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Ring transformations of aziridinyl 2-phosphonates: synthesis of 5-phosphono-2-oxazolidinones and 5-phosphono-2-imidazolidinones

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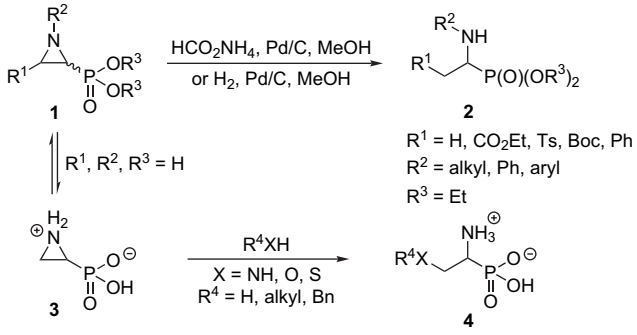
Abstract—Syntheses of 5-phosphono-2-oxazolidinones and 5-phosphono-2-imidazolidinones were achieved from the corresponding 1-vinyl-2-phosphonoaziridines. Regioselective aziridine ring opening employing methyl chloroformate affords 1-amido-2-chloroethyl-phosphonates, which were easily transformed into the corresponding 2-oxazolidinones upon heating in dimethyl sulfoxide. Treatment of the aziridine ring opening products with ammonia furnishes vinylphosphonates, which undergo a Michael type addition with several amines. In situ ring closure of the addition products yields the corresponding phosphonylated 2-imidazolidinones.

1. Introduction

The synthesis of azaheterocyclic phosphonates is recently getting more attention in search of new physiologically active compounds because of the mimicking potential of phosphonic acids in relation to the corresponding amino acids.[1] Because of the important ring strain of aziridines, ring opening reactions are a predominant feature in their chemistry.[2,3] Although the reactivity of aziridinyl carboxylates is well documented,[2,3] the ring fission of the corresponding aziridinyl 2-phosphonates **1** is poorly covered in the literature. Except for their conversion into the corresponding α-aminophosphonates **2** by hydrogenolysis (Scheme 1),[4,5] ring opening reactions of phosphonylated aziridines have not been studied in detail. On the other hand, the reactivity of aziridinyl 2-phosphonic acid **3** was studied in the early 1980s. Treating these aziridines with different nucleophiles, including halides, alkoxides, thiolates, and amines, the ring opening was successfully achieved (Scheme 1).[6] Because of the protonation in the corresponding zwitterionic structure **3**, the aziridine ring is activated toward ring fission allowing the synthesis of 1-amino-2-functionalized ethylphosphonic acids **4**.

In comparison with aziridinyl 2-carboxylates and their derivatives, which are useful intermediates for the synthesis of various amine-substituted molecules,[2,3] phosphonylated



Scheme 1. Hydrogenolysis of α-aminophosphonates and ring opening of aminophosphonic acids by several nucleophiles.

aziridines may allow straightforward synthesis of the corresponding α-amino-phosphonates or may be transformed into five-membered heterocyclic aminophosphonates.[7] Considering the importance of acyclic and heterocyclic aminophosphonates in synthetic, agrochemical, and medicinal chemistry,[8] the potential transformation to phosphonylated 2-oxazolidinones and 2-imidazolidinones from the corresponding aziridines was considered to be worthwhile. Indeed, the synthesis of phosphonylated 2-oxazolidinones is very scarcely covered in the literature. 4-Phosphono-[9] as well as 5-phosphono-2-oxazolidinones[10] are exclusively prepared from α-amino-β-hydroxyphosphonates and β-amino-α-hydroxyphosphonates, respectively, upon reaction with 1,1′-carbonyldiimidazole (CDI) or phosgene. Recently, a straightforward procedure was reported disclosing the preparation of oxazolidine-2-thiones **8** from isothiocyanomethyl phosphonate **6** and several aldehydes **5** (Scheme 2).[11]

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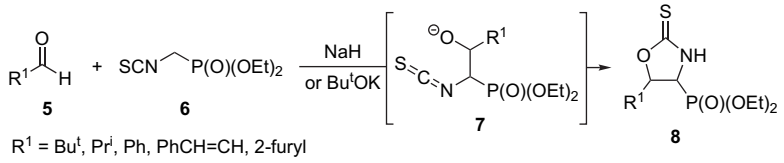
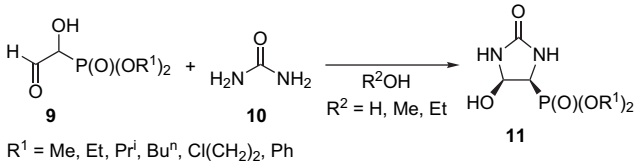


Scheme 2. Preparation of oxazolidine-2-thiones **8** from isothiocyano-methylphosphonate **6** and aldehydes **5**.

Despite the observation that certain phosphonylated 2-pyrrolidinones exhibit antibiotic[12] and enzyme-inhibiting activities,[13] the related phosphonylated 2-imidazolidinones are also poorly investigated. A rare example expounds the straightforward procedure toward **11** using the reaction of urea **10** with phosphonylated aldehydes **9** (Scheme 3).[14]



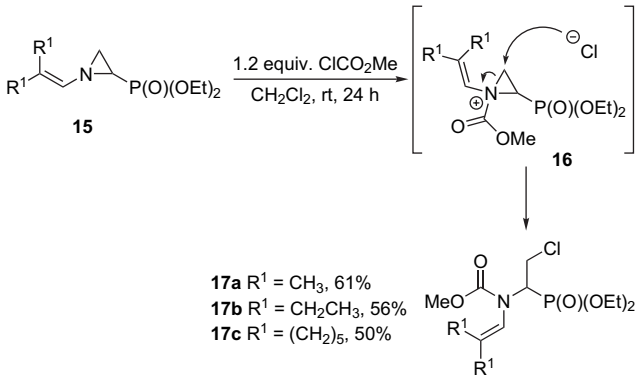
Scheme 3. Preparation of phosphonylated 2-imidazolidinones **11** from aldehydes **9** and urea **10**.

On the other hand, 4-oxo-5-phosphono-2-imidazolidinone has received considerably more attention,[15] especially since this compound has been abundantly utilized as a Horner–Wadsworth–Emmons reagent for the introduction of a C-5 unsaturated hydantoin functionality in organic molecules.[16] The synthesis of 5-phosphono-2-imidazolones **14** may also be mentioned here (Scheme 4).

β-Enaminophosphonates **12** react with diethyl azodicarboxylate (DEAD) affording functionalized enamines **13**, which undergo cyclocondensation to give 2-imidazolones **14** upon treatment with sodium hydride.

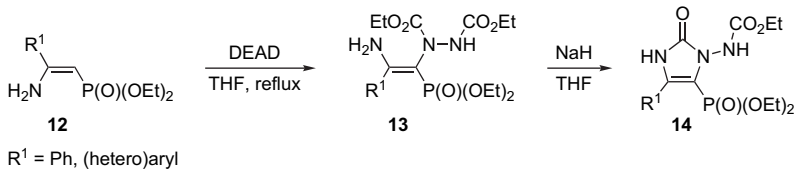
2. Results and discussion

Recently we reported on the synthesis of electron poor 1-phosphono-2-aza-1,3-dienes and their aziridination toward the corresponding 1-vinyl-2-phosphonoaziridines **15** upon treatment with diazomethane or other diazo compounds.[17] In the context of our continuing interest on the synthesis of heterocyclic aminophosphonates for agrochemical and pharmaceutical applications,[18] the ring transformation of these aziridines was investigated. Activation of the aziridines toward nucleophilic ring opening was evaluated using methyl chloroformate as counterattack reagent. Initially aziridines **15** were dissolved in anhydrous acetonitrile/toluene (8:2) and heated to 80 °C after addition of methyl chloroformate. After 2 h, TLC analysis revealed complete conversion and compounds **17** were isolated in 85–90% purity. Performing the reaction at room temperature needed 24 h to go to completion, but led to a more pure reaction product. Finally, evaluating CH_2Cl_2 as a solvent at room temperature gave the best results (Scheme 5).



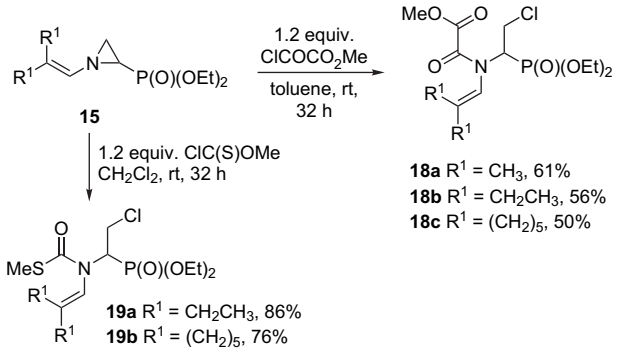
Scheme 5.

After quaternization toward **16**, chloride opens the three-membered ring with complete regioselectivity at C-3. The observed C-3 regioselectivity is opposite to the one observed for the reaction of the non-activated aziridinyl 2-carboxylates with methyl chloroformate.[19] The latter undergo nucleophilic substitution at C-2, which can be explained by the enhanced S_N2 at the α-position with respect to a carbonyl group. Hence, the observed regioselectivity for aziridinyl 2-phosphonates might be the result of a less efficient overlap of the LUMO of the phosphonate functionality with the LUMO of the carbon nitrogen bond (σ^*_{C-N}) so that no combined molecular LUMO, lower in energy than either, is formed. This, possibly combined with the increased steric hindrance caused by the tetragonal phosphonate moiety compared to the trigonal carboxyl group, favors nucleophilic attack at C-3. The aziridinium-initiated ring opening was also expanded to other counterattack reagents (Scheme 6). Thus, reaction of **15** with monomethyl oxalyl chloride successfully produced derivatives **18** whereas reaction with methyl chlorothioformate led to the sulfur containing derivatives **19**. Unfortunately, treatment of aziridines **15** with benzyloxy acetylchloride or methyl 2-bromoacetate led to complex reaction mixtures. Despite the fact that no formation of 2-oxazolidinones was observed during the synthesis



Scheme 4. Preparation of 5-phosphono-2-imidazolones **14**.

