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Synthesis and Reactivity of Imines Derived from Bisphosphonates and 3-Phosphorylated 2-Aza-1,3-dienes

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Abstract—The synthesis and some reactions of imines derived from aminoalkylbisphosphonates and 2-aza-1,3-butadienes is described. Bisphosphonylalkylimino compounds are useful intermediates in the preparation of aminoalkylbisphosphonate derivatives by reduction of the imino linkage with sodium triacetoxyborohydride as well as in the synthesis of 2-aza-1,3-butadienes by an olefination reaction. The electrocyclization of phosphorylated 2-aza-1,3,5-trienes afforded substituted 2-phosphorylated pyridines.

Aminophosphonic acids, which are analogues of amino acids, and their phosphapeptide derivatives are both mimetics of amino acids and peptides, with interesting biological properties.[1,2] For instance, α-amino phosphonates have been used as haptens for the preparation of catalytic monoclonal antibodies[3a] and as enzymatic inhibitors with therapeutic use,[3b] while β-aminophosphonates have been found to be potent and selective inhibitors of farnesyl protein transferase (FPT) and therefore they may prove useful as antitumor agents.[3c] Furthermore, some aminoalkylbisphosphonic acid derivatives have been used as spin traps[4] and have recently gained importance in medicinal chemistry as antiinflammatory agents and for the treatment of bone diseases related to calcium metabolism.[5] These include acyclic compounds such as pamidronate **1a** (n=1) or alendronate **2b** (n=2) or cyclic derivatives such as pyridyl- (NE-97220) **2a** or cycloheptyl-aminomethylbisphosphonic acids (cimadronate, YM-175) **2b**, which show increasing antiresorptive activity compared to previous bisphosphonate derivatives which lack N-containing functionalities such as clodronate or etidronate (Fig. 1).[6]

Taking this into account, we decided to devise a route for the preparation of new aminophosphonic derivatives such as iminoalkylphosphonates **3** and phosphorylated 2-aza-1,3-butadienes **4** (Fig. 2). 2-Azadienes represent an important class of compounds and have become useful key intermediates in organic synthesis for the construction of both heterocyclic systems and open chain polyfunctionalized compounds.[7] These heterodienes **4**, analogues of 2-azadienes derived from α-amino acids[8] **5**, where the carboxylate group has been isosterically replaced by a phosphonate, may be useful intermediates for the synthesis of more complex cyclic and acyclic α-aminophosphonate derivatives with potentially increased biological activity.

We envisaged obtaining compounds of type **3** and **4** according to the following retrosynthetic scheme where, after condensation of aminomethyldiphosphonate **6** with a carbonyl compound, the resulting imine **3** could be olefinated by means of a Wadsworth–Emmons reaction with the appropriate aldehyde to give rise to 3-phosphorylated 2-aza-1,3-butadiene **4**. This would be a highly versatile route starting from very simple precursors, which would allow the introduction of a great variety of functional groups in positions 1 and 4 of the azadiene (Scheme 1).

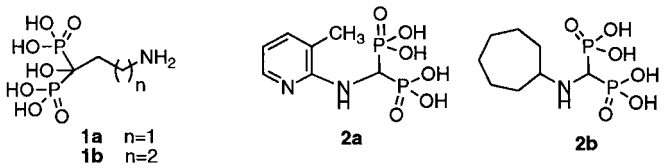

Figure 1.

Keywords: aminobisphosphonates; 2-aza-1,3-dienes; 2-aza-1,3,5-trienes; 2-phosphoryl pyridines.
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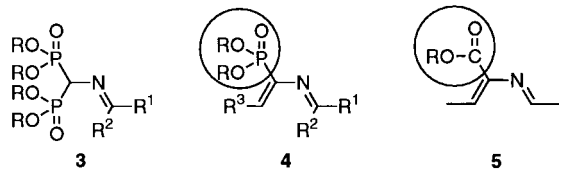
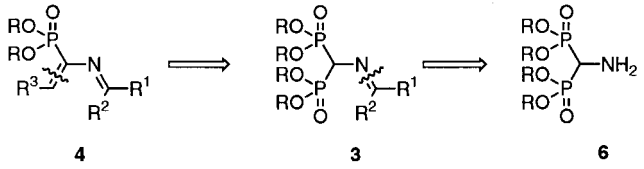


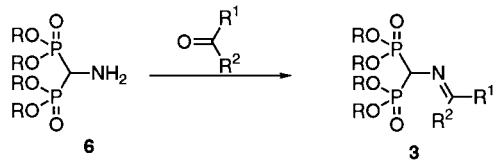
Figure 2.



Scheme 1.

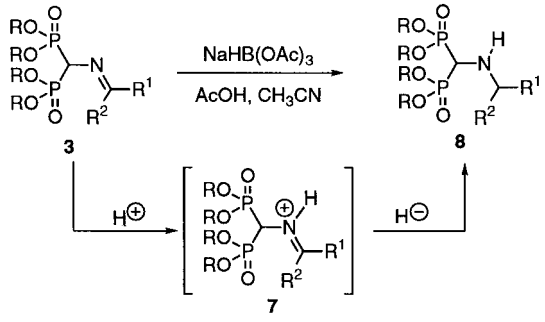
Imines **3** were easily obtained by simple condensation of aminomethyldiphosphonate **6**[9] and aromatic (Table 1, entries 1–3), heteroaromatic (Table 1, entries 4–6), α,β-unsaturated aldehydes (Table 1, entry 7) and ketones such as cycloheptanone, norbornan-2-one (Table 1, entries 8 and 9) and diethyl ketomalonate (Table 1, entry 10) (Scheme 2). Compounds **3** were characterized by their spectroscopic data. Thus, in the ^{1}H NMR spectrum of iminebisphosphonate **3b** the methine proton resonates at δ_H 4.31 ppm as a triplet with coupling constant $^2J_{HP}$=18.3 Hz, and the imine hydrogen appears at δ_H 8.25 ppm also as a triplet ($^4J_{HP}$=4.2 Hz), while the ^{13}C NMR shows a triplet ($^1J_{CP}$=149.5 Hz) corresponding to the methine carbon at δ_C 68.1 ppm and another triplet (δ_C 167.5, $^3J_{CP}$=15.1 Hz) for the imine carbon. The phosphonate group resonates at δ_P 16.0 ppm in the ^{31}P NMR spectrum.

Taking into account the importance of aminoalkylbisphosphonate derivatives as antiinflammatory agents and for the treatment of bone diseases related to calcium metabolism[5,6] we decided to further explore the reactivity of imines **3** with nucleophiles, in order to prepare funtionalized aminoalkylphosphonates with structures similar to compounds **2** (Fig. 1), and, therefore, with potential biological activity on the metabolism of calcium in bones. Although several different nucleophiles including methyl lithium, acetylacetone enolate, piperidine, triethylamine or sodium borohydride were used, no reaction was detected in any case. Therefore, we performed the reduction of some of the imines in the presence of acetic acid with $NaHB(OAc)_3$ prepared in situ,[10] and obtained the expected aminoalkylphosphonates **8** with acceptable yields (see Scheme 3 and Table 2). The structure of compounds **8** were confirmed by means of spectroscopic data. Thus, the ^{1}H NMR spectrum of compound **8a** shows a triplet ($^2J_{HP}$=21.3 Hz) at δ_H 3.25 ppm assignable to the methine proton, and the signal corresponding to the benzylic protons at δ_H 3.93 ppm. The methine carbon resonates at δ_C 53.1 ppm as a triplet ($^1J_{CP}$=146.0 Hz), while the benzylic one appears at 54.6 as a singlet. Formation of aminophosphonates **8** could be explained by initial protonation of the imine moiety of compound **3** followed by nucleophilic addition of the hydride to the iminium salts **7** (see Scheme 3).



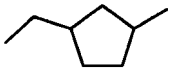
Scheme 2.

Following our synthetic plan to make derivatives of α-aminophosphonates (Scheme 1) we investigated a route towards 2-aza-1,3-butadienes **4** based on the olefination reaction of aldehydes and functionalized imines **3**. In this context, we have previously used β-functionalized imines or



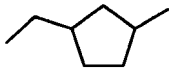
Scheme 3.

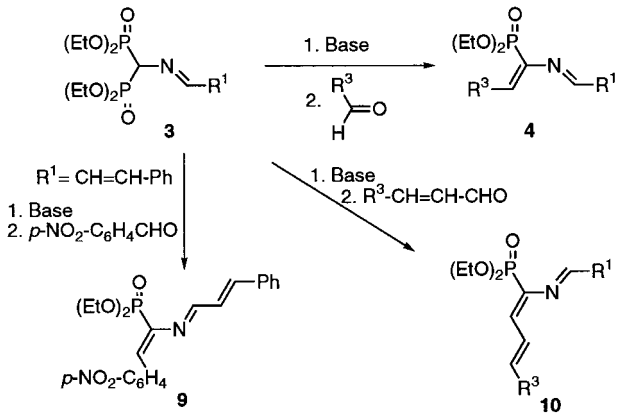
Table 1. Imines **3** obtained

Entry	Compound	R^1	R^2	Yield (%)[a]
1	**3a**	Ph	H	60
2	**3b**	*p*-Me–C_6H_4	H	87
3	**3c**	*o*-(CH_2=CH–CH_2O)C_6H_4	H	70
4	**3d**		H	92
5	**3e**		H	70
6	**3f**		H	65
7	**3g**	(*E*)-Ph–CH=CH	H	70
8	**3h**	–CH_2–CH_2–CH_2–CH_2–CH_2–CH_2–		70
9	**3i**			60
10	**3j**	CO_2Et	CO_2Et	40

[a] Yield of products after flash chromatography.

