85 (m, 2H), 3.75 (dd, J_{4-3}=9.9 Hz, $^2J_{3-P}$=7.2 Hz, 1H, *H*–C3), 3.08 (d, *J*=0.9 Hz, 3H, C*H*$_3$N), 1.26 (t, *J*=6.9 Hz, 3H), 1.02 (t, *J*=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 195.14 (d, *J*=5.2 Hz, C=O), 137.98 (C_{ipso}), 137.59 (C_{ipso}), 133.32, 128.65, 128.58, 128.48, 128.44, 126.79, 82.83 (d, $^3J_{PCCC}$=3.7 Hz, C5), 69.34 (d, $^1J_{PC}$=172.6 Hz, C3), 63.45 (d, *J*=6.6 Hz), 62.82 (d, *J*=7.2 Hz), 58.43 (s, C4), 47.55 (d, *J*=8.9 Hz, *C*H$_3$N), 16.53 (d, *J*=6.0 Hz), 16.20 (d, *J*=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 18.88. Anal. Calcd for $C_{21}H_{26}NO_5P$: C, 62.52; H, 6.50; N, 3.47. Found: C, 62.52; H, 6.65; N, 3.66.

4.3.18.2. Diethyl 5-benzyl-2-methyl-4-phenylisoxazolidin-3-yl-3-phosphonate 8j. IR (film): *ν*=2985, 2909, 1680, 1596, 1449, 1252, 1240, 1027, 969 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.70–7.67 (m, 2H), 7.55–7.4 (m, 1H), 7.4–7.2 (m, 7H), 5.20 (d, J_{4-5}=7.8 Hz, 1H, *H*–C5), 4.71 (ddd, J_{4-P}=17.7 Hz, J_{4-5}=7.8 Hz, J_{4-3}=7.2 Hz, 1H, *H*–C4), 4.25–4.08 (m, 4H), 3.86 (dd, J_{4-3}=7.2 Hz, $^2J_{3-P}$=6.0 Hz, 1H, *H*–C3), 3.06 (s, 3H, C*H*$_3$N), 1.28 (t, *J*=7.2 Hz, 3H), 1.17 (t, *J*=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 196.98 (s, *J*=4.0 Hz, C=O), 137.17 (C_{ipso}), 136.20 (C_{ipso}), 133.76, 128.81, 128.73, 128.66, 128.52, 127.05, 83.33 (d, $^3J_{PCCC}$=5.4 Hz, C5), 69.03 (d, $^1J_{PC}$=174.6 Hz, C3), 63.38 (d, *J*=6.6 Hz), 62.94 (d, *J*=6.9 Hz), 61.39 (d, *J*=1.7 Hz, C4), 47.06 (d, *J*=12.6 Hz, *C*H$_3$N), 16.62 (d, *J*=6.0 Hz), 16.42 (d, *J*=6.0 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 22.67. Anal. Calcd for $C_{21}H_{26}NO_5P$: C, 62.52; H, 6.50; N, 3.47. Found: C, 62.62; H, 6.57; N, 3.64.

4.3.18.3. Diethyl 4-benzyl-2-methyl-5-phenylisoxazolidin-3-yl-3-phosphonate 10j. Colourless oil. IR (film): *ν*=2982, 2930, 1690, 1447, 1247, 1240, 1025, 971 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 8.0–7.94 (m, 2H), 7.6–7.5 (m, 1H), 7.5–7.24 (m, 7H), 5.10 (d, J_{4-5}=4.2 Hz, 1H, *H*–C5), 4.64 (ddd, J_{4-P}=17.1 Hz, J_{4-3}=8.7 Hz, J_{4-5}=4.2 Hz, 1H, *H*–C4), 4.20–3.80 (m, 4H), 3.13 (dd, J_{4-3}=8.7 Hz, $^2J_{3-P}$=3.0 Hz, 1H, *H*–C3), 3.02 (d, *J*=1.2 Hz, 3H, C*H*$_3$N),

1.29 (t, J=7.2 Hz, 3H), 1.07 (t, J=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 196.56 (s, C=O), 140.85 (C_{ipso}), 134.97 (C_{ipso}), 133.28, 129.33, 128.92, 128.43, 128.23, 127.54, 86.31 (d, $^3J_{PCCC}$=9.2 Hz, C5), 74.36 (d, $^1J_{PC}$= 162.9 Hz, C3), 63.89 (d, J=6.3 Hz), 62.34 (d, J=6.6 Hz), 53.99 (C4), 46.18 (CH_3N), 16.61 (d, J=6.3 Hz), 16.27 (d, J=6.3 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 20.95. Anal. Calcd for $C_{21}H_{26}NO_5P$: C, 62.52; H, 6.50; N, 3.47. Found: C, 62.28; H, 6.52; N, 3.70.