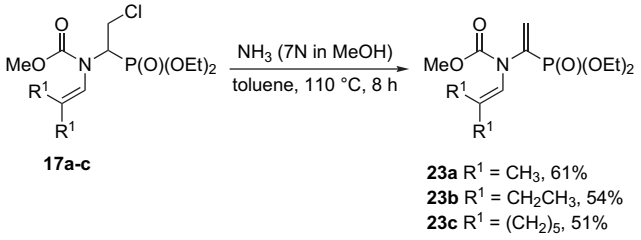
of compounds **17**, an attempt was made to obtain these compounds by refluxing **17** in CH_3CN. As expected, only starting material could be recovered. The addition of NaI as a nucleophilic catalyst, or AgO or $LiClO_4$ as Lewis acids, did not lead to a better result.



Scheme 6.

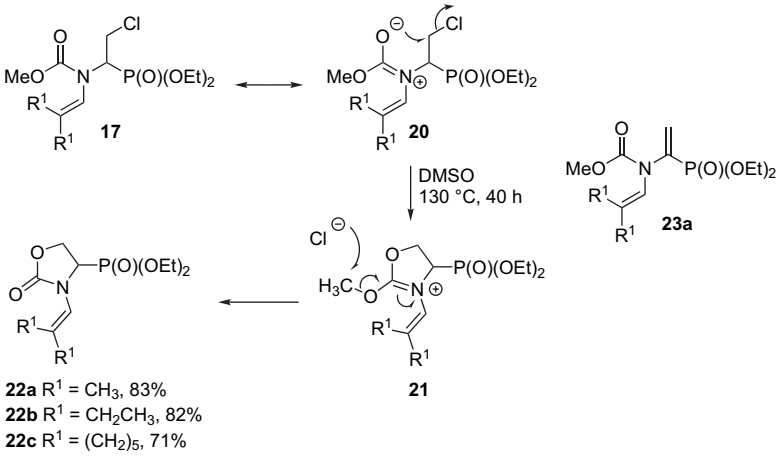
It was reasoned, however, that using dipolar solvents could favor the mesomeric structure **20** of enamides **17** due to the polarity of the medium. This can be expected to facilitate the intramolecular substitution leading to the formation of the corresponding 2-oxazolidinones **22**. Performing the reaction in DMF at 130 °C for 24 h did furnish some promising results. Two products could be identified in the reaction mixture namely compounds **22** and **23**, the latter obviously formed after elimination of hydrogen chloride with DMF acting as a base. Therefore, a less basic solvent, namely DMSO, was evaluated. Indeed, heating enamide **17a** in DMSO at 130 °C for 40 h resulted in the formation of 2-oxazolidinone **22a** in good yield and high purity after work-up (Scheme 7). In this case, the elimination product **23a** was not formed. Comparable results were obtained with enamides **17b–c**. Further purification using column chromatography yielded pure 2-oxazolidinones **22** in good yield.

Unfortunately, applying the same conditions to ring-opened compounds **18** and **19** did not lead to cyclization. Compounds **18** decomposed to a complex mixture whereas compounds **19** were recovered unchanged after refluxing in THF, toluene, CH_3CN, CH_3NO_2, CH_3NO_2/HMPA (9:1) or decomposed when heated in DMSO or diglyme. Some attention was given to the preparation of vinylphosphonates such as **23a** from the corresponding enamides **17** in order to evaluate Michael type additions of amines to these substrates. Treating enamine **17a** with triethylamine in refluxing dichloromethane or acetonitrile led to the recovery of starting material. The same outcome was obtained when pyridine or diisopropylamine was employed as a base. Next, enamide **17a** was reacted with ammonia (added as a solution in methanol, 7 N) in dichloromethane. At room temperature, no elimination was observed and starting material was isolated. Under reflux, the formation of vinylphosphonate **23a** took place, yet additional amounts of ammonia had to be added repeatedly to compensate for losses caused by evaporation. To compensate for this disadvantage, the reaction was executed in a sealed vessel. When the elimination was performed in acetonitrile at 80 °C, conversion was finished after 24 h. The elimination was completed only after 8 h, however, using toluene at 110 °C (Scheme 8). Hence, vinylphosphonate **23a** was isolated in good yield and with high purity (>95%), and could be further purified utilizing column chromatography. Employing the same procedure, derivatives **23b** and **23c** were prepared in comparable yields.

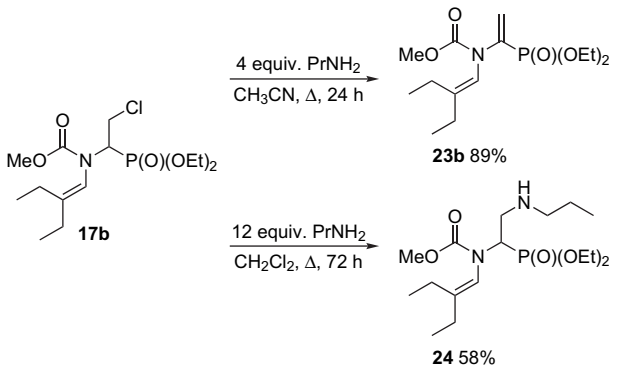


Scheme 8.

Primary amines were also used to evaluate the substitution reaction. When enamide **17b** was stirred together with 4.0 equiv of propylamine in refluxing acetonitrile, the elimination product **23b** was produced (Scheme 9). Next, the reaction was repeated in refluxing dichloromethane. Rather surprisingly, the substitution product **24** was formed instead and isolated in good yield after purification by flash chromatography.

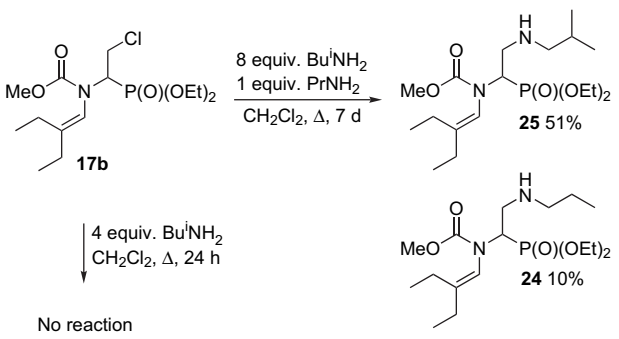


Scheme 7.



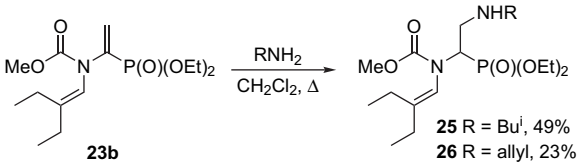
Scheme 9.

Importantly, to drive the reaction to completion, two times 4.0 equiv of propylamine were added during the course of the reaction. With the spectral data of β-aminophosphonate **24** in hand, it became clear that also in refluxing acetonitrile amine **24** was formed, however, only in a very small amount. It was unlikely to believe that only the difference in polarity of the applied solvents could be responsible for the different outcome of both reaction set-ups. The hypothesis that instead of the substitution of the chlorine atom, the elimination of hydrogen chloride takes place first, followed by a Michael type addition to vinylphosphonate **23b**, was assumed more plausible. The different outcome when the reaction is performed in acetonitrile should simply be attributed to the higher boiling point of acetonitrile causing bigger losses of propylamine (bp 48 °C) during the course of the reaction. Indeed, even in dichloromethane, additional amounts of propylamine had to be added in order to complete the reaction. The fact that a Michael type addition is involved in the preparation of substitution products like amine **24** was further confirmed when isobutylamine was applied as a nucleophile. Stirring enamide **17b** with 4.0 equiv of isobutylamine under reflux for 24 h did not result in any reaction and only starting material was isolated (Scheme 10). However, when 1 equiv of propylamine was added to the reaction mixture, mainly β-aminophosphonate **25** was obtained together with small amounts of amine **24**. Apparently, isobutylamine does not induce elimination, probably because of steric hindrance. When propylamine is added, vinylphosphonate **23b** is formed, which subsequently undergoes a Michael type addition by isobutylamine and propylamine resulting in a mixture of β-aminophosphonates **25** and **24**, respectively.



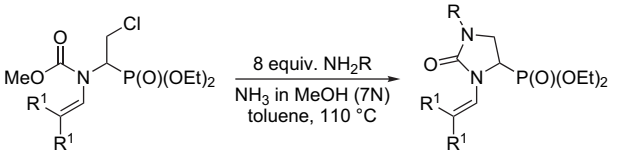
Scheme 10.

Having access to pure vinylphosphonates **23**, the Michael type addition with isobutylamine and allylamine was evaluated in order to prepare the corresponding β-aminophosphonates **25** and **26**. Prompted by the promising results with propylamine, dichloromethane was selected as solvent. Enamide **23b** was stirred together with 4.0 equiv of isobutylamine under reflux and the course of the reaction was followed by ^{31}P NMR spectroscopy (Scheme 11). After 4 days, the reaction mixture still contained starting material and no further conversion was observed. Consequently, an additional 4.0 equiv of isobutylamine was added. The reaction was stopped after 7 days although a small amount of starting material (<5%) was still present. After work-up and purification by means of column chromatography, amine **25** was isolated in moderate yield. Similarly, 12.0 equiv of allylamine was added to enamide **23b** and after 10 days of reflux the reaction was stopped because of the formation of unidentified side products. After purification by column chromatography, amine **26** was isolated, however, only in poor yield.



Scheme 11.