Table 2. Aminoalkylbisphosphonates **8** obtained

Entry	Compound	R^1	R^2	Yield (%)
1	**8a**	*p*-Me–C_6H_4	H	60
2	**8b**		H	40
3	**8c**	–CH_2–CH_2–CH_2–CH_2–CH_2–CH_2–		71
4	**8d**			67



Scheme 4.

enamines derived from phosphazenes, phosphonium salts, phosphine oxides and phosphonates for the construction of carbon–carbon double bonds in the synthesis of acyclic derivatives such as oximes,[11a,b] allylamines,[11c] hydrazones,[11d] and β-amino functionalized compounds.[11e] Both the synthesis and some reactions of electronically neutral 2-azadienes[12] or electron-rich heterodienes[13] have been reported. However, electron-poor dienes have received much less attention. In fact, azabutadienes of this type were limited to 3- or 4-substituted electron-deficient heterodienes derived from α-[14] or β-amino acids[15] as well as to 4,4-[16] and 3,4-electron-withdrawing substituted 2-azadienes.[15,17] Likewise, we reported the preparation of azadienes substituted with a phosphine oxide group[18] in the 4 position, and while developing this work[19] the synthesis of azadienes substituted with a phosphonyl group[20] in the 4 position was reported elsewhere.

According to this synthetic design, the olefination reaction of imines **3** was initially carried out using several different bases including methyl and butyl lithium, potassium *tert*-butoxide and the superbase *t*-butyl-tris(tetramethylene)-phosphazene (BTPP), but taking into account the partially stabilized nature of the carbanion we reasoned that a weaker base such as cesium carbonate in THF/*i*-PrOH would suffice.[21] In fact, the use of this base provided good yields of the 2-azadienes **4** (Scheme 4 and Table 3) when aliphatic, aromatic or heteroaromatic aldehydes were used, in shorter reaction times and with the advantage that the reaction could be run at room temperature and worked-up in a very easy way. These azadienes **4** were identified by means of spectroscopic data. The most characteristic signal in the ^{1}H NMR spectrum of compound **4ba** is the doublet (δ_H 7.05 ppm, $^2J_{HP}$=16.6 Hz) corresponding to the vinylic proton coupled with the vicinal phosphorus nucleus. According to this coupling constant[22] and the NOE experiments carried out on some of the azadienes, we conclude that only the *E* isomer is formed in the olefination reaction of imines derived from bisphosphonates, since no traces of the *Z* compound are observed.

This methodology can also be applied to the synthesis of 3-azatriene **9** (Scheme 4) when the corresponding α,β-unsaturated imine derived from (*E*)-cinnamaldehyde **3g** was used (Table 4, entry 1). Selective decoupling and

Table 3. 2-Aza-1,3-butadienes **4** obtained

Entry	Compound	R^1	R^3	Base	Yield (%)[a]
1	**4aa**	Ph	Me	MeLi	48
				BuLi	50
				t-BuOK	55
2	**4ab**	Ph	*p*-Me–C_6H_4	BTPP	50
				t-BuOK	55
3	**4ac**	Ph	Ph	BTPP	45
				Cs_2CO_3	65
4	**4ad**	Ph	CO_2Et	BTPP	50
5	**4ba**	*p*-Me-C_6H_4	*p*-Me–C_6H_4	MeLi	47
				Cs_2CO_3	67
6	**4bb**	*p*-Me–C_6H_4	H	BTPP	80[a]
7	**4bc**	*p*-Me–C_6H_4		Cs_2CO_3	50
8	**4bd**	*p*-Me–C_6H_4		Cs_2CO_3	50
9	**4ca**	*o*-(CH_2=CH–CH_2O)C_6H_4	*p*-NO_2–C_6H_4	BuLi	30
				Cs_2CO_3	60
10	**4cb**	*o*-(CH_2=CH–CH_2O)C_6H_4	Me	BuLi	71
11	**4da**		*p*-Me–C_6H_4	Cs_2CO_3	60
12	**4ea**		*p*-Me–C_6H_4	Cs_2CO_3	55
13	**4fa**		Me	BuLi	70

[a] Yield of product without purification.

Table 4. Azatrienes **9** and **10** obtained

Entry	Comp.	R^1	R^3	Base	Yield (%)
1	**9**	–	–	BTPP	59
				Cs_2CO_3	64
2	**10be**	*p*-Me–C_6H_4	Ph	BTPP	40
				Cs_2CO_3	60
3	**10bf**	*p*-Me–C_6H_4	CH_3	BTPP	40
				Cs_2CO_3	70
4	**10eb**		Ph	Cs_2CO_3	50

NOE experiments were carried out on ^{1}H NMR in order to assign the vinylic protons and to establish the stereochemistry of this azatriene. For instance, when selective saturation of the doublet at δ_H 8.4 ppm corresponding to the imine proton in 3-azatriene **9** was performed, NOE effect (32%) was observed for the vinylic proton close to the phenyl group and also for the protons in the phosphonate group (18%).

In a similar way, the preparation of 2-azatrienes **10** by olefination reaction of the imines **3** with crotonaldehyde or cinnamaldehyde (Table 4, entries 2–4) can be performed. The spectrum of 2-azatriene **10bf** shows a multiplet for the vinylic proton close to the methyl group at δ_H 6.06 ppm, a double doublet at δ_H 6.74 ppm with $^3J_{HP}$=18.9 Hz, and $^3J_{HH}$=11.0 Hz, assignable to the proton vicinal to the phosphonate group and another double doublet at δ_H 6.75 ppm ($^3J_{HH}$=23.4 and $^3J_{HH}$=10.5 Hz) corresponding to the middle vinylic proton.

Electron-poor 2-azadienes derived from amino acids have been used in the synthesis of heterocyclic systems through cycloaddition reactions[8,14–17] and, therefore, we hoped that azadienes **4** derived from aminophosphonates would react with dienophiles in inverse demand hetero-Diels–Alder reactions to provide substituted pyridine and related heterocyclic systems. Nevertheless, azadienes **4** did not react with electron-rich dienophiles such as cyclohexanone–pyrrolidine enamine, nor with electron-poor dienophiles including tetracyanoethylene, dimethyl acetylenedicarboxylate and 4-phenyl-1,2,4-triazoline-3,5-dione. Even the $LiClO_4$ promoted intramolecular cycloaddition[12a,15b] reaction on compound **4ca** also failed, showing the remarkable inertness of these azadienes in [4+2] cycloaddition reactions.

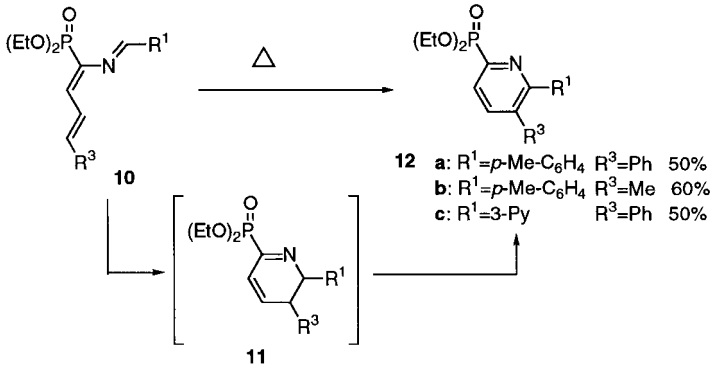
Therefore, we explored the potential utility of azatrienes in intramolecular electrocyclization reactions, since thermal 6π-electrocyclization processes have been already described for azatrienes derived from α-amino acids.[23] Heating 3-azatriene **9** did not produce the heterocyclic compound, but in the case of 2-azatrienes **10** it did eventually provide 2-phosphonylpyridine derivatives **12** with moderate yields (Scheme 5). We would like to note the low value of the coupling constant between the phosphorus and the vicinal proton in the pyridine ring ($^3J_{HP}$=6.5 Hz) compared to the value found in the open chain precursor ($^3J_{HP}$=14–18 Hz). This change is not detected in the ^{13}C NMR spectra, where the coupling constants remain similar to those in the precursor azatrienes. Formation of pyridines **12** can be explained by thermal 6π-electrocyclization of 2-azatrienes **10** followed by aromatization of dihydropyridines **11**, as has been reported for azatrienes derived from α-amino acids.[23a] These results are consistent with thermal rearrangements of 2-azatrienes[24] to obtain pyridine derivatives, while electrocyclizations of 3-azatrienes were performed with more difficulty and required very high temperatures.[25]