4.3.19. Phosphonates obtained from 1a and ethyl cinnamate (7k–10k). From nitrone **1a** (0.781 g, 4.00 mmol) and **6h** (0.705 g, 4.00 mmol), pure **7k** (0.192 g, 13%) and **8k** (0.103 g, 7%) were obtained after purification on silica gel with ethyl acetate–hexane (2:1).

4.3.19.1. Ethyl 3-diethoxyphosphoryl-2-methyl-5-phenylisoxazolidine-4-carboxylate 7k. Colourless oil. IR (film): ν=2983, 2909, 1737, 1455, 1378, 1243, 1187, 1050, 1027, 971 cm^{-1}. ^{1}H NMR (C_6D_6, 300 MHz): 7.45–7.40 (m, 2H), 7.15–7.00 (m, 3H), 5.82 (d, J=8.7 Hz, 1H, *H*–C5), 4.20–3.95 (m, 6H, 2×CH_2OP and CH_2–CH_3), 3.51 (ddd, J=17.4, 10.2, 8.7 Hz, 1H, *H*–C4), 3.45 (dd, J=10.2, 6.8 Hz, 1H, *H*–C3), 2.89 (s, 3H), 1.11 (t, J=7.0 Hz, 6H), 0.99 (t, J=7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 169.17 (d, J=6.6 Hz, C=O), 137.57 (C_{ipso}), 128.50, 128.37, 126.57, 82.11 (d, $^3J_{PCCC}$=4.6 Hz, C5), 67.97 (d, $^1J_{PC}$=169.2 Hz, C3), 63.14 (d, J=6.8 Hz), 63.10 (d, J=6.6 Hz), 61.37 (s, CH_3CH_2O(O)C), 56.72 (s, C4), 46.83 (d, J=7.4 Hz, CH_3N), 16.55 (d, J=5.4 Hz), 16.49 (d, J=5.7 Hz), 14.07 (s, CH_3CH_2O(O)C). ^{13}C NMR (C_6D_6, 75.5 MHz): 169.79 (d, J=6.6 Hz, C=O), 137.01 (C_{ipso}), 129.14, 128.90, 127.50, 82.92 (d, $^3J_{PCCC}$=4.3 Hz, C5), 69.05 (d, $^1J_{PC}$=167.2 Hz, C3), 63.48 (d, J=6.3 Hz), 63.31 (d, J=6.6 Hz), 61.67 (s, CH_3CH_2O(O)C), 57.90 (s, C4), 47.14 (d, J=7.2 Hz, CH_3N), 17.05 (d, J=6.0 Hz), 16.97 (d, J=5.7 Hz), 14.50 (s, CH_3CH_2O(O)C). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 19.32. Anal. Calcd for $C_{17}H_{26}NO_6P$: C, 54.98; H, 7.06; N, 3.77. Found: C, 55.04; H, 7.30; N, 3.96.