Guided by the findings that Michael type additions of amines to vinylphosphonates proceed well in alcoholic solvents,[20] the addition was evaluated in methanol. Considering the facile generation of vinylphosphonates **23** from enamides **17** using ammonia in methanol, it was judged appropriate to endeavor the preparation of β-aminophosphonates from the corresponding enamides **17** in one single step, without the isolation of the intermediate vinylphosphonates **23**. However, when enamide **17a** was dissolved in methanol and reacted with isobutylamine in the presence of ammonia (sealed vessel, 60 °C), the elimination reaction was observed to be very slow; after 24 h of stirring, only a trace of elimination product could be detected. The reaction was repeated, but this time toluene was applied as solvent and the reaction mixture was heated to 110 °C (Scheme 12). Following the reaction with ^{31}P NMR spectroscopy did show the conversion of enamide **17a** (~20.8 ppm) into vinylphosphonate **23a** (~12.5 ppm). Except for these two signals, three other signals (~16–17 ppm; ~22.3 ppm; ~24.3 ppm) appeared in the ^{31}P NMR spectra. During the course of the reaction, the signal of vinylphosphonate **23a** disappeared in favor for these new signals. Gradually, the signal with a chemical shift of 24.3 ppm completely vanished leaving only the signal with a chemical shift of 22.3 ppm. It was concluded that



Scheme 12.

these signals could be assigned to the corresponding β-aminophosphonate and the 2-imidazolidinone **27a**, respectively. The reaction was stopped when the 2-imidazolidinone **27a** (22.3 ppm) and the side product (~16–17 ppm) were the only products present in the reaction mixture, at least according to the ^{31}P NMR spectrum. After work-up, only small amounts of crude reaction product could be isolated from which 2-imidazolidinone **27a** could not be obtained completely pure.

Analogous results were obtained when enamides **17a** and **17c** were treated with allylamine resulting in the isolation of 2-imidazolidinones **27b** and **27c**, however, in poor yields. Compound **27c** could also not be obtained completely pure. With isobutylamine as well as with allylamine, the crude reaction product only showed one signal assigned to 2-imidazolidinones **27a–c**. Hence, the side product (~16–17 ppm) was not recovered. This, together with the minor amounts of crude reaction product isolated, led to the conclusion that a water-soluble compound was formed during the reaction, which is subsequently lost during work-up. Possibly, 5-phosphonylated 2-imidazolidinones **27a–c** are converted to the corresponding phosphonic acids. Prolonged heating in the presence of ammonium chloride, which is generated by the elimination reaction, may create a chemical environment effective to transform the phosphonates into the phosphonic acids. Trying to avoid the formation of this side product, the preparation of 5-phosphonylated 2-imidazolidinones **27** was evaluated in methanol from the corresponding vinylphosphonates **23a–c**, hence, avoiding the formation of ammonium chloride in the reaction medium (Scheme 13). Utilizing ^{31}P NMR spectroscopy to monitor the reaction, the formation of 2-imidazolidinones **27** was established and moreover, no side product could be detected.

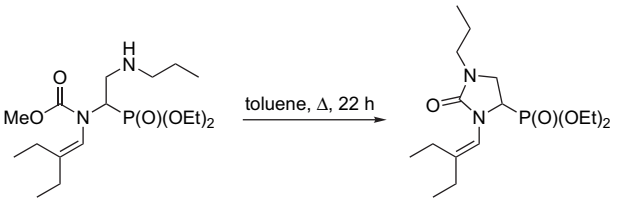
23b $R^1 = CH_2CH_3$
23c $R^1 = (CH_2)_5$

27c $R^1 = (CH_2)_5$, R = allyl, 44%
27d $R^1 = (CH_2)_5$, R = Pr, 41%
27e $R^1 = CH_2CH_3$, R = Bu^i, 33%
27f $R^1 = CH_2CH_3$, R = allyl, 52%
27g $R^1 = (CH_2)_5$, R = Bn, 44%

Scheme 13.

Of course, ring closure of β-aminophosphonate **24**, prepared from the corresponding vinylphosphonate **17b** and propylamine in dichloromethane, was also evaluated (Scheme 14). As could be expected, refluxing β-aminophosphonate **24** in toluene followed by purification afforded the corresponding 2-imidazolidinone **27h**.

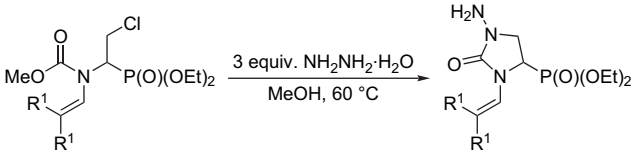
While applying different amines in order to prepare several 2-imidazolidinones from the corresponding vinylphosphonates, an unexpected chemical behavior of hydrazine was noticed. As was outlined before, the preparation of several 2-imidazolidinones (**27a–c**) from the corresponding 2-chloro-1-aminophosphonates (**17a–c**) was also possible, however, this entry was accompanied with the formation of a (unidentified) side product. When hydrazine was added



24 **27h** 41%

Scheme 14.

to vinylphosphonate **23b**, only a complex reaction mixture could be isolated in which none of the corresponding addition product or 2-imidazolidinone **28b** could be detected. Rather remarkably, 2-imidazolidinone **28b** was formed when 2-chloro-1-aminophosphonate **17b** was applied as starting material instead. Heating **17b** in the presence of hydrazine monohydrate afforded 1-amino-2-imidazolidinone **28b**, which could be isolated in moderate yield after purification by flash chromatography (Scheme 15). Noteworthy, no potassium carbonate had to be added to obtain **28b** within an acceptable time span. Applying this procedure on 2-chloro-1-aminophosphonate **17c** led to the formation of 2-imidazolidinone **28c** in a comparable yield.



17b $R^1 = CH_2CH_3$
17c $R^1 = (CH_2)_5$

28b $R^1 = CH_2CH_3$, 44%
28c $R^1 = (CH_2)_5$, 49%

Scheme 15.

3. Conclusion

In conclusion, the ring opening chemistry of 1-vinyl-2-phosphonoaziridines has been evaluated and used for the synthesis of 2-oxazolidinones and 2-imidazolidinones. The ring opening of the aziridines with methyl chloroformate as counterattack reagent occurs with complete regioselectivity at C-3. The resulting 1-amido-2-chloroethylphosphonates were transformed to the corresponding 2-oxazolidinones by heating in DMSO. Treatment of the ring-opened products with ammonia in methanol gave rise to the corresponding vinylphosphonates, by elimination of HCl. These vinylphosphonates were easily transformed to the 2-imidazolidinones by treatment with primary amines in methanol after Michael type addition followed by cyclization.

4. Experimental

4.1. General methods

Flash chromatography was performed on silica gel (Acros, 0.035–0.070 mm). ^{1}H NMR spectra were recorded at 300 MHz. ^{13}C NMR and ^{31}P NMR experiments were acquired at 75 MHz and 121 MHz, respectively. Chemical shifts (δ) are reported in parts per million from TMS as an internal reference. Coupling constants (J) are given in Hertz.

IR spectra were recorded with a FTIR spectrometer. Low-resolution mass spectra (MS) were obtained at 70 eV or using ES (4000 V). High-resolution mass spectra were recorded on a Finnigan MAT 95 XP-API-GC-Trap tandem Mass Spectrometer system. Solvents were dried extensively over calcium hydride (dichloromethane) or sodium/benzophenone ketyl (toluene) or used as such (methanol).

4.1.1. General procedure for the ring opening of 2-phosphonoaziridines with methyl chloroformate or methyl chlorothioformate. In a flask of 50 mL, 2-phosphonoaziridine **15a–c** (5.0 mmol) was dissolved in 30 mL of anhydrous dichloromethane and methyl chloroformate (6.0 mmol) (or methyl chlorothioformate (6.0 mmol) for the preparation of enamides **19a–b**) was added. The flask was fitted with a calcium chloride tube and stirred at room temperature for 24 h (the reaction with methyl chlorothioformate needed 48 h of stirring). The solvent was evaporated under reduced pressure furnishing the crude reaction mixture, which was purified by flash chromatography (using a mixture of ethyl acetate and petroleum ether as the eluent) leading to the isolation of enamide **17a–c**, **19a–b** (50–86%).

4.1.1.1. Diethyl 2-chloro-1-[(methoxycarbonyl)(2-methyl-1-propenyl)amino]ethylphosphonate 17a. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.32 (6H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.67 (3H, s, CH_3), 1.77 (3H, s, CH_3), 3.77 (4H, m, CH_2Cl, OCH_3), 3.88 (1H, dt, J=11.8 Hz, J=3.3 Hz, CH_2Cl), 4.15 (4H, sextet, J=7.3 Hz, P(O)OCH_2CH$_3$), 4.88 (1H, ddd, J_{HP}=19.0 Hz, J=11.5 Hz, J=3.0 Hz, CHP), 5.68 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.36 (P(O)OCH$_2$CH_3), 16.44 (P(O)OCH$_2$CH_3), 18.22 (CH_3), 22.42 (CH_3), 40.62 (d, J_{CP}=16.1 Hz, CH_2Cl), 53.45 (OCH_3), 56.13 (d, J_{CP}=147.7 Hz, CHP), 62.67 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 62.82 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 117.31 (CH), 138.03 (C_{quat}), 156.71 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 20.53; IR (neat) ν 1707, 1678 cm^{-1}; MS m/z 330/328 [M+H$^+$]; HRMS calcd for $C_{12}H_{23}{}^{35}ClNO_5P$ (M+H$^+$) 328.1075; found 328.1081; R_f (EtOAc/PET 9:1)=0.47.

4.1.1.2. Diethyl 2-chloro-1-[(2-ethyl-1-butenyl)(methoxycarbonyl)amino]ethylphosphonate 17b. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (3H, t, J=7.4 Hz, CH_3), 1.03 (3H, t, J=7.5 Hz, CH_3), 1.30 (6H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 2.11 (4H, quintet, J=7.4 Hz, CH_2), 3.72 (4H, m, OCH_3, CH_2Cl), 3.85 (1H, dt, J=11.8 Hz, J=2.9 Hz, CH_2Cl), 4.13 (4H, sextet, J=7.0 Hz, P(O)OCH_2CH$_3$), 4.86 (1H, ddd, J_{HP}=20.0 Hz, J=11.3 Hz, J=2.6 Hz, CHP), 5.65 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.09 (CH_3), 12.54 (CH_3), 16.40 (P(O)OCH$_2$CH_3), 16.46 (P(O)OCH$_2$CH_3), 22.16 (CH_2), 25.61 (CH_2), 40.63 (d, J_{CP}=16.7 Hz, CH_2Cl), 53.30 (OCH_3), 56.34 (d, J_{CP}=148.3 Hz, CHP), 62.64 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 62.78 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 116.07 (CH), 148.15 (C_{quat}), 156.90 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 20.72; IR (neat) ν 1709, 1662 cm^{-1}; MS m/z 358/356 [M+H$^+$]; HRMS calcd for $C_{14}H_{27}{}^{35}ClNO_5P$ (M+H$^+$) 356.1388; found 356.1396; R_f (EtOAc/PET 9:1)=0.38.