In conclusion, we describe here a straightforward method for the synthesis of imines **3** or amines **8** derived from bisphosphonates as well as azadienes **4**, azatrienes **9**, **10** and pyridines **12** derived from aminophosphonates. Aminophosphonates show interesting biological properties[1,3] while aminoalkylphosphonate derivatives have generated great interest in medicinal chemistry as anti-inflammatory agents and for the treatment of bone diseases.[5,6]

Experimental

General

Chemicals were purchased from Aldrich Chemical Company. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with Merck



Scheme 5.

silica gel 60 F_{254} plates. Visualization was accomplished by UV light and $KMnO_4$ solution. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM). Melting points were determined with an Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^1H (300 MHz), ^{13}C (75 MHz) and ^{31}P NMR (120 MHz) spectra were recorded on a Varian UnityPlus 300 MHz spectrometer using $CDCl_3$ solutions with TMS as an internal reference for ^1H and ^{13}C NMR spectra and phosphoric acid (85%) for ^{31}P NMR spectra. Chemical shifts (δ) are reported in ppm and coupling constants (J) are reported in Hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EIMS) on a Hewlett–Packard 5971 spectrometer. Data are reported in the form m/z (intensity relative to base=100). Infrared spectra (IR) were recorded on a Nicolet IRFT Magna 550 spectrometer for neat oils. Peaks are reported in cm^{-1}. Elemental analyses were performed in a LECO CHNS-932 apparatus. Aminomethyldiphosphonate tetraethyl ester **6** was synthesized according to the literature procedure.[9]

General procedure for the preparation of iminophosphonates 3

A carbonyl compound (aldehyde or ketone, about 6 mmol) was added to a solution of an equimolecular amount of aminomethyldiphosphonate tetraethyl ester in dry benzene (20 mL) and the stirred mixture was heated at reflux in a Dean–Stark for 4 h. The solvent was removed at reduced pressure and the crude product was purified by flash chromatography eluting with ethyl acetate to provide the pure compounds as yellow–orange oils.

Tetraethyl (*E*)-*N*-(benzyliden)aminomethyldiphosphonate (3a). Starting from 6.6 mmol of benzaldehyde, 1.5 g (60%) were obtained; ^1H NMR (δ) 8.28 (t, 1H, $^4J_{HP}$=4.2 Hz, CH=N), 7.20–7.84 (m, 5H, Harom), 4.30 (t, 1H, $^2J_{HP}$=18.0 Hz, CHP), 4.20 (m, 8H, 4×CH_2),1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 167.3 (t, $^3J_{CP}$=15.3 Hz, C=N), 135.2 (*C*arom–C), 131.4, 131.2, 128.4, 128.2 and 128.0 (Carom–H), 67.9 (t, $^1J_{CP}$=149, CHP), 63.4, 63.3, 63.2, 63.1 (4×CH_2), 16.2, 16.1 (2×CH_3); ^{31}P NMR (δ) 15.8; IR (NaCl, ν_{max}) 1629 (C=N), 1257 (P=O), 1030 (P–O); EIMS m/z 288 ($M^+-NCC_6H_5$, 100). Anal. Calcd for $C_{16}H_{27}NO_6P_2$: C, 49.10; H, 6.92; N, 3.55. Found: C, 49.20; H, 6.90; N, 3.65.

Tetraethyl (*E*)-*N*-(4-methylbenzyliden)aminomethyldiphosphonate (3b). Starting from 6.2 mmol of *p*-tolualdehyde, 2.2 g (87%) were obtained; ^1H NMR (δ) 8.25 (t, 1H, $^4J_{HP}$=4.2 Hz, CH=N), 7.63 (d, 2H, $^3J_{HH}$=9.1 Hz, Ph–H), 7.18 (d, 2H, $^3J_{HH}$=9.1 Hz, Ph–H), 4.31 (t, 1H, $^2J_{HP}$=18.3 Hz, CHP), 4.20 (m, 8H, 4×CH_2), 2.35 (s, 3H, $PhCH_3$), 1.30 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 167.5 (t, $^3J_{CP}$=15.1 Hz, C=N), 141.9 and 132.9 (*C*arom–C), 129.3 and 128.5 (Carom–H), 68.05 (t, $^1J_{CP}$=149.5 Hz, CHP), 63.6, 63.5, 63.4, 63.3, 63.2 (6×CH_2), 21.5 ($PhCH_3$), 16.4, 16.1 (2×CH_3); ^{31}P NMR (δ) 16.0; IR (NaCl, ν_{max}) 1632 (C=N), 1261 (P=O), 1029 (P–O); EIMS m/z 288 ($M^+-NCC_6H_4CH_3$, 100). Anal. Calcd for $C_{17}H_{29}NO_6P_2$: C, 50.37; H, 7.21; N, 3.46. Found: C, 50.25; H, 7.45; N, 3.50.

Tetraethyl (*E*)-*N*-(2-allyloxybenzyliden)aminomethyldiphosphonate (3c). Starting from 6.4 mmol of 2-allyloxybenzaldehyde, 2 g (70%) were obtained; ^1H NMR (δ) 8.72 (t, 1H, $^4J_{HP}$=4.3 Hz, CH=N), 7.96–6.83 (m, 4H, Ph–H), 6.12–5.91 (m, 1H, CH_2=C*H*), 5.37 (dd, 1H, $^3J_{HH}$=17.2 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=C*Htrans*), 5.26 (dd, 1H, $^3J_{HH}$=10.5 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=C*Hcis*), 4.53 (dd, 2H, $^3J_{HH}$=5.2 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=CH_2), 4.32 (t, 1H, $^2J_{HP}$=18.3 Hz, CHP), 4.17 (m, 8H, 4×OCH_2CH_3), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 163.1 (t, $^3J_{CP}$=15.4 Hz, C=N), 157.6 (*C*arom–C), 132.3 (–*C*H=CH_2), 127.9, 127.0 (Carom–H), 123.6 (*C*arom–C), 120.4 (Carom–H), 117.2 (=CH_2), 111.9 (Carom–H), 68.6 (OCH_2CH=CH_2), 68.1 (t, $^1J_{CP}$=149.6 Hz, CHP), 63.4, 63.3, 63.1, 63.0 (4×OCH_2CH_3), 16.1, 15.9 (2×CH_3); ^{31}P NMR (δ) 15.8; IR (NaCl, ν_{max}) 1623 (C=N), 1300 (P=O), 1023 (P–O); EIMS m/z 447 (M^+, 5). Anal. Calcd for $C_{19}H_{31}NO_7P_2$: C, 51.01; H, 6.98; N, 3.13. Found: C, 51.25; H, 6.80; N, 3.10.

Tetraethyl (*E*)-*N*-(2-pyridylmethyliden)aminomethyldiphosphonate (3d). Starting from 2.5 mmol of 2-pyridinecarbaldehyde, 0.9 g (92%) were obtained; ^1H NMR (δ) 8.33 (t, 1H, $^4J_{HP}$=4.2 Hz, CH=N), 8.57–7.24 (m, 4H, Pyr–H), 4.37 (t, 1H, $^2J_{HP}$=18.0 Hz, CHP), 4.18 (m, 8H, 4×CH_2), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 168.2 (t, $^3J_{CP}$=15.0 Hz, C=N), 153.5 (C_{Pyr}–C), 149.2, 136.4, 125.2, 121.1 (C_{Pyr}–H), 67.9 (t, $^1J_{CP}$=149.0 Hz, CHP), 63.4, 63.3, 63.2, 63.1 (4×CH_2), 16.2, 16.1 (2×CH_3); ^{31}P NMR (δ) 15.3; IR (NaCl, ν_{max}) 1650 (C=N), 1250 (P=O), 1050 (P–O); EIMS m/z 347 ($M^+-OCH_2CH_3$, 3). Anal. Calcd for $C_{15}H_{26}N_2O_6P_2$: C, 45.91; H, 6.68; N, 7.14. Found: C, 46.00; H, 6.60; N, 7.10.

Tetraethyl (*E*)-*N*-(3-pyridylmethyliden)aminomethyldiphosphonate (3e). Starting from 2.5 mmol of 3-pyridincarbaldehyde, 0.5 g (70%) were obtained; ^1H NMR (δ) 8.86 (s, 1H, CH=N_{Pyr}), 8.63 (d, 1H, $^3J_{HH}$=3.3 Hz, Pyr–H), 8.32 (t, 1H, $^4J_{HP}$=4.2 Hz, CH=N), 8.10 (dd, 1H, $^3J_{HH}$=6.0 and $^4J_{HH}$=1.5 Hz, Pyr–H), 7.30 (m, 1H, Pyr–H), 4.30 (t, 1H, $^2J_{HP}$=18.0 Hz, CHP), 4.20 (m, 8H, 4×CH_2), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 164.5 (t, $^3J_{CP}$=15.6 Hz, C=N), 151.8 (C_{Pyr}–N), 149.8 (C_{Pyr}–H), 134.6 (C_{Pyr}–H), 130.7 (C_{Pyr}–C), 123.39 (C_{Pyr}–H), 67.8 (t, $^1J_{CP}$=149.0 Hz, CHP), 63.4, 63.3, 63.2, 63.1 (4×CH_2), 16.2, 16.1 (2×CH_3); ^{31}P NMR (δ) 15.4; IR (NaCl, ν_{max}) 1630 (C=N), 1250 (P=O), 1050 (P–O); EIMS m/z 392 (M^+, 2). Anal. Calcd for $C_{15}H_{26}N_2O_6P_2$: C, 45.91; H, 6.68; N, 7.14. Found: C, 46.10; H, 6.55; N, 7.05.