4.3.19.2. Ethyl 3-diethoxyphosphoryl-2-methyl-5-phenylisoxazolidine-4-carboxylate 8k. Colourless oil. IR (film): ν=2983, 2910, 1735, 1447, 1375, 1253, 1180, 1024, 971 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.47–7.42 (m, 2H), 7.40–7.25 (m, 3H), 5.26 (d, J_{5-4}=7.0 Hz, 1H, *H*–C5), 4.30–4.10 (m, 6H), 3.69 (dd, J_{3-4}=7.5 Hz, $J_{3\text{-}P}$= 5.7 Hz, 1H, *H*–C3), 3.64 (ddd, $J_{4\text{-}P}$=13.5 Hz, J_{4-3}=7.5 Hz, J_{4-5}=7.0 Hz, 1H, *H*–C4), 3.00 (d, J=0.6 Hz, 3H), 1.30 (t, J=7.0 Hz, 3H), 1.26 (t, J=7.0 Hz, 3H), 1.24 (t, J=7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 170.85 (d, J=5.4 Hz, C=O), 137.99 (C_{ipso}), 128.51, 128.39, 126.68, 81.57 (d, $^3J_{PCCC}$=5.4 Hz, C5), 68.20 (d, $^1J_{PC}$=173.8 Hz, C3), 63.62 (d, J=6.6 Hz), 62.86 (d, J=6.9 Hz), 61.78 (s, CH_3CH_2O-(O)C), 59.38 (s, C4), 46.88 (d, J=11.5 Hz, CH_3N), 16.57 (d, J=6.0 Hz), 14.36 (s, CH_3CH_2O(O)C). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 21.84. Anal. Calcd for $C_{17}H_{26}NO_6P$: C, 54.98; H, 7.06; N, 3.77. Found: C, 54.86; H, 7.20; N, 4.00.

4.4. General procedure for the cycloaddition of nitrone 1a to alkene in the presence of $ZnCl_2$

Nitrone **1a** (1.0 mmol) and alkene (2.0 mmol) in methylene chloride (2 mL) were stirred at room temperature in the presence of $ZnCl_2$ (1.00 mmol) until the nitrone disappeared. Crude product was purified by column chromatography on silica gel.

4.4.1. Isoxazolidines 3a and 4a. From nitrone **1a** (1.03 g, 5.28 mmol) and allyl alcohol (0.720 mL, 10.56 mmol), pure **3a** (0.633 g, 47%) and **4a** (0.045 g, 3%) were obtained after purification by column chromatography.

4.4.2. Isoxazolidines 3d and 4d. From nitrone **1a** (0.256 g, 1.31 mmol) and alkene **2d** (0.416 mL, 2.62 mmol), pure **3d** (0.081 g, 20%) and **4d** (0.028 g, 7%) were obtained, after purification by column chromatography.

*Compound **4d***: IR (film): ν=2981, 2955, 2911, 1249, 1050, 1027 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.30–4.13 (m, 5H, H-C5 and 2×CH_2–O–P), 3.10 (ddd, $J_{3-4\beta}$=9.0 Hz, $J_{3-4\alpha}$=8.4 Hz, $J_{3\text{-}P}$=4.8 Hz, 1H, *H*–C3), 2.78 (d, J=0.9 Hz, 3H, CH_3–N), 2.60 (dddAB, J_{AB}=12.3 Hz, J=6.6 Hz, $J_{4\alpha-3}$= 8.4 Hz, J=5.4 Hz, 1H, *Hα*–C4), 2.03 (dddAB, J_{AB}= 12.3 Hz, $J_{4\beta\text{-}P}$=18.6 Hz, $J_{4\beta-5}$=9.3 Hz, $J_{4\beta-3}$=9.0 Hz, 1H, *Hβ*–C4), 1.34 (t, J=7.1 Hz, 6H, 2×CH_3–CH_2–O–P), 1.07 (dAB, J_{AB}=14.1 Hz, $J_{5-1'a}$=6.0 Hz, 1H, *Ha*–C1′), 0.87 (dAB, J_{AB}=14.1 Hz, $J_{5-1'b}$=8.3 Hz, 1H, *Hb*–C1′), 0.05 (s, 9H, C(CH_3)$_3$). ^{13}C NMR ($CDCl_3$, 75.5 MHz): 73.82 (d, $^3J_{PCCC}$=7.5 Hz, C5), 64.71 (d, $^1J_{PC}$=169.0 Hz, C3), 62.95 (d, J=6.6 Hz, C–O–P), 62.48 (d, J=6.8 Hz, C–O–P), 46.31 (d, J=4.5 Hz, H_3C–N–C–P), 40.34 (d, $^2J_{PCC}$=3.8 Hz, C4), 21.98 (s, C1′), 16.63 (d, J=5.5 Hz, *C*–C–O–P), −0.70 (s, C(CH_3)$_3$). ^{31}P NMR ($CDCl_3$, 121.5 MHz): 24.42. Anal. Calcd for $C_{12}H_{28}NO_4PSi$: C, 46.58; H, 9.12; N, 4.53. Found: C, 46.37; H, 9.23; N, 4.52.

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