4.1.1.3. Diethyl 2-chloro-1-[(cyclohexylidenemethyl)(methoxycarbonyl)amino]ethylphosphonate 17c. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (3H, t, J=7.0 Hz, P(O)-OCH$_2$CH_3), 1.33 (3H, t, J=7.1 Hz, P(O)OCH$_2$CH_3), 1.60 (6H, m, CH_2), 2.13 (4H, m, CH_2), 3.73 (3H, s, OCH_3), 3.79 (1H, td, J=11.8 Hz, J=3.9 Hz, CH_2Cl), 3.88 (1H, dt, J=11.8 Hz, J=3.1 Hz, CH_2Cl), 4.14 (2H, sextet, J=7.0 Hz, P(O)OCH_2CH$_3$), 4.15 (2H, sextet, J=7.0 Hz, P(O)OCH_2CH$_3$), 4.92 (1H, ddd, J_{HP}=20.1 Hz, J=11.5 Hz, J=2.9 Hz, CHP), 5.66 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.39 (P(O)OCH$_2$CH_3), 16.44 (P(O)OCH$_2$CH_3), 26.41 (CH_2), 26.57 (CH_2), 28.04 (CH_2), 28.67 (CH_2), 33.43 (CH_2), 40.58 (d, J_{CP}=16.1 Hz, CH_2Cl), 53.35 (OCH_3), 55.87 (d, J_{CP}=147.7 Hz, CHP), 62.71 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 62.76 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 113.95 (CH), 144.96 (C_{quat}), 156.77 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 20.56; IR (neat) ν 1706 cm^{-1}; MS m/z 370/368 [M+H$^+$]; HRMS calcd for $C_{15}H_{27}{}^{35}ClNO_5P$ (M+H$^+$) 368.1388; found 368.1404; R_f (EtOAc/PET 7:3)=0.33.

4.1.1.4. Diethyl 2-chloro-1-{(2-ethyl-1-butenyl)[(methylsulfanyl)carbonyl]amino}ethylphosphonate 19a. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (3H, t, J=7.4 Hz, CH_3), 1.09 (3H, t, J=7.6 Hz, CH_3), 1.32 (6H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 2.19 (3H, m, CH_2), 2.27 (3H, s, SCH_3), 2.39 (1H, m, CH_2), 3.71 (1H, td, J=11.5 Hz, J=3.6 Hz, CH_2Cl), 3.89 (1H, dt, J=11.8 Hz, J=3.3 Hz, CH_2Cl), 4.13 (2H, quintet, J=7.1 Hz, P(O)OCH_2CH$_3$), 4.15 (2H, quintet, J=7.1 Hz, P(O)OCH_2CH$_3$), 5.18 (1H, ddd, J_{HP}=18.7 Hz, J=11.2 Hz, J=2.7 Hz, CHP), 5.77 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.18 (CH_3), 11.95 (CH_3), 13.47 (SCH_3), 16.28 (d, J_{CP}=5.8 Hz, P(O)OCH$_2$CH_3), 16.35 (d, J_{CP}=5.8 Hz, P(O)OCH$_2$CH_3), 22.06 (CH_2), 25.69 (CH_2), 40.27 (d, J_{CP}=16.1 Hz, CH_2Cl), 55.66 (d, J_{CP}=147.7 Hz, CHP), 62.64 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 62.78 (d, J_{CP}=5.7 Hz, P(O)OCH$_2$CH$_3$), 116.60 (CH), 153.83 (C_{quat}), 171.74 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 19.74; IR (neat) ν 1664, 1645 cm^{-1}; MS m/z 374/372 [M+H$^+$]; HRMS calcd for $C_{14}H_{27}{}^{35}ClNO_4PS$ (M+H$^+$) 372.1160; found 372.1171; R_f (EtOAc/PET 1:1)=0.33.

4.1.1.5. Diethyl 2-chloro-1-{(cyclohexylidenemethyl)[(methylsulfanyl)carbonyl]amino}ethylphosphonate 19b. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (6H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.61 (6H, m, CH_2), 2.18 (3H, m, CH_2), 2.28 (3H, s, SCH_3), 2.39 (1H, m, CH_2), 3.74 (1H, td, J=11.7 Hz, J=3.8 Hz, CH_2Cl), 3.89 (1H, dt, J=12.1 Hz, J=3.3 Hz, CH_2Cl), 4.14 (2H, sextet, J=7.1 Hz, P(O)-OCH_2CH$_3$), 4.15 (2H, sextet, J=7.4 Hz, P(O)OCH_2CH$_3$), 5.20 (1H, ddd, J_{HP}=20.1 Hz, J=11.1 Hz, J=2.9 Hz, CHP), 5.52 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.29 (SCH_3), 16.18 (2×P(O)OCH$_2$CH_3), 26.09 (CH_2), 26.30 (CH_2), 27.32 (CH_2), 28.59 (CH_2), 33.31 (CH_2), 40.12 (d, J_{CP}=16.1 Hz, CH_2Cl), 55.17 (d, J_{CP}=147.7 Hz, CHP), 62.62 (2C, d, J_{CP}=3.5 Hz, P(O)OCH$_2$CH$_3$), 114.52 (CH), 150.69 (C_{quat}), 171.32 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 19.57; IR (neat) ν 1667, 1650 cm^{-1}; MS m/z 386/384 [M+H$^+$]; HRMS calcd for $C_{15}H_{27}{}^{35}ClNO_4PS$ (M+H$^+$) 384.1160; found 384.1172; R_f (EtOAc/PET 6:4)=0.18.

4.1.2. General procedure for the ring opening of 2-phosphonoaziridines with monomethyl oxalyl chloride. In a flask of 25 mL, phosphonoaziridine **15a–c** (2.0 mmol) was dissolved in 20 mL of anhydrous dichloromethane and monomethyl oxalyl chloride (2.4 mmol) was added. The reaction was protected from moisture by a calcium chloride

tube and the mixture was stirred for 32 h at room temperature. Next, the reaction mixture was extracted with 3×15 mL of water and dried over magnesium sulfate. The solvent was evaporated under reduced pressure. The crude enamide **18a–c** was purified by flash chromatography (using a mixture of ethyl acetate and petroleum ether as the eluent) furnishing enamide **18a–c** (45–56%).

4.1.2.1. Methyl [[2-chloro-1-(diethoxyphosphoryl)-ethyl](2-methyl-1-propenyl)amino](oxo)acetate 18a. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, t, J=7.1 Hz, P(O)OCH$_2$CH_3), 1.34 (3H, t, J=7.1 Hz, P(O)OCH$_2$CH_3), 1.77 (6H, s, CH_3), 3.77 (4H, m, OCH_3, CH_2Cl), 3.95 (1H, dt, J=12.1 Hz, J=3.3 Hz, CH_2Cl), 4.17 (2H, quintet, J=7.3 Hz, P(O)OCH_2CH$_3$), 4.18 (2H, quintet, J=7.2 Hz, P(O)OCH_2CH$_3$), 5.12 (1H, ddd, J_{HP}=19.7 Hz, J=11.4 Hz, J=2.9 Hz, CHP), 5.88 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.37 (2C, d, J_{CP}=5.8 Hz, P(O)OCH$_2$CH_3), 18.60 (CH_3), 22.57 (CH_3), 39.72 (d, J_{CP}=13.8 Hz, CH_2Cl), 52.47 (OCH_3), 53.35 (d, J_{CP}=150.0 Hz, CHP), 63.16 (d, J_{CP}=6.9 Hz, P(O)OCH_2CH$_3$), 63.29 (d, J_{CP}=6.9 Hz, P(O)-OCH_2CH$_3$), 117.89 (CH), 142.63 (C_{quat}), 162.81 (C═O), 163.09 (C═O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 18.42; IR (neat) ν 1749, 1679 cm^{-1}; MS m/z 358/356 [M+H$^+$]; HRMS calcd for $C_{13}H_{23}{}^{35}ClNO_6P$ (M+H$^+$) 356.1024; found 356.1031; R_f (EtOAc/PET 7:3)=0.24.

4.1.2.2. Methyl [[2-chloro-1-(diethoxyphosphoryl)-ethyl](2-ethyl-1-butenyl)amino](oxo)acetate 18b. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (3H, t, J=7.5 Hz, CH_3), 1.01 (3H, t, J=7.5 Hz, CH_3), 1.34 (3H, t, J=7.1 Hz, P(O)OCH$_2$CH_3), 1.35 (3H, t, J=7.3 Hz, P(O)OCH$_2$CH_3), 2.11 (3H, m, CH_2), 2.40 (1H, m, CH_2), 3.73 (1H, td, J=11.8 Hz, J=3.8 Hz, CH_2Cl), 3.78 (3H, s, OCH_3), 3.94 (1H, dt, J=12.1 Hz, J=3.3 Hz, CH_2Cl), 4.18 (4H, quintet, J=7.2 Hz, P(O)OCH_2CH$_3$), 5.15 (1H, ddd, J_{HP}=20.1 Hz, J=11.3 Hz, J=2.9 Hz, CHP), 5.89 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.40 (CH_3), 12.47 (CH_3), 16.14 (d, J_{CP}=5.8 Hz, P(O)OCH$_2$CH_3), 16.21 (d, J_{CP}=4.6 Hz, P(O)OCH$_2$CH_3), 21.51 (CH_2), 25.41 (CH_2), 39.58 (d, J_{CP}=13.8 Hz, CH_2Cl), 52.07 (OCH_3), 53.43 (d, J_{CP}=147.7 Hz, CHP), 62.95 (d, J_{CP}=5.8 Hz, P(O)OCH_2CH$_3$), 63.03 (d, J_{CP}=5.8 Hz, P(O)OCH_2CH$_3$), 116.84 (CH), 152.06 (C_{quat}), 162.52 (d, J_{CP}=2.3 Hz, C═O), 162.69 (C═O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 18.48; IR (neat) ν 1749, 1678 cm^{-1}; MS m/z 386/384 [M+H$^+$]; HRMS calcd for $C_{15}H_{27}{}^{35}ClNO_6P$ (M+H$^+$) 384.1337; found 384.1353; R_f (EtOAc/PET 1:1)=0.16.