Tetraethyl (*E*)-*N*-(2-thiophenemethyliden)aminomethyldiphosphonate (3f). Starting from 2.5 mmol of 2-thiophenylcarbaldehyde, 0.5 g (70%) were obtained; ^1H NMR (δ) 8.38 (t, 1H, $^4J_{HP}$=4.1 Hz, CH=N), 7.79–7.01 (m, 3H, TioPh–H), 4.34 (t, 1H, $^2J_{HP}$=18.5 Hz, CHP), 4.20 (m, 8H, 4×CH_2), 1.28 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 160.3 (t, $^3J_{CP}$=15.8 Hz, C=N), 134.3 (C_{Thio}–C), 131.9, 130.2, 127.4 (C_{Thio}–H), 67.2 (t, $^1J_{CP}$=148.6 Hz, CHP), 63.4, 63.4, 63.2, 63.1 (4×CH_2), 16.2, 16.1 (CH_3); ^{31}P NMR (δ) 15.4; IR (NaCl, ν_{max}) 1630 (C=N), 1250 (P=O), 1050 (P–O); EIMS m/z 288 ($M^+-NCC_4H_3S$, 100). Anal. Calcd for $C_{14}H_{25}NO_6P_2S$: C, 42.32; H, 6.34; N, 3.52; S, 8.07. Found: C, 42.25; H, 6.25; N, 3.45; S, 8.00.

Tetraethyl (*E*)-*N*-(3-phenylprop-2-enyliden)aminomethyldiphosphonate (3g). Starting from 2.4 mmol of cinnamaldehyde, 0.7 g (70%) were obtained; ^{1}H NMR (δ) 8.00 (m, 1H, CH=N), 6.97–7.44 (m, 7H, Ph–H, –C*H*=C*H*–), 4.25 (m, 9H, 4×CH_2, CHP), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 169.2 (t, $^3J_{CP}$=15.4 Hz, C=N), 143.8 (Ph–CH=*C*H), 135.2 (Ph–*C*H), 129.6–127.5 (Carom), 67.0 (t, $^1J_{CP}$=149.5 Hz, CHP), 63.2 (CH_2), 16.1 (CH_3); ^{31}P NMR (δ) 16.0; IR (NaCl, ν_{max}) 1633 (C=N), 1255 (P=O), 1036 (P–O); EIMS *m/z* 314 (M^+−Ph–CH=CH, 1). Anal. Calcd for $C_{18}H_{29}NO_6P_2$: C, 51.80; H, 7.00; N, 3.36. Found: C, 51.70; H, 6.90; N, 3.45.

Tetraethyl *N*-(cycloheptyliden)aminomethyldiphosphonate (3h). Starting from 3.6 mmol of cycloheptanone, 1 g (70%) was obtained; ^{1}H NMR (δ) 4.55 (t, 1H, $^2J_{HP}$= 18.6 Hz, CHP), 4.11 (m, 8H, 4×OCH_2), 2.50 (m, 4H, 2×CH_2), 1.51 (m, 8H, 4×CH_2), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 182.1 (t, $^3J_{CP}$=15.1 Hz, C=N), 63.3, 63.2, 62.9, 62.8 (4×OCH_2), 58.8 (t, $^1J_{CP}$=153.5 Hz, CHP), 53.5, 48.8, 31.4, 29.6, 26.4, 24.3 (6×CH_2), 16.2, 16.1, 15.8, 15.7 (4×CH_3); ^{31}P NMR (δ) 16.9; IR (NaCl, ν_{max}) 1633 (C=N), 1248 (P=O), 1029 (P–O); EIMS *m/z* 397 (M^+, 2). Anal. Calcd for $C_{16}H_{33}NO_6P_2$: C, 48.36; H, 8.37; N, 3.52. Found: 48.50; H, 8.25; N, 3.45.

Tetraethyl *N*-(norborn-2-yliden)aminomethyldiphosphonate (3i). Starting from 3.3 mmol of norbornan-2-one, 0.8 g (60%) were obtained; ^{1}H NMR (δ) 4.50 (t, 1H, $^2J_{HP}$=18.5 Hz, CHP), 4.11 (m, 8H, 4×OCH_2), 2.18–1.66 (m, 10H, 4×CH_2, 2×CH_{norbor}), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 187.2 (t, $^3J_{CP}$=14.6 Hz, C=N), 62.6, 62.5, 62.4, 62.3 (4×OCH_2), 56.3 (t, $^1J_{CP}$=152.3 Hz, CHP), 42.8 (CH), 32.9 (CH_2), 32.5 (CH_2), 30.5 (CH), 21.4, 19.4 (2×CH_2), 16.1, 15.8 (2×CH_3); ^{31}P NMR (δ) 16.8; IR (NaCl, ν_{max}) 1666 (C=N), 1255 (P=O), 1023 (P–O); EIMS *m/z* 395 (M^+, 8). Anal. Calcd for $C_{16}H_{31}NO_6P_2$: C, 48.61; H, 7.90; N, 3.54. Found: 48.70; H, 7.75; N, 3.45.

Tetraethyl *N*-[bis(ethoxycarbonyl)methyliden]aminomethyldiphosphonate (3j). Diethyl ketomalonate (0.56 g, 3.23 mmol) and molecular sieve (0.4 nm) were added to a solution of aminomethyldiphosphonate tetraethyl ester (0.98 g, 3.23 mmol) in dry dichloromethane (10 mL) and the stirred mixture was heated at reflux for 12 h. The solvent was removed at reduced pressure and the crude product was purified by flash chromatography eluting with ethyl acetate to provide 1.5 g (40%) of the compound as a yellow oil; ^{1}H NMR (δ) 5.20 (t, 1H, $^2J_{HP}$=17.1 Hz, CHP), 4.33 (m, 12H, 6×CH_2), 1.30 (m, 18H, 6×CH_3); ^{13}C NMR (δ) 168.4 (CO_2Et), 168.1 (C=N), 64.1, 63.8, 63.7, 63.3, 62.6, 62.5 (6×CH_2), 47.1 (t, $^1J_{CP}$=150.0 Hz, CHP), 16.3, 16.2, 13.9, 13.8 (4×CH_3); ^{31}P NMR (δ) 12.9; IR (NaCl, ν_{max}) 1739 (C=N), 1248 (P=O), 1023 (P–O); EIMS *m/z* 288 (M^+−$NCC_6H_{10}O_4$, 100). Anal. Calcd for $C_{16}H_{31}NO_{10}P_2$: C, 41.83; H, 6.80; N, 3.05. Found: C, 42.00; H, 6.70; N, 3.10.

Synthesis of aminoalkylphosphonates 8

General procedure: $NaBH_4$ (3–4 mmol) was added over glacial acetic acid (3 mL) at about 15°C under inert atmosphere and the resulting mixture was stirred at room temperature until evolving of gas (H_2) ceased thus ensuring that $NaBH(OAc)_3$ formation had taken place. Then dry acetonitrile (5 mL) was added, the reaction vessel cooled to 0°C, the imine **3** (1–1.5 mmol) added and the reaction stirred for 1 h at 0°C. Acetic acid and acetonitrile were removed at reduced pressure and the crude product was purified by flash chromatography eluting with ethyl acetate to provide the pure compounds as yellow–orange oils (see Table 4).

Tetraethyl *N*-(4-methylbenzyl)aminomethyldiphosphonate (8a). According to general procedure, imine **3b** (0.5 g, 1.23 mmol), $NaBH_4$ (0.13 g, 3.42 mmol), glacial acetic acid (3 mL) and dry acetonitrile (5 mL) were used. The crude residue was purified by flash chromatography to yield 0.3 g (60%) of **8a**; ^{1}H NMR (δ) 7.18 (d, 2H, $^3J_{HH}$=7.9 Hz, Ph–H), 7.06 (d, 2H, $^3J_{HH}$=7.9 Hz, Ph–H), 4.15 (m, 8H, 4×OCH_2), 3.93 (s, 2H, NCH_2), 3.25 (t, 1H, $^2J_{HP}$=21.3 Hz, CHP), 2.27 (s, 3H, $PhCH_3$), 2.12 (s, 1H, NH), 1.28 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 136.7, 135.4 (2×*C*arom–C), 128.7–128.3 (Carom–H), 62.4, 54.6 (2×CH_2), 53.1 (t, $^1J_{CP}$=146.0 Hz, CHP), 20.7 ($PhCH_3$), 16.1 (CH_3); ^{31}P NMR (δ) 20.0; IR (NaCl, ν_{max}) 3489 (NH), 1248 (P=O), 1029 (P–O); EIMS *m/z* 288 (M^+−CH_3PhCH_2NH, 100). Anal. Calcd for $C_{17}H_{31}NO_6P_2$: C, 50.12; H, 7.67; N, 3.44. Found: C, 50.25; H, 7.75; N, 3.55.