4.1.2.3. Methyl [[2-chloro-1-(diethoxyphosphoryl)-ethyl] (cyclohexylidenemethyl)amino](oxo)acetate 18c. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, t, J=7.1 Hz, P(O)OCH$_2$CH_3), 1.34 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.55 (6H, m, CH_2), 2.06 (2H, m, CH_2), 2.20 (1H, m, CH_2), 2.39 (1H, m, CH_2), 3.77 (4H, m, OCH_3, CH_2Cl), 3.94 (1H, dq, J=12.1 Hz, J=3.0 Hz, CH_2Cl), 4.17 (2H, quintet, J=7.3 Hz, P(O)OCH_2CH$_3$), 4.18 (2H, quintet, J=7.2 Hz, P(O)OCH_2CH$_3$), 5.15 (1H, ddd, J_{HP}=19.8 Hz, J=11.3 Hz, J=2.7 Hz, CHP), 5.87 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.33 (d, J_{CP}=4.6 Hz, P(O)OCH$_2$CH_3), 16.40 (d, J_{CP}=5.8 Hz, P(O)OCH$_2$CH_3), 26.06 (CH_2), 26.96 (CH_2), 27.89 (CH_2), 28.51 (CH_2), 33.58 (CH_2), 39.72 (d, J_{CP}=13.8 Hz, CH_2Cl), 52.42 (OCH_3), 53.39 (d, J_{CP}=145.4 Hz, CHP), 63.18 (d, J_{CP}=5.8 Hz, P(O)OCH_2CH$_3$), 63.23 (d, J_{CP}=5.8 Hz, P(O)OCH_2CH$_3$), 114.98 (CH), 148.98 (C_{quat}), 162.61 (C═O), 162.87 (C═O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 18.33; IR (neat) ν 1749, 1682 cm^{-1}; MS m/z 398/396 [M+H$^+$]; HRMS calcd for $C_{16}H_{27}{}^{35}ClNO_6P$ (M+H$^+$) 396.1337; found 396.1341; R_f (EtOAc/PET 7:3)=0.33.

4.1.3. General procedure for the preparation of phosphonylated 2-oxazolidinones. In a flask of 25 mL, enamide **17** (1.0 mmol) was dissolved in 15 mL of anhydrous dimethyl sulfoxide (DMSO) and heated to 120–130 °C. After maintaining this temperature for 40 h, the solvent was distilled off under high vacuum (50–60 °C/0.10 mmHg) where upon the residue was dissolved in 20 mL of diethyl ether. The solution was extracted with brine (3×10 mL) and dried over magnesium sulfate. Evaporating the solvent under reduced pressure afforded oxazolidinone **22a–c** (71–83%, purity>95%). Further purification might be performed by flash chromatography using ethyl acetate and petroleum ether as the eluents (isolated yields: 51–62%).

4.1.3.1. Diethyl 3-(2-methyl-1-propenyl)-2-oxo-1,3-oxazolidin-4-ylphosphonate 22a. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.35 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.71 (3H, s, CH_3), 1.79 (3H, s, CH_3), 4.06 (1H, ddd, J_{HP}=8.7 Hz, J=7.3 Hz, J=1.9 Hz, CHP), 4.16 (2H, quintet, J=7.2 Hz, P(O)OCH_2CH$_3$), 4.18 (2H, quintet, J=7.1 Hz, P(O)OCH_2CH$_3$), 4.52 (2H, m, OCH_2), 5.69 (1H, t, J=1.4 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.48 (P(O)OCH$_2$CH_3), 16.56 (P(O)OCH$_2$CH_3), 18.27 (CH_3), 22.36 (CH_3), 54.07 (d, J_{CP}=163.8 Hz, CHP), 62.82 (OCH_2), 62.94 (d, J_{CP}=13.8 Hz, P(O)OCH_2CH$_3$), 63.18 (d, J_{CP}=8.1 Hz, P(O)OCH_2CH$_3$), 117.39 (CH), 135.67 (C_{quat}), 156.11 (C═O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 19.93; IR (neat) ν 1766 cm^{-1}; MS m/z 278 [M+H$^+$]; HRMS calcd for $C_{11}H_{20}NO_5P$ (M+H$^+$) 278.1152; found 278.1153; R_f (EtOAc/PET 9:1)=0.18.

4.1.3.2. Diethyl 3-(2-ethyl-1-butenyl)-2-oxo-1,3-oxazolidin-4-ylphosphonate 22b. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, t, J=7.7 Hz, CH_3), 1.07 (3H, t, J=7.7 Hz, CH_3), 1.34 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.35 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 2.14 (4H, q, J=7.5 Hz, CH_2), 4.04 (1H, ddd, J_{HP}=8.3 Hz, J=6.8 Hz, J=1.9 Hz, CHP), 4.16 (2H, quintet, J=7.2 Hz, P(O)OCH_2CH$_3$), 4.18 (2H, quintet, J=7.0 Hz, P(O)OCH_2CH$_3$), 4.52 (2H, m, OCH_2), 5.66 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.61 (CH_3), 12.30 (CH_3), 16.51 (P(O)OCH$_2$CH_3), 16.59 (P(O)-OCH$_2$CH_3), 22.90 (CH_2), 25.99 (CH_2), 54.49 (d, J_{CP}=162.7 Hz, CHP), 62.77 (d, J_{CP}=3.5 Hz, OCH_2), 63.02 (d, J_{CP}=6.9 Hz, P(O)OCH_2CH$_3$), 63.16 (d, J_{CP}=6.9 Hz, P(O)OCH_2CH$_3$), 116.15 (CH), 146.26 (C_{quat}), 156.43 (d, J_{CP}=4.6 Hz, C═O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 20.13; IR (neat) ν 1769 cm^{-1}; MS m/z 306 [M+H$^+$]; HRMS calcd for $C_{13}H_{24}NO_5P$ (M+H$^+$) 306.1465; found 306.1480; R_f (EtOAc/PET 9:1)=0.25.

4.1.3.3. Diethyl 3-(cyclohexylidenemethyl)-2-oxo-1,3-oxazolidin-4-ylphosphonate 22c. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (6H, t, J=7.4 Hz, P(O)OCH$_2$CH_3), 1.57 (6H, m, CH_2), 2.15 (4H, m, CH_2), 4.05 (1H, ddd, J_{HP}=8.7 Hz, J=6.9 Hz, J=1.8 Hz, CHP), 4.20 (4H, m,

P(O)OCH_2CH$_3$), 4.51 (2H, m, OCH$_2$), 5.64 (1H, s, CH); ^{13}C NMR (75 MHz, CDCl$_3$) δ 16.51 (P(O)OCH$_2$*C*H$_3$), 16.59 (P(O)OCH$_2$*C*H$_3$), 26.30 (CH$_2$), 26.74 (CH$_2$), 27.80 (CH$_2$), 28.76 (CH$_2$), 33.12 (CH$_2$), 54.38 (d, J_{CP}=163.8 Hz, CHP), 62.71 (d, J_{CP}=2.3 Hz, OCH$_2$), 63.07 (d, J_{CP}=6.9 Hz, P(O)-O*C*H$_2$CH$_3$), 63.16 (d, J_{CP}=8.1 Hz, P(O)O*C*H$_2$CH$_3$), 114.29 (CH), 142.78 (C$_{quat}$), 156.35 (d, J_{CP}=4.6 Hz, C=O); ^{31}P NMR (121 MHz, CDCl$_3$) δ 20.03; IR (neat) ν 1767 cm^{-1}; MS *m*/*z* 318 [M+H$^+$]; HRMS calcd for C$_{14}$H$_{24}$NO$_5$P (M+H$^+$) 318.1465; found 318.1468; R_f (EtOAc/PET 7:3)=0.14.

4.1.4. General procedure for the preparation of vinylphosphonates 23a–c. In a sealed vessel, enamide **17a–c** (5.0 mmol) was dissolved in 20 mL of toluene and 5.7 mL of ammonia (40 mmol) (7 M in MeOH) was added. The reaction mixture was heated in an oil bath of 120 °C for 8 h after which the reaction mixture was extracted using 30 mL of dichloromethane and 3×40 mL of water. The organic layer was dried over magnesium sulfate, which was subsequently filtered off and the solvent was evaporated under reduced pressure. Vinylphosphonate **23a–c** (72–83%, purity>95%) was obtained, which might be further purified by flash chromatography using a mixture of ethyl acetate and petroleum ether as the eluent (isolated yields: 51–61%).

4.1.4.1. Diethyl 1-[(methoxycarbonyl)(2-methyl-1-propenyl)amino]vinylphosphonate 23a. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.31 (3H, t, *J*=7.0 Hz, P(O)OCH$_2$C*H*$_3$), 1.32 (3H, t, *J*=7.0 Hz, P(O)OCH$_2$C*H*$_3$), 1.62 (3H, d, *J*=0.8 Hz, CH$_3$), 1.73 (3H, d, *J*=1.4 Hz, CH$_3$), 3.74 (3H, s, OCH$_3$), 4.08 (2H, octet, *J*=7.2 Hz, P(O)OC*H*$_2$CH$_3$), 4.11 (2H, octet, *J*=7.3 Hz, P(O)OC*H*$_2$CH$_3$), 5.82 (1H, s, CH), 5.90 (1H, d, J_{HP}=38.2 Hz, CH$_2$), 6.16 (1H, d, J_{HP}=13.5 Hz, CH$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 16.28 (P(O)OCH$_2$*C*H$_3$), 16.38 (P(O)OCH$_2$*C*H$_3$), 17.78 (CH$_3$), 22.30 (CH$_3$), 53.29 (OCH$_3$), 62.39 (2C, d, J_{CP}=4.6 Hz, P(O)O*C*H$_2$CH$_3$), 121.66 (CH), 128.63 (d, J_{CP}=23.1 Hz, CH$_2$), 134.15 (C$_{quat}$), 138.38 (d, J_{CP}=205.4 Hz, CP), 155.04 (C=O); ^{31}P NMR (121 MHz, CDCl$_3$) δ 12.76; IR (neat) ν 1721 cm^{-1}; MS *m*/*z* 292 [M+H$^+$]; HRMS calcd for C$_{12}$H$_{22}$NO$_5$P (M+H$^+$) 292.1308; found 292.1312; R_f (EtOAc/PET 7:3)=0.21.

4.1.4.2. Diethyl 1-[(2-ethyl-1-butenyl)(methoxycarbonyl)amino]vinylphosphonate 23b. ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.96 (3H, t, *J*=7.5 Hz, CH$_3$), 1.04 (3H, t, *J*=7.4 Hz, CH$_3$), 1.32 (6H, t, *J*=7.1 Hz, P(O)OCH$_2$C*H*$_3$), 2.08 (2H, q, *J*=7.4 Hz, CH$_2$), 2.09 (2H, q, *J*=7.1 Hz, CH$_2$), 3.73 (3H, s, OCH$_3$), 4.09 (2H, octet, *J*=7.1 Hz, P(O)-OC*H*$_2$CH$_3$), 4.12 (2H, octet, *J*=7.2 Hz, P(O)OC*H*$_2$CH$_3$), 5.80 (1H, s, CH), 5.90 (1H, d, J_{HP}=38.2 Hz, CH$_2$), 6.14 (1H, d, J_{HP}=13.2 Hz, CH$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 11.31 (CH$_3$), 12.31 (CH$_3$), 16.30 (P(O)OCH$_2$*C*H$_3$), 16.39 (P(O)OCH$_2$*C*H$_3$), 22.10 (CH$_2$), 25.98 (CH$_2$), 53.20 (OCH$_3$), 62.39 (2C, d, J_{CP}=5.8 Hz, P(O)O*C*H$_2$CH$_3$), 120.50 (CH), 128.15 (d, J_{CP}=21.9 Hz, CH$_2$), 138.86 (d, J_{CP}=205.4 Hz, CP), 144.66 (C$_{quat}$), 155.21 (C=O); ^{31}P NMR (121 MHz, CDCl$_3$) δ 12.84; IR (neat) ν 1722 cm^{-1}; MS *m*/*z* 320 [M+H$^+$]; HRMS calcd for C$_{14}$H$_{26}$NO$_5$P (M+H$^+$) 320.1621; found 320.1633; R_f (EtOAc/PET 7:3)=0.27.

4.1.4.3. Diethyl 1-[(cyclohexylidenemethyl)(methoxycarbonyl)amino]vinylphosphonate 23c. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.33 (6H, t, *J*=7.1 Hz, P(O)OCH$_2$C*H*$_3$), 1.54 (6H, m, CH$_2$), 2.11 (4H, m, CH$_2$), 3.73 (3H, s, OCH$_3$), 4.09 (2H, octet, *J*=7.1 Hz, P(O)OC*H*$_2$CH$_3$), 4.12 (2H, octet, *J*=7.1 Hz, P(O)OC*H*$_2$CH$_3$), 5.76 (1H, s, CH), 5.88 (1H, d, J_{HP}=38.2 Hz, CH$_2$), 6.13 (1H, d, J_{HP}=13.2 Hz, CH$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 16.25 (P(O)OCH$_2$*C*H$_3$), 16.35 (P(O)OCH$_2$*C*H$_3$), 26.32 (2×CH$_2$), 27.72 (CH$_2$), 28.12 (CH$_2$), 33.02 (CH$_2$), 53.16 (OCH$_3$), 62.34 (2C, d, J_{CP}= 5.8 Hz, P(O)O*C*H$_2$CH$_3$), 118.60 (CH), 128.08 (d, J_{CP}= 21.9 Hz, CH$_2$), 139.03 (d, J_{CP}=206.5 Hz, CP), 141.19 (C$_{quat}$), 155.06 (C=O); ^{31}P NMR (121 MHz, CDCl$_3$) δ 12.73; IR (neat) ν 1721 cm^{-1}; MS *m*/*z* 332 [M+H$^+$]; HRMS calcd for C$_{15}$H$_{26}$NO$_5$P (M+H$^+$) 332.1621; found 332.1627; R_f (EtOAc/PET 1:1)=0.11.

4.1.5. Experimental procedure for the preparation of diethyl 1-[(2-ethyl-1-butenyl)(methoxycarbonyl)amino]-2-(propylamino)ethylphosphonate 24. In a flask of 25 mL, 0.35 g of 2-chloro-1-aminophosphonate **17b** (1.0 mmol) and 0.24 g of propylamine (4.0 mmol) were dissolved in 10 mL of dichloromethane. The reaction mixture was heated under reflux for 72 h (to compensate for the loss of propylamine by evaporation, 0.24 g of propylamine (4.0 mmol) was added to the reaction mixture after 24 and 48 h). Next, the reaction mixture was extracted with 10 mL of dichloromethane and 3×10 mL of 0.1 M sodium bicarbonate after which the organic layer was dried over magnesium sulfate. Filtering off the drying agent and evaporating the solvent under reduced pressure afforded 0.32 g of crude reaction mixture from which 0.22 g of 2-propylamino-1-aminophosphonate **24** (58%) was isolated upon purification by flash chromatography.

^{1}H NMR (300 MHz, CDCl$_3$) δ 0.90 (3H, d, *J*=7.4 Hz, CH$_3$), 0.97 (3H, d, *J*=7.3 Hz, CH$_3$), 1.04 (3H, t, *J*=7.4 Hz, CH$_3$), 1.31 (6H, t, *J*=7.0 Hz, P(O)OCH$_2$C*H*$_3$), 1.46 (2H, sextet, *J*= 7.2 Hz, CH$_2$), 2.07 (4H, m, CH$_2$), 2.49 (1H, dt, *J*=11.5 Hz, *J*=7.1 Hz, NCH$_2$), 2.61 (1H, dt, *J*=11.3 Hz, *J*=7.1 Hz, NCH$_2$), 2.96 (2H, m, NCH$_2$), 3.70 (3H, s, OCH$_3$), 4.12 (2H, quintet, *J*=7.2 Hz, P(O)OC*H*$_2$CH$_3$), 4.14 (2H, quintet, *J*=7.1 Hz, P(O)OC*H*$_2$CH$_3$), 4.85 (1H, m, CHP), 5.71 (1H, s CH); ^{13}C NMR (75 MHz, CDCl$_3$) δ 10.88 (CH$_3$), 11.72 (CH$_3$), 12.44 (CH$_3$), 16.38 (P(O)OCH$_2$*C*H$_3$), 16.44 (P(O)-OCH$_2$*C*H$_3$), 21.99 (CH$_2$), 23.15 (CH$_2$), 25.48 (CH$_2$), 46.44 (NCH$_2$), 50.79 (NCH$_2$), 52.92 (d, J_{CP}=148.8 Hz, CHP), 53.06 (OCH$_3$), 62.15 (2C, d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 117.07 (CH), 145.89 (C$_{quat}$), 156.87 (C=O); ^{31}P NMR (121 MHz, CDCl$_3$) δ 24.39; IR (neat) ν 1705 cm^{-1}; MS *m*/*z* 379 [M+H$^+$]; HRMS calcd for C$_{17}$H$_{35}$N$_2$O$_5$P (M+H$^+$) 379.2356; found 379.2372; R_f (EtOAc/PET 9:1)=0.10.

4.1.6. Experimental procedure for the preparation of diethyl 1-[(2-ethyl-1-butenyl)(methoxycarbonyl)amino]-2-(isobutylamino)ethylphosphonate 25. In a flask of 25 mL, 0.32 g of vinylphosphonate **23b** (1.0 mmol) and 0.29 g of isobutylamine (4.0 mmol) were dissolved in 10 mL of dichloromethane and the reaction mixture was heated under reflux for 7 days. After 4 days, 0.29 g of isobutylamine (4.0 mmol) was added to compensate the loss of amine by evaporation. The work-up performed was identical to that for derivative **24** and afforded 0.36 g of crude reaction mixture. Purification by flash chromatography yielded 0.19 g of 2-isobutylamino-1-aminophosphonate **25** (49%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (3H, d, J=6.6 Hz, CH_3), 0.89 (3H, d, J=6.9 Hz, CH_3), 0.96 (3H, t, J=7.3 Hz, CH_3), 1.04 (3H, t, J=7.4 Hz, CH_3), 1.31 (6H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.69 (1H, nonnet, J=6.6 Hz, CH), 2.07 (4H, m, CH_2), 2.34 (1H, dd, J=11.3 Hz, J=6.6 Hz, NCH_2), 2.45 (1H, dd, J=11.3 Hz, J=6.9 Hz, NCH_2), 2.95 (2H, m, NCH_2), 3.70 (3H, s, OCH_3), 4.12 (2H, quintet, J=7.2 Hz, P(O)OCH_2CH$_3$), 4.14 (2H, quintet, J=7.1 Hz, P(O)OCH_2CH$_3$), 4.84 (1H, m, CHP), 5.71 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.92 (CH_3), 12.47 (CH_3), 16.39 (P(O)OCH$_2$CH_3), 16.47 (P(O)OCH$_2$CH_3), 20.59 (CH_3), 20.67 (CH_3), 22.04 (CH), 25.52 (CH_2), 28.48 (CH_2), 46.76 (NCH_2), 53.00 (d, J_{CP}=147.7 Hz, CHP), 53.06 (NCH_2), 57.05 (OCH_3), 62.18 (2×P(O)OCH$_2$CH$_3$), 117.16 (CH), 145.86 (C_{quat}), 156.89 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.51; IR (neat) ν 1706 cm^{-1}; MS m/z 393 [M+H$^+$]; HRMS calcd for $C_{18}H_{37}N_2O_5P$ (M+H$^+$) 393.2513; found 393.2530; R_f (EtOAc/PET 6:4)=0.14.