Tetraethyl *N*-(2-pyridylmethyl)aminomethyldiphosphonate (8b). According to general procedure, imine **3d** (0.5 g, 1.27 mmol), $NaBH_4$ (0.14 g, 3.68 mmol), glacial acetic acid (3 mL) and dry acetonitrile (5 mL) were used. The crude residue was purified by flash chromatography to yield 0.2 g (40%) of **8b**; ^{1}H NMR (δ) 8.48 (d, 1H, $^3J_{HH}$=4.8 Hz, Pyr–H), 7.60 (t, 1H, $^3J_{HH}$=5.0 Hz, Pyr–H), 7.35 (d, 1H, $^3J_{HH}$=7.8 Hz, Pyr–H), 7.10 (t, 1H, $^3J_{HH}$= 6.1 Hz, Pyr–H), 4.15 (m, 8H, 4×CH_2), 4.11 (s, 2H, NCH_2), 3.40 (t, 1H, $^2J_{HP}$=21.3 Hz, CHP), 2.85 (br s, 1H, NH), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 158.6 (C_{Pyr}–C), 148.8, 136.1, 122.1, 121.8 (C_{Pyr}–H), 62.4, 54.6 (2×CH_2), 53.1 (t, $^1J_{CP}$=146.0 Hz, CHP), 16.1 (CH_3); ^{31}P NMR (δ) 19.8; IR (NaCl, ν_{max}) 3456 (NH), 1235 (P=O), 1016 (P–O); EIMS *m/z* 394 (M^+, 2). Anal. Calcd for $C_{15}H_{28}N_2O_6P_2$: C, 45.69; H, 7.16; N, 7.10. Found: C, 45.55; H, 7.10; N, 7.15.

Tetraethyl *N*-(cycloheptyl)aminomethyldiphosphonate (8c). According to general procedure, imine **3h** (0.49 g, 1.23 mmol), $NaBH_4$ (0.13 g, 3.42 mmol), glacial acetic acid (3 mL) and dry acetonitrile (5 mL) were used. The crude residue was purified by flash chromatography to yield 0.35 g (71%) of **8c**; ^{1}H NMR (δ) 4.11 (m, 8H, 4×OCH_2), 3.30 (t, 1H, $^2J_{HP}$=21.9 Hz, CHP), 2.91 (m, 1H, C*H*NH), 2.10 (br s, 1H, NH), 1.72 (m, 4H, 2×CH_2), 1.52 (m, 8H, 4×CH_2), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 62.8, 62.2 (2×OCH_2), 57.7 (CH–NH), 51.1 (t, $^1J_{CP}$=145.5 Hz, CHP), 33.8, 27.9, 23.4 (3×CH_2), 15.9 (CH_3); ^{31}P NMR (δ) 20.1; IR (NaCl, ν_{max}) 3482 (NH), 1241 (P=O), 1023 (P–O); EIMS *m/z* 399 (M^+, 1). Anal. Calcd for $C_{16}H_{35}NO_6P_2$: C, 48.12; H, 8.83; N, 3.51. Found: C, 48.00; H, 8.80; N, 3.50.

Tetraethyl *N*-(norborn-2-yl)aminomethyldiphosphonate (8d). According to general procedure, imine **3i** (0.45 g,

1.23 mmol), $NaBH_4$ (0.14 g, 3.68 mmol), glacial acetic acid (3 mL) and dry acetonitrile (5 mL) were used. The crude residue was purified by flash chromatography to yield 0.3 g (67%) of **8d**; ^{1}H NMR (δ) 4.11 (m, 8H, 4×OCH_2), 3.28 (m, C*H*NH), 3.20 (t, 1H, $^2J_{HP}$=21.6 Hz, CHP), 1.66–2.18 (m, 10H, 4×CH_2, 2×CH_{norbor}), 1.27 (m, 12H, 4×CH_3); ^{13}C NMR (δ) 62.9, 62.5 (OCH_2), 58.9 (CHN), 52.7 (t, $^1J_{CP}$=145.0 Hz, CHP), 39.5 (CH), 37.7, 36.8 (2×CH_2), 36.6 (CH), 29.9, 20.3 (2×CH_2), 16.1 (CH_3); ^{31}P NMR (δ) 20.4; IR (NaCl, ν_{max}) 3469 (NH), 1241 (P=O), 1016 (P–O); EIMS *m/z* 397 (M^+, 1). Anal. Calcd for $C_{16}H_{33}NO_6P_2$: C, 48.36; H, 8.37; N, 3.52. Found: C, 48.25; H, 8.40; N, 3.55.

Synthesis of azadienes 4 and azatrienes 9 and 10

General procedure A: Base (MeLi, BuLi, K^{t}BuO or BTPP) (about 6 mmol) was added to a solution of an equimolecular amount of imine **3** in dry THF (10 mL) at −78°C. After 1 h the aldehyde was added, the mixture was allowed to warm to room temperature and stirred overnight. The solvent was removed at reduced pressure and the crude product was purified by flash chromatography eluting with the appropriate solvent to provide the pure compounds as yellow–orange oils (see Table 2).

Synthesis of azadienes 4 and azatrienes 9 and 10

General procedure B: Excess of Cs_2CO_3 (about 5 mmol) was added to a solution of imine **3** (about 4 mmol) and aldehyde (about 4 mmol) in THF/*i*-PrOH (4:1, 10 mL) at room temperature. The mixture was stirred for 1 to 4 days. The solvent was removed at reduced pressure and then dichloromethane was added, the organic layer washed with water (3×25 mL), dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography eluting with the appropriate solvent to provide the pure compounds as yellow–orange oils (see Table 2).