4.1.7. Experimental procedure for the preparation of diethyl 2-(allylamino)-1-[(2-ethyl-1-butenyl)(methoxycarbonyl)amino]ethylphosphonate 26. Following the procedure for the preparation of derivative **25** with 0.32 g of vinylphosphonate **23b** (1.0 mmol) and 0.68 g of allylamine (12 mmol) afforded 0.33 g of crude reaction mixture (reflux, 10 days) from which 0.09 g of 2-allylamino-1-aminophosphonate **26** (23%) was isolated by flash chromatography.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (3H, t, J=7.4 Hz, CH_3), 1.04 (3H, t, J=7.6 Hz, CH_3), 1.31 (6H, t, J=7.1 Hz, P(O)OCH$_2$CH_3), 1.76 (1H, s, NH), 2.07 (4H, m, CH_2), 2.96 (2H, m, NCH_2), 3.19 (1H, dd, J=13.9 Hz, J=6.1 Hz, NCH_2), 3.29 (1H, dd, J=13.8 Hz, J=5.8 Hz, NCH_2), 3.70 (3H, s, OCH_3), 4.12 (2H, quintet, J=7.2 Hz, P(O)-OCH_2CH$_3$), 4.14 (2H, quintet, J=7.1 Hz, P(O)OCH_2CH$_3$), 4.80 (1H, m, CHP), 5.09 (1H, d, J=10.4 Hz, CH_2), 5.17 (1H, dd, J=17.1 Hz, J=1.4 Hz, CH_2), 5.72 (1H, s, CH), 5.85 (1H, ddt, J=16.8 Hz, J=10.4 Hz, J=6.0 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.97 (CH_3), 12.54 (CH_3), 16.45 (P(O)OCH$_2$CH_3), 16.53 (P(O)OCH$_2$CH_3), 22.09 (CH_2), 25.55 (CH_2), 45.80 (NCH_2), 51.49 (NCH_2), 53.05 (d, J_{CP}= 147.7 Hz, CHP), 53.17 (OCH_3), 62.29 (2×P(O)OCH$_2$CH$_3$), 116.32 (CH_2), 117.15 (CH), 136.46 (CH), 146.06 (C_{quat}), 156.93 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 24.18; IR (neat) ν 1705 cm^{-1}; MS m/z 377 [M+H$^+$]; HRMS calcd for $C_{17}H_{33}N_2O_5P$ (M+H$^+$) 377.2200; found 377.2217; R_f (EtOAc/PET 8:2)=0.19.

4.1.8. General procedure for the preparation of 2-imidazolidinones 27d,e,g from vinylphosphonates 23b–c. In a sealed vessel, vinylphosphonate **23b–c** (1.0 mmol) and the appropriate amine (6.0 mmol) were dissolved in 10 mL of methanol and the reaction mixture was heated in an oil bath of 50–60 °C. After 4–14 days of heating (a sample from the reaction mixture showed a ~1:1 ratio of addition product (~24.6 ppm) vs ring closed product **27** (~23.5 ppm), all starting material (~13.3 ppm) was consumed; determined by ^{31}P NMR), potassium carbonate (1.0 mmol) was added and the reaction was heated for an additional 2 days until ring closure was complete. The solvent was evaporated under reduced pressure and the residue was extracted with 10 mL of dichloromethane and was washed with 3×10 mL of water. The crude reaction mixture was purified by flash chromatography affording 2-imidazolidinone **27a–f** (33–44%).

4.1.8.1. Diethyl 3-(cyclohexylidenemethyl)-2-oxo-1-propyl-4-imidazolidinylphosphonate 27d (potassium carbonate was added after 4 days of heating). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (3H, d, J=7.4 Hz, CH_3), 1.32 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.33 (3H, t, J=7.0 Hz, P(O)OCH$_2$CH_3), 1.56 (8H, m, CH_2), 2.20 (4H, m, CH_2), 3.15 (1H, dt, J=13.6 Hz, J=7.0 Hz, NCH_2), 3.20 (1H, dt, J=13.6 Hz, J=7.3 Hz, NCH_2), 3.58 (2H, m, NCH_2), 3.86 (1H, m, CHP), 4.12 (4H, m, P(O)OCH_2CH$_3$), 5.54 (1H, s CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.20 (CH_3), 16.53 (P(O)OCH$_2$CH_3), 16.60 (P(O)OCH$_2$CH_3), 20.80 (CH_2), 26.48 (CH_2), 26.94 (CH_2), 27.95 (CH_2), 29.02 (CH_2), 33.23 (CH_2), 43.78 (NCH_2), 45.83 (NCH_2), 52.26 (d, J_{CP}= 165.0 Hz, CHP), 62.61 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 62.74 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 116.81 (CH), 139.89 (C_{quat}), 158.92 (d, J_{CP}=6.9 Hz, C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.42; IR (neat) ν 1716 cm^{-1}; MS m/z 359 [M+H$^+$]; HRMS calcd for $C_{17}H_{31}N_2O_4P$ (M+H$^+$) 359.2094; found 359.2095; R_f (EtOAc/PET 9:1)=0.11.

4.1.8.2. Diethyl 3-(2-ethyl-1-butenyl)-1-isobutyl-2-oxo-4-imidazolidinylphosphonate 27e (potassium carbonate was added after 8 days of heating). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (3H, d, J=6.6 Hz, CH_3), 0.92 (3H, d, J=6.6 Hz, CH_3), 1.02 (3H, t, J=7.5 Hz, CH_3), 1.06 (3H, t, J=7.5 Hz, CH_3), 1.32 (6H, t, J=7.1 Hz, P(O)-OCH$_2$CH_3), 1.86 (1H, nonnet, J=6.8 Hz, CH), 2.14 (4H, m, CH_2), 2.98 (1H, dd, J=13.7 Hz, J=7.4 Hz, NCH_2), 3.04 (1H, dd, J=13.6 Hz, J=7.5 Hz, NCH_2), 3.59 (2H, m, NCH_2), 3.86 (1H, ddd, J_{HP}=9.6 Hz, J=7.1 Hz, J=1.5 Hz, CHP), 4.13 (4H, m, P(O)OCH_2CH$_3$), 5.56 (1H, d, J=0.8 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.78 (CH_3), 12.54 (CH_3), 16.53 (P(O)OCH$_2$CH_3), 16.60 (P(O)OCH$_2$CH_3), 19.98 (CH_3), 20.09 (CH_3), 22.93 (CH_2), 26.03 (CH_2), 27.00 (CH), 44.50 (NCH_2), 51.97 (NCH_2), 52.35 (d, J_{CP}=165.0 Hz, CHP), 62.58 (d, J_{CP}=4.6 Hz, P(O)OCH$_2$CH$_3$), 62.67 (d, J_{CP}=4.6 Hz, P(O)OCH$_2$CH$_3$), 118.63 (CH), 143.38 (C_{quat}), 159.20 (d, J_{CP}=5.8 Hz, C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.51; IR (neat) ν 1716 cm^{-1}; MS m/z 361 [M+H$^+$]; HRMS calcd for $C_{17}H_{33}N_2O_4P$ (M+H$^+$) 361.2251; found 361.2259; R_f (EtOAc/PET 8:2)=0.15.

4.1.8.3. Diethyl 1-benzyl-3-(cyclohexylidenemethyl)-2-oxo-4-imidazolidinylphosphonate 27g (potassium carbonate was added after 14 days of heating). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, t, J=7.1 Hz, P(O)-OCH$_2$CH_3), 1.30 (3H, t, J=6.9 Hz, P(O)OCH$_2$CH_3), 1.61 (6H, m, CH_2), 2.21 (4H, m, CH_2), 3.46 (2H, m, NCH_2), 3.83 (1H, ddd, J_{HP}=9.8 Hz, J=7.3 Hz, J=1.1 Hz, CHP), 4.07 (4H, m, P(O)OCH_2CH$_3$), 4.35 (1H, d, J=14.8 Hz, CH_2), 4.44 (1H, d, J=14.8 Hz, CH_2), 5.56 (1H, d, J=0.8 Hz, CH), 7.32 (5H, m, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.51 (P(O)OCH$_2$CH_3), 16.59 (P(O)OCH$_2$CH_3), 26.53 (CH_2), 27.00 (CH_2), 27.99 (CH_2), 29.11 (CH_2), 33.28 (CH_2), 43.32 (NCH_2), 48.39 (NCH_2), 52.15 (d, J_{CP}= 166.1 Hz, CHP), 62.64 (d, J_{CP}=9.2 Hz, P(O)OCH$_2$CH$_3$), 62.74 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 116.66 (CH), 127.66 (CH), 128.31 (2×CH), 128.72 (2×CH), 136.73 (C_{quat}), 140.43 (C_{quat}), 158.75 (d, J_{CP}=6.9 Hz, C=O); ^{31}P

NMR (121 MHz, $CDCl_3$) δ 22.10; IR (neat) ν 1716 cm^{-1}; MS *m/z* 407 [M+H$^+$]; HRMS calcd for $C_{21}H_{31}N_2O_4P$ (M+H$^+$) 407.2094; found 407.2102; R_f (EtOAc/PET 8:2)=0.15.

4.1.9. General procedure for the preparation of diethyl 1-allyl-2-oxo-4-imidazolidinylphosphonates 27b,f. Following the procedure for the preparation of 2-imidazolidinones **27**, vinylphosphonate **23a**,**b** (1.0 mmol) and 0.34 g of allylamine (6.0 mmol) were heated for 6 days (a sample from the reaction mixture showed that ring closure was complete; determined by ^{31}P NMR). After work-up, the crude reaction mixture was purified by flash chromatography affording 2-imidazolidinone **27b**,**c**,**f** (44–52%).