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-4-methyl-1-phenyl-2-azabuta-1,3-diene 4aa. According to general procedure A, imine **3a** (2.28 g, 5.8 mmol), acetaldehyde (0.33 mL, 5.8 mmol) and an equimolecular amount of base (MeLi, BuLi and K^{t}BuO) were used (see Table 2). The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 2:1 to yield 2.28 g (48%, from MeLi), 2.35 g (50%, from BuLi) and 2.45 g (55%, from K^{t}BuO) of **4aa** as a pale yellow oil; ^{1}H NMR (δ) 8.45 (s, 1H, CH=N), 7.22–7.83 (m, 5H, Ph–H), 6.42 (dq, 1H, $^3J_{HH}$=7.0 Hz, $^3J_{HP}$=15.3 Hz, CH=C), 4.10 (q, 4H, $^3J_{HH}$=7.1 Hz, 2×CH_2), 1.89 (dd, 3H, $^3J_{HH}$=7.0 Hz, $^4J_{HP}$=3.2 Hz, CH_3), 1.27 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 161.6 (d, $^3J_{CP}$=9.5 Hz, C=N), 139.2 (d, $^1J_{CP}$=181.8 Hz, C=*C*P), 136.1 (*C*arom–C), 134.3 (d, $^2J_{CP}$=24.2 Hz, *C*=CP), 131.2, 128.7, 128.4 (Carom–H), 62.0 (CH_2), 16.2 (CH_3), 12.8 (d, $^3J_{CP}$=14.1 Hz, CH_3); ^{31}P NMR (δ) 13.5; IR (NaCl, ν_{max}) 1622 (C=N), 1248 (P=O), 1023 (P–O); EIMS *m/z* 281 (M^+, 100). Anal. Calcd for $C_{14}H_{20}NO_3P$: C, 59.78; H, 7.17; N, 4.98. Found: 59.85; H, 7.05; N, 5.05.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-4-(4-methylphenyl)-1-phenyl-2-azabuta-1,3-diene 4ab. According to general procedure A, imine **3a** (1 g, 2.5 mmol), *p*-tolualdehyde (0.31 mL, 2.5 mmol) and an equimolecular amount of base (BTPP and K^{t}BuO) were used (see Table 2). The crude residue was purified by flash chromatography eluting with hexane to yield 0.4 g (50%, from BTPP) and 2.45 g (0.44 g, from K^{t}BuO) of **4ab** as a pale yellow oil; ^{1}H NMR (δ) 8.60 (s, 1H, CH=N), 7.07–7.80 (m, 9H, Ph–H), 7.05 (d, 1H, $^3J_{HP}$=16.8 Hz, CH=C), 4.15 (m, 4H, 2×CH_2), 2.27 (s, 3H, $PhCH_3$), 1.26 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 162.1 (d, $^3J_{CP}$=9.6 Hz, C=N), 138.7 (*C*arom–C), 135.8 (d, $^1J_{CP}$=175.7 Hz, C=*C*P), 134.3, 136.1 (*C*arom–C), 132.4 (d, $^2J_{CP}$=22.2 Hz, *C*=CP), 131.7 (d, $^3J_{CP}$=19.1 Hz, *C*arom–C), 131.3, 131.2, 128.8, 128.1, 128.6 (Carom–H), 62.0 (CH_2), 21.1 ($PhCH_3$), 16.1 (CH_3); ^{31}P NMR (δ) 14.4; IR (NaCl, ν_{max}) 1612 (C=N), 1245 (P=O), 1028 (P–O); EIMS *m/z* 357 (M^+, 100). Anal. Calcd for $C_{20}H_{24}NO_3P$: C, 67.22; H, 6.77; N, 3.92. Found: C, 67.15; H, 6.8; N, 3.85.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1,4-diphenyl-2-azabuta-1,3-diene 4ac. According to general procedure A, imine **3a** (2.6 g, 6.7 mmol), benzaldehyde (0.68 mL, 6.7 mmol) and BTPP (2.1 mL, 6.87 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 15:1 to yield 1 g (45%) of **4ac**. According to general procedure B, imine **3a** (2.5 g, 6.4 mmol), benzaldehyde (0.7 mL, 7 mmol) and Cs_2CO_3 (2.7 g, 8.3 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 1.4 g (65%) of **4ac** as a pale yellow oil; ^{1}H NMR (δ) 8.58 (s, 1H, CH=N), 7.20–7.80 (m, 10H, Ph–H), 7.01 (d, 1H, $^3J_{HP}$=16.8 Hz, CH=C), 4.15 (m, 4H, 2×CH_2), 1.25 (t, 6H, $^3J_{HH}$=7.1 Hz, 2×CH_3); ^{13}C NMR (δ) 162.6 (d, $^3J_{CP}$=9.8 Hz, C=N), 137.0 (d, $^1J_{CP}$=175.4 Hz, C=*C*P), 134.6 (d, $^3J_{CP}$=19.1 Hz, *C*arom–C), 132.4 (d, $^2J_{CP}$=21.6 Hz, *C*=CP), 132.1–128.0 (Carom), 61.9 (CH_2), 16.1 (CH_3); ^{31}P NMR (δ) 14.0; IR (NaCl, ν_{max}) 1619 (C=N), 1261 (P=O), 1035 (P–O); EIMS *m/z* 342 (M^+-1, 100). Anal. Calcd for $C_{19}H_{22}NO_3P$: C, 66.46; H, 6.46; N, 4.08. Found: C, 66.55; H, 6.35; N, 4.15.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1-phenyl-4-(ethoxycarbonyl)-2-azabuta-1,3-diene 4ad. According to general procedure A, imine **3a** (1.7 g, 4.3 mmol), ethyl glioxalate (0.46 mL, 4.3 mmol) and BTPP (1.32 mL, 4.3 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 5:1 to yield 0.7 g (50%) of **4ad** as a pale yellow oil; ^{1}H NMR (δ) 8.15 (s, 1H, CH=N), 7.25–7.82 (m, 5H, Ph–H), 6.03 (d, 1H, $^3J_{HP}$=18.2 Hz, CH=C), 4.20 (m, 4H, 2×CH_2), 4.09 (m, 2H, CH_2), 1.27 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3), 1.10 (t, 3H, $^3J_{HH}$=6.9 Hz, CH_3); ^{13}C NMR (δ) 164.3 (d, $^2J_{CP}$=24.6 Hz, *C*=CP), 162.5 (d, $^3J_{CP}$=11.6 Hz, C=N), 154.6 (d, $^1J_{CP}$=109.3 Hz, C=*C*P), 134.9 (*C*arom–C), 128.6–130.4 (Carom), 63.3, 60.3 (CH_2), 16.1, 13.9 (2×CH_3); ^{31}P NMR (δ) 9.4; IR (NaCl, ν_{max}) 1646 (C=N), 1268 (P=O), 1023 (P–O); EIMS *m/z* 339 (M^+, 1). Anal. Calcd for $C_{16}H_{22}NO_5P$: C, 56.63; H, 6.54; N, 4.13. Found: C, 56.60; H, 6.45; N, 4.10.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1,4-bis(4-methylphenyl)-2-azabuta-1,3-diene 4ba. According to general procedure A, imine **3b** (2 g, 5 mmol), *p*-tolualdehyde (0.6 mL, 5 mmol) and MeLi (1.6 M, 3.2 mL) were used. The crude residue was purified by flash chromatography eluting with