4.1.9.1. Diethyl 1-allyl-3-(2-methyl-1-propenyl)-2-oxo-4-imidazolidinylphosphonate 27b. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (6H, t, *J*=7.0 Hz, P(O)OCH$_2$C*H*$_3$), 1.70 (3H, d, *J*=1.1 Hz, CH$_3$), 1.76 (3H, d, *J*=1.1 Hz, CH$_3$), 3.56 (2H, m, NCH$_2$), 3.83 (2H, m, NCH$_2$), 3.89 (1H, ddd, J_{HP}=9.7 Hz, *J*=6.8 Hz, *J*=1.2 Hz, CHP), 4.12 (4H, m, P(O)OC*H*$_2$CH$_3$), 5.20 (1H, dq, *J*=10.0 Hz, *J*=1.3 Hz, CH$_2$), 5.24 (1H, dq, *J*=16.9 Hz, *J*=1.5 Hz, CH$_2$), 5.62 (1H, sextet, *J*=1.3 Hz, CH), 5.75 (1H, ddt, *J*=17.1 Hz, *J*=9.9 Hz, *J*=6.1 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.56 (2×P(O)OCH$_2$*C*H$_3$), 18.50 (CH$_3$), 22.42 (CH$_3$), 43.58 (NCH$_2$), 47.02 (NCH$_2$), 51.89 (d, J_{CP}=166.1 Hz, CHP), 62.61 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 62.81 (d, J_{CP}=6.9 Hz, P(O)OCH$_2$CH$_3$), 118.17 (CH$_2$), 119.68 (CH), 132.93 (CH), 133.21 (C$_{quat}$), 158.57 (C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.27; IR (neat) ν 1716 cm^{-1}; MS *m/z* 317 [M+H$^+$]; HRMS calcd for $C_{14}H_{25}N_2O_5P$ (M+H$^+$) 317.1625; found 317.1632; R_f (EtOAc/PET 8:2)=0.13.

4.1.9.2. Diethyl 1-allyl-3-(2-ethyl-1-butenyl)-2-oxo-4-imidazolidinylphosphonate 27f. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (3H, t, *J*=7.5 Hz, CH$_3$), 1.06 (3H, t, *J*=7.4 Hz, CH$_3$), 1.32 (6H, t, *J*=7.0 Hz, P(O)OCH$_2$C*H*$_3$), 2.14 (4H, m, CH$_2$), 3.56 (2H, m, NCH$_2$), 3.83 (2H, m, NCH$_2$), 3.86 (1H, ddd, J_{HP}=9.6 Hz, *J*=6.7 Hz, *J*=1.2 Hz, CHP), 4.12 (4H, m, P(O)OC*H*$_2$CH$_3$), 5.20 (1H, dq, *J*=10.0 Hz, *J*=1.5 Hz, CH$_2$), 5.24 (1H, dq, *J*=17.1 Hz, *J*=1.5 Hz, CH$_2$), 5.56 (1H, d, *J*=0.8 Hz, CH), 5.75 (1H, ddt, *J*=17.2 Hz, *J*=10.0 Hz, *J*=6.1 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.80 (CH$_3$), 12.56 (CH$_3$), 16.53 (P(O)OCH$_2$*C*H$_3$), 16.60 (P(O)OCH$_2$*C*H$_3$), 22.94 (CH$_2$), 26.01 (CH$_2$), 43.57 (NCH$_2$), 47.06 (NCH$_2$), 52.35 (d, J_{CP}=165.0 Hz, CHP), 62.55 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 62.74 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 118.12 (CH$_2$), 118.49 (CH), 132.96 (CH), 143.68 (C$_{quat}$), 158.67 (d, J_{CP}=6.9 Hz, C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.45; IR (neat) ν 1718 cm^{-1}; MS *m/z* 345 [M+H$^+$]; HRMS calcd for $C_{16}H_{29}N_2O_4P$ (M+H$^+$) 345.1938; found 345.1940; R_f (EtOAc/PET 9:1)=0.13.

4.1.10. Experimental procedure for the preparation of diethyl 3-(2-ethyl-1-butenyl)-2-oxo-1-propyl-4-imidazolidinylphosphonate 27h by ring closure of 2-propylamino-1-aminophosphonate 24. In a flask of 25 mL, 0.22 g of 2-propylamino-1-aminophosphonate **24** (0.58 mmol) was dissolved in 5 mL of anhydrous toluene. The reaction mixture was heated under reflux for 22 h where upon the solvent was evaporated under reduced pressure affording 0.20 g of crude reaction mixture. Purification by flash chromatography led to the isolation of 0.08 g of 2-imidazolidinone **27h** (41%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (3H, t, *J*=7.4 Hz, CH$_3$), 1.02 (3H, t, *J*=7.7 Hz, CH$_3$), 1.05 (3H, t, *J*=7.4 Hz, CH$_3$), 1.32 (6H, t, *J*=7.0 Hz, P(O)OCH$_2$C*H*$_3$), 1.54 (2H, sextet, *J*=7.3 Hz, CH$_2$), 2.12 (4H, m, CH$_2$), 3.16 (1H, dt, *J*=13.7 Hz, *J*=7.1 Hz, NCH$_2$), 3.20 (1H, dt, *J*=13.7 Hz, *J*=7.1 Hz, NCH$_2$), 3.59 (2H, m, NCH$_2$), 3.86 (1H, m, CHP), 4.15 (4H, m, P(O)OC*H*$_2$CH$_3$), 5.56 (1H, s CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.23 (CH$_3$), 11.81 (CH$_3$), 12.57 (CH$_3$), 16.54 (P(O)OCH$_2$*C*H$_3$), 16.62 (P(O)OCH$_2$*C*H$_3$), 20.85 (CH$_2$), 22.93 (CH$_2$), 26.03 (CH$_2$), 43.87 (NCH$_2$), 45.87 (NCH$_2$), 52.42 (d, J_{CP}=165.0 Hz, CHP), 62.56 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 62.74 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 118.63 (CH), 143.39 (C$_{quat}$), 159.06 (d, J_{CP}=4.6 Hz, C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.63; IR (neat) ν 1714 cm^{-1}; MS *m/z* 347 [M+H$^+$]; HRMS calcd for $C_{16}H_{31}N_2O_4P$ (M+H$^+$) 347.2094; found 347.2105; R_f (EtOAc/PET 8:2)=0.14.

4.1.11. Experimental procedure for the preparation of diethyl 1-amino-3-(2-ethyl-1-butenyl)-2-oxo-4-imidazolidinylphosphonate 28b. In a sealed vessel, 0.35 g of 2-chloro-1-aminophosphonate **17b** (1.0 mmol) and 0.15 g of hydrazine monohydrate (3.0 mmol) were dissolved in 10 mL of methanol. The reaction mixture was heated in an oil bath of 60 °C for 4 days after which the solvent was evaporated under reduced pressure affording 0.31 g of crude reaction mixture. Purification by flash chromatography led to the isolation of 0.14 g of 2-imidazolidinone **28b** (44%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (3H, t, *J*=7.7 Hz, CH$_3$), 1.06 (3H, t, *J*=7.4 Hz, CH$_3$), 1.33 (6H, t, *J*=7.1 Hz, P(O)OCH$_2$C*H*$_3$), 2.14 (4H, m, CH$_2$), 3.68 (4H, m, NCH$_2$, NH$_2$), 3.81 (1H, dd, J_{HP}=9.3 Hz, *J*=6.0 Hz, CHP), 4.19 (4H, m, P(O)OC*H*$_2$CH$_3$), 5.55 (1H, d, *J*=0.8 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.76 (CH$_3$), 12.44 (CH$_3$), 16.51 (P(O)OCH$_2$*C*H$_3$), 16.59 (P(O)OCH$_2$*C*H$_3$), 22.93 (CH$_2$), 25.95 (CH$_2$), 48.59 (NCH$_2$), 51.34 (d, J_{CP}=166.1 Hz, CHP), 62.62 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 62.87 (d, J_{CP}=6.9 Hz, P(O)O*C*H$_2$CH$_3$), 117.92 (CH), 144.77 (C$_{quat}$), 160.75 (d, J_{CP}=4.6 Hz, C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 21.84; IR (neat) ν 3327, 3211, 1723 cm^{-1}; MS *m/z* 320 [M+H$^+$]; HRMS calcd for $C_{13}H_{26}N_3O_4P$ (M+H$^+$) 320.1734; found 320.1746; R_f (EtOAc/MeOH 8:2)=0.20.

4.1.12. Experimental procedure for the preparation of diethyl 1-amino-3-(cyclohexylidenemethyl)-2-oxo-4-imidazolidinylphosphonate 28c. Applying the procedure for the preparation of 2-imidazolidinone **28b** on 0.37 g of 2-chloro-1-aminophosphonate **17c** led to 0.32 g of crude reaction mixture from which 0.16 g of 2-imidazolidinone **28c** (49%) was isolated.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (6H, t, *J*=7.2 Hz, P(O)OCH$_2$C*H*$_3$), 1.57 (6H, m, CH$_2$), 2.16 (4H, m, CH$_2$), 3.62 (2H, m, NCH$_2$), 3.81 (1H, dd, J_{HP}=9.5 Hz, *J*=6.4 Hz, CHP), 3.94 (2H, s, NH$_2$), 4.15 (4H, m, P(O)OC*H*$_2$CH$_3$), 5.54 (1H, s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.54 (P(O)OCH$_2$*C*H$_3$), 16.62 (P(O)OCH$_2$*C*H$_3$), 26.41 (CH$_2$),

26.93 (CH_2), 27.92 (CH_2), 28.96 (CH_2), 33.17 (CH_2), 48.58 (NCH_2), 51.26 (d, J_{CP}=166.1 Hz, CHP), 62.65 (d, J_{CP}=6.9 Hz, P(O)OCH_2CH_3), 62.88 (d, J_{CP}=6.9 Hz, P(O)-OCH_2CH_3), 116.12 (CH), 141.30 (C_{quat}), 160.67 (d, J_{CP}=5.8 Hz, C=O); ^{31}P NMR (121 MHz, $CDCl_3$) δ 21.68; IR (neat) ν 3326, 3211, 1724 cm^{-1}; MS *m/z* 332 [M+H$^+$]; HRMS calcd for $C_{14}H_{26}N_3O_4P$ (M+H$^+$) 332.1734; found 332.1747; R_f (EtOAc/MeOH 9:1)=0.16.

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