hexane/ethyl acetate 15:1 to yield 0.87 g (47%) of **4ba**. According to general procedure B, imine **3b** (1.7 g, 4.2 mmol), *p*-tolualdehyde (0.5 mL, 4.5 mmol) and Cs_2CO_3 (1.8 g, 5.4 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 1.07 g (67%) of **4ba** as a pale yellow oil; ^{1}H NMR (δ) 8.56 (s, 1H, CH=N), 7.09–7.70 (m, 8H, Ph–H), 7.05 (d, 1H, $^3J_{HP}$=16.6 Hz, CH=C), 4.11 (m, 4H, 2×CH_2), 2.35 (s, 3H, $PhCH_3$), 2.26 (s, 3H, $PhCH_3$), 1.26 (t, 6H, $^3J_{HH}$=7.1 Hz, 2×CH_3); ^{13}C NMR (δ) 162.1 (d, $^3J_{CP}$=9.6 Hz, C=N), 138.7, 142.1 (*C*arom–C), 136.2 (d, $^1J_{CP}$=175.2 Hz, C=*C*P), 133.7 (*C*arom–C), 132.6 (d, $^2J_{CP}$=22.7 Hz, *C*=CP), 131.9 (d, $^3J_{CP}$=19.1 Hz, *C*arom–C), 131.3, 129.4, 128.9, 128.7 (Carom–H), 62.1 (CH_2), 21.5, 21.3 (2×$PhCH_3$), 16.2 (CH_3); ^{31}P NMR (δ) 14.3; IR (NaCl, ν_{max}) 1608 (C=N), 1247 (P=O), 1023 (P–O); EIMS *m*/*z* 371 (M^+, 100). Anal. Calcd for $C_{21}H_{26}NO_3P$: C, 67.91; H, 7.06; N, 3.77. Found: C, 68.05; H, 7.10; N, 3.80.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1-(4-methylphenyl)-2-azabuta-1,3-diene 4bb. According to general procedure A, formaldehyde was bubbled into the solution of imine **3b** (0.95 g, 2.42 mmol) and BTPP (0.74 mL, 2.42 mmol). The crude (0.5 g, 80%) could not be purified by crystallization, by flash chromatography or distillation and was used as obtained; ^{1}H NMR (δ) 8.25 (s, 1H, CH=N), 7.63 (d, 2H, $^3J_{HH}$=8.1 Hz, Ph–H), 7.17 (d, 2H, $^3J_{HH}$=7.8 Hz, Ph–H), 5.38 (d, 1H, $^3J_{HP}$=14.7 Hz, CH=C*cis*), 5.52 (d, 1H, $^3J_{HP}$=39.3 Hz, CH=C*trans*), 4.10 (m, 4H, 2×CH_2), 2.35 (s, 3H, $PhCH_3$), 1.26 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 161.3 (d, $^3J_{CP}$=12.5 Hz, C=N), 150.1 (d, $^1J_{CP}$=193.8 Hz, C=*C*P), 141.9, 132.8 (*C*arom–C), 129.1, 128.5 (Carom–H), 115.0 (d, $^2J_{CP}$=19.6 Hz, *C*=CP), 62.0 (CH_2), 21.5 ($PhCH_3$), 16.2 (CH_3); ^{31}P NMR (δ) 12.1; IR (NaCl, ν_{max}) 1659 (C=N), 1235 (P=O), 1069 (P–O); EIMS *m*/*z* 281 (M^+, 100). Anal. Calcd for $C_{14}H_{20}NO_3P$: C, 59.78; H, 7.17; N, 4.98. Found: C, 59.85; H, 7.20; N, 5.05.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1-(4-methylphenyl)-4-(2-pyridyl)-2-azabuta-1,3-diene 4bc. According to general procedure B, imine **3b** (1.3 g, 3.3 mmol), 2-pyridinecarbaldehyde (0.3 mL, 3.6 mmol) and Cs_2CO_3 (1.37 g, 4.3 mmol) were used. The oily crude (0.4 g, 50%) could not be purified by crystallization, by flash chromatography or distillation and was used as obtained; ^{1}H NMR (δ) 8.56 (br s, 1H, CH=N_{Pyr}), 8.36 (d, 1H, $^3J_{HH}$=3.1 Hz, Pyr–H), 7.80–7.23 (m, 5H, Ph–H, Pyr–H), 7.10 (m, 1H, Pyr–H), 7.03 (d, 1H $^3J_{HP}$=16.8 Hz, CH=C), 4.14 (m, 4H, 2×CH_2), 2.37 (s, 3H, $PhCH_3$), 1.27 (m, 6H, 2×CH_3); ^{13}C NMR (δ) 158.2 (d, $^3J_{CP}$=22.1 Hz, C=N), 148.7, 147.7 (C_{Pyr}–H), 145.3 (C_{Pyr}–C), 138.1 (d, $^1J_{CP}$=166.2 Hz, C=*C*P), 135.3 (*C*arom–C), 130.9–126.3 (Carom–H), 122.2, 119.1 (C_{Pyr}–H), 115.3 (d, $^2J_{CP}$=15.6 Hz, *C*=CP), 62.5 (CH_2), 21.5 ($PhCH_3$), 16.2 (CH_3); ^{31}P NMR (δ) 12.5; IR (NaCl, ν_{max}) 1640 (C=N), 1202 (P=O), 1036 (P–O); EIMS *m*/*z* 256 (M^+-CH_3–Ph–CH, 100). Anal. Calcd for $C_{19}H_{23}N_2O_3P$: C, 63.68; H, 6.47; N, 7.82. Found: C, 63.60; H, 6.55; N, 7.90.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1-(4-methylphenyl)-4-(3-pyridyl)-2-azabuta-1,3-diene 4bd. According to general procedure B, imine **3b** (1.3 g, 3.3 mmol), 3-pyridincarbaldehyde (0.3 mL, 3.6 mmol) and Cs_2CO_3 (1.37 g, 4.3 mmol) were used. The crude residue was purified by flash chromatography in alumina eluting with hexane/ethyl acetate 3:1 to yield 0.4 g (50%) of **4bd** as a pale yellow oil; ^{1}H NMR (δ) 8.94 (s, 1H, Pyr–H), 8.56 (s, 1H, CH=N), 8.42 (d, 1H, $^3J_{HH}$=4.8 Hz, Pyr–H), 8.05 (d, 1H, $^3J_{HH}$=8.1 Hz, Pyr–H), 7.80–7.18 (m, 4H, Ph–H), 7.10 (m, 1H, Pyr–H), 7.03 (d, 1H, $^3J_{HP}$=16.8 Hz, CH=C) 4.14 (m, 4H, 2×CH_2), 2.37 (s, 3H, $PhCH_3$), 1.27 (t, 6H, $^3J_{HH}$=7.1 Hz, 2×CH_3); ^{13}C NMR (δ) 163.2 (d, $^3J_{CP}$=9.5 Hz, C=N), 151.8 (C_{Pyr}), 148.7 (C_{Pyr}), 142.6 (*C*arom–C), 138.2 (C_{Pyr}), 137.9 (d, $^1J_{CP}$=167.2 Hz, C=*C*P), 133.3 (*C*arom–C), 130.9–127.3 (Carom–H), 123.1 (C_{Pyr}–H), 115.3 (d, $^2J_{CP}$= 18.6 Hz, *C*=CP), 62.5 (CH_2), 21.5 ($PhCH_3$), 16.2 (CH_3); ^{31}P NMR (δ) 13.0; IR (NaCl, ν_{max}) 1659 (C=N), 1427 (P=O), 1202 (P–O); EIMS *m*/*z* 357 (M^+, 50). Anal. Calcd for $C_{19}H_{23}N_2O_3P$: C, 63.68; H, 6.47; N, 7.82. Found: C, 63.75; H, 6.50; N, 7.85.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-4-(4-nitrophenyl)-1-(2-allyloxyphenyl)-2-azabuta-1,3-diene 4ca. According to general procedure A, imine **3c** (2.64 g, 5.91 mmol), *p*-nitrobenzaldehyde (0.91 g, 6 mmol) and BuLi (1.6 M, 3.8 mL) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 15:1 to yield 0.79 g (30%) of **4ca**. According to general procedure B, imine **3c** (2.7 g, 6.04 mmol), *p*-nitrobenzaldehyde (0.94 g, 6.2 mmol) and Cs_2CO_3 (2.02 g, 6.2 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 1.61 g (60%) of **4ca** as a pale yellow oil; ^{1}H NMR (δ) 8.50 (s, 1H, CH=N), 7.10–8.00 (m, 8H, Ph–H), 7.05 (d, 1H, $^3J_{HP}$=16.8 Hz, CH=CP), 6.00–6.10 (m, 1H, CH_2=C*H*), 5.42 (dd, 1H, $^3J_{HH}$=17.2 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=C*Htrans*), 5.30 (dd, 1H, $^3J_{HH}$=10.5 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=C*Hcis*), 4.60 (dd, 2H, $^3J_{HH}$=5.1 Hz, $^4J_{HH}$=1.3 Hz, O*C*H_2CH=CH_2), 4.20 (q, 4H, $^3J_{HH}$=7.2 Hz, 2×O*C*H_2CH_3), 1.26 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 159.9 (d, $^3J_{CP}$=9.0 Hz, C=N), 159.1 (Carom–O), 142.7 (d, $^1J_{CP}$=176.5 Hz, C=*C*P), 141.1 (Carom–NO_2), 133.6 (–*C*H=CH_2), 128.5 (d, $^2J_{CP}$=19.1 Hz, *C*=CP), 131.5–121.2 (Carom), 117.7 (=CH_2), 69.5 (O*C*H_2CH=CH_2), 62.5 (O*C*H_2CH_2), 16.2 (CH_3); ^{31}P NMR (δ) 12.6; IR (NaCl, ν_{max}) 1595 (C=N), 1534 (NO_2), 1242 (P=O), 1016 (P–O); EIMS *m*/*z* 414 (M^+, 100). Anal. Calcd for $C_{22}H_{25}N_2O_6P$: C, 59.46; H, 5.67; N, 6.30. Found: C, 59.35; H, 5.75; N, 6.25.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1-(2-allyloxyphenyl)-2-azapenta-1,3-diene 4cb. According to general procedure A, imine **3c** (1.2 g, 2.68 mmol), acetaldehyde (0.15 mL, 2.7 mmol) and BuLi (1.6 M, 1.7 mL) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 2:1 to yield 0.64 g (71%) of **4cb** as a pale yellow oil; ^{1}H NMR (δ) 8.50 (s, 1H, CH=N), 7.40–6.85 (m, 4H, Ph–H), 6.40 (dq, 1H, $^3J_{HH}$=7.0 Hz, $^4J_{HP}$=15.5 Hz, CH=CP), 5.98–6.03 (m, 1H, CH_2=C*H*), 5.35 (dd, 1H, $^3J_{HH}$=17.2 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=C*H-trans*), 5.24 (dd, 1H, $^3J_{HH}$=10.5 Hz, $^4J_{HH}$=1.3 Hz, OCH_2CH=C*Hcis*), 4.54 (dd, 2H, $^3J_{HH}$=5.2 Hz, $^4J_{HH}$= 1.3 Hz, O*C*H_2CH=CH_2), 4.07 (q, 4H, $^3J_{HH}$=7.0 Hz, 2×O*C*H_2CH_3), 1.87 (dd, 3H, $^3J_{HH}$=7.0 Hz, $^3J_{HP}$=3.2 Hz, =CHC*H*$_3$), 1.25 (t, 6H, $^3J_{HH}$=7.1 Hz, 2×CH_2C*H*$_3$); ^{13}C NMR (δ) 158.0 (*C*arom–O), 157.5 (d, $^3J_{CP}$=9.6 Hz,

C═N), 139.2 (d, $^{1}J_{CP}$=181.3 Hz, C═*C*P), 133.5 (d, $^{2}J_{CP}$=22.2 Hz, *C*═CP), 132.3, 132.2 (Carom, –*C*H═CH_2), 126.6, 124.6, 120.4 (Carom), 116.8 (═CH_2), 111.9 (Carom), 68.4 (O*C*H_2CH═CH_2), 61.5 (O*C*$H_2$$CH_2$), 15.9 ($CH_3$), 12.5 (d, $^{3}J_{CP}$=14.6 Hz, CH_3); ^{31}P NMR (δ) 13.9; IR (NaCl, ν_{max}) 1598 (C═N), 1246 (P═O), 1023 (P–O); EIMS *m/z* 337 (M^+, 18). Anal. Calcd for $C_{17}H_{24}NO_4P$: C, 60.53; H, 7.17; N, 4.15. Found: C, 60.60; H, 7.10; N, 4.10.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-4-(4-methylphenyl)-1-(2-pyridyl)-2-azabuta-1,3-diene 4da. According to general procedure B, imine **3d** (0.9 g, 2.29 mmol), *p*-tolualdehyde (0.3 mL, 2.5 mmol) and Cs_2CO_3 (0.96 g, 2.94 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 0.49 g (60%) of **4da** as a yellow–orange oil; ^{1}H NMR (δ) 8.68 (s, 1H, CH═N), 8.66 (br d, 1H, $^{3}J_{HH}$=4.8 Hz, Pyr–H), 8.11 (d, 1H, $^{3}J_{HH}$=7.9 Hz, Pyr–H), 7.76 (bt, 1H, $^{3}J_{HH}$=7.7 Hz, Pyr–H), 7.62 (d, 2H, $^{3}J_{HH}$=8.1 Hz, Ph–H), 7.32 (dd, 1H, $^{3}J_{HH}$=7.4 Hz, $^{3}J_{HH}$=4.8 Hz, Pyr–H), 7.17 (d, 1H, $^{3}J_{HP}$=16.5 Hz, CH═CP), 7.11 (d, 2H, $^{3}J_{HH}$=8.4 Hz, Ph–H), 4.15 (m, 4H, 2×CH_2), 2.29 (s, 3H, PhCH_3), 1.27 (t, 6H, $^{3}J_{HH}$=7.2 Hz, 2×CH_2CH_3); ^{13}C NMR (δ) 162.8 (d, $^{3}J_{CP}$=9.0 Hz, C═N), 149.7 (C_{Pyr}–H), 139.3 (*C*arom–C), 136.5 (C_{Pyr}–H), 135.3 (d, $^{2}J_{CP}$=20.6 Hz, *C*═CP), 133.2 (d, $^{1}J_{CP}$=172.0 Hz, C═*C*P), 125.5 (*C*arom–C), 131.6–129.0 (Carom), 125.1, 121.3 (C_{Pyr}–H), 62.2 (CH_2), 21.3 (PhCH_3), 16.2 (CH_3); ^{31}P NMR (δ) 13.9; IR (NaCl, ν_{max}) 1630 (C═N), 1400 (P═O), 1100 (P–O); EIMS *m/z* 359 (M^+, 3). Anal. Calcd for $C_{19}H_{23}N_2O_3P$: C, 63.68; H, 6.47; N, 7.82. Found: C, 63.70; H, 6.55; N, 7.80.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-4-(4-methylphenyl)-1-(3-pyridyl)-2-azabuta-1,3-diene 4ea. According to general procedure B, imine **3e** (0.8 g, 2.04 mmol), *p*-tolualdehyde (0.2 mL, 2.23 mmol) and Cs_2CO_3 (0.85 g, 2.61 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 0.4 g (55%) of **4ea** as a yellow–orange oil;.^{1}H NMR (δ) 8.94 (s, 1H, Pyr–H), 8.72 (s, 1H, CH═N), 8.66 (d, 1H, $^{3}J_{HH}$=4.8 Hz, Pyr–H), 8.2 (d, 1H, $^{3}J_{HH}$=7.9 Hz, Pyr–H), 7.65 (d, 2H, $^{3}J_{HH}$=8.2 Hz, Ph–H), 7.37 (dd, 1H, $^{3}J_{HH}$=8.1 Hz, $^{3}J_{HH}$=4.8 Hz, Pyr–H), 7.25 (d, 2H, $^{3}J_{HH}$=8.1 Hz, Ph–H), 7.11 (d, 1H, $^{3}J_{HP}$=16.0 Hz, CH═CP), 4.15 (m, 4H, 2×CH_2), 2.29 (s, 3H, PhCH_3), 1.27 (t, 6H, $^{3}J_{HH}$=7.2 Hz, 2×CH_2CH_3); ^{13}C NMR (δ) 162.8 (d, $^{3}J_{CP}$=9.0 Hz, C═N), 155.3 (C_{Pyr}–H), 149.7 (C_{Pyr}–H), 139.6 (*C*arom–C), 137.8 (d, $^{2}J_{CP}$=20.6 Hz, *C*═CP), 136.5 (C_{Pyr}–H), 135.8 (d, $^{1}J_{CP}$=172.3 Hz, C═*C*P), 131.6–129.0 (Carom), 125.9 (*C*arom–C), 125.1 (C_{Pyr}–H), 62.2 (CH_2), 21.3 (PhCH_3), 16.2 (CH_3); ^{31}P NMR (δ) 12.5; IR (NaCl, ν_{max}) 1633 (C═N), 1350 (P═O), 1040 (P–O); EIMS *m/z* 359 (M^+, 3). Anal. Calcd for $C_{19}H_{23}N_2O_3P$: C, 63.68; H, 6.47; N, 7.82. Found: C, 63.65; H, 6.50; N, 7.90.

(1*E*,3*E*)-3-(Diethoxyphosphoryl)-1-(2-thiophenyl)-2-azapenta-1,3-diene 4fa. According to general procedure A, imine **3f** (0.7 g, 1.76 mmol), acetaldehyde (0.10 mL, 1.8 mmol) and BuLi (1.6 M, 1.2 mL) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 2:1 to yield 0.37 g (70%) of **4fa** as a pale yellow oil; ^{1}H NMR (δ) 8.59 (s, 1H, CH═N), 7.45–7.03 (m, 3H, TioPh–H), 6.43 (dq, 1H, $^{3}J_{HH}$=7.0 Hz, $^{3}J_{HP}$=14.8 Hz, CH═C), 4.06 (q, 4H, $^{3}J_{HH}$=7.3 Hz, 2×CH_2), 1.90 (dd, 3H, $^{3}J_{HH}$=7.0 Hz, $^{3}J_{HH}$=3.2 Hz, CH_3), 1.26 (t, 6H, $^{3}J_{HH}$=7.1 Hz, 2×CH_3); ^{13}C NMR (δ) 154.4 (t, $^{3}J_{CP}$=9.6 Hz, CH═N), 143.4 (C_{Thio}–C), 138.3 (d, $^{1}J_{CP}$=177.8 Hz, CH═*C*), 136.3 (d, $^{2}J_{CP}$=22.7 Hz, *C*H═C), 127.6, 130.2, 131.9 (C_{Thio}–H), 62.0 (CH_2), 16.2 (CH_3), 13.1 (d, $^{3}J_{CP}$=14.1 Hz, CH_3); ^{31}P NMR (δ) 13.4; IR (NaCl, ν_{max}) 1630 (C═N), 1250 (P═O), 1050 (P–O); EIMS *m/z* 287 (M^+, 100). Anal. Calcd for $C_{12}H_{18}NO_3PS$: C, 50.16; H, 6.31; N, 4.88; S, 11.16. Found: C, 50.15; H, 6.25; N, 4.80; S, 11.15.

(1*E*,3*E*, 5*E*)-2-(Diethoxyphosphoryl)-6-phenyl-1-(4-nitrophenyl)-3-azahexa-1,3,5-triene 9. According to general procedure A, imine **3g** (0.65 g, 1.55 mmol), *p*-nitrobenzaldehyde (0.24 g, 1.59 mmol) and BTPP (0.48 mL, 1.57 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 15:1 to yield 0.3 g (59%) of **9**. According to general procedure B, imine **3g** (2.7 g, 6.47 mmol), *p*-nitrobenzaldehyde (1.09 g, 7.2 mmol) and Cs_2CO_3 (2.7 g, 8.3 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield a pale yellow oil. This product was crystallized from hexane yielding 1.7 g (64%) of **9** as a yellow solid; mp 95–96°C, ^{1}H NMR (δ) 8.40 (d, 1H, $^{3}J_{HH}$=8.4 Hz, CH═N), 8.15 (d, 2H, $^{3}J_{HH}$=8.7 Hz, NO_2–Ph–H), 7.84 (d, 2H, $^{3}J_{HH}$=8.7 Hz, NO_2–Ph–H), 7.58–7.32 (m, 5H, Ph–H), 7.16 (d, 1H, $^{3}J_{HH}$=15.9 Hz, PhC*H*═CH), 7.03 (dd, 1H, $^{3}J_{HH}$=15.9 Hz, $^{3}J_{HH}$=8.7 Hz, PhCH═C*H*), 7.00 (d, 1H, $^{3}J_{HP}$=16.5 Hz, CH═CP), 4.20 (q, 4H, $^{3}J_{HH}$=7.2 Hz, 2×CH_2), 1.26 (t, 6H, $^{3}J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 165.7 (d, $^{3}J_{CP}$=10.1 Hz, C═N), 146.9 (Carom–NO_2), 146.1 (*C*═C–Ph), 141.7 (d, $^{1}J_{CP}$=173.7 Hz, C═*C*P), 141.0 (d, $^{3}J_{CP}$=19.6 Hz, *C*arom–C═CP), 135.5 (*C*arom–C═C), 131.6–123.6 (Carom), 128.6 (d, $^{2}J_{CP}$=22.7 Hz, *C*═CP), 128.2 (C═*C*–Ph), 62.5 (CH_2), 16.2 (CH_3); ^{31}P NMR (δ) 12.6; IR (NaCl, ν_{max}) 1627 (C═N), 1516 (NO_2), 1246 (P═O), 1017 (P–O); EIMS *m/z* 414 (M^+, 100). Anal. Calcd for $C_{21}H_{23}N_2O_5P$: C, 60.87; H, 5.59; N, 6.76. Found: C, 60.95; H, 5.60; N, 6.80.

(1*E*,3*E*,5*E*)-3-(Diethoxyphosphoryl)-6-phenyl-1-(4-methylphenyl)-2-azahexa-1,3,5-triene 10be. According to general procedure A, imine **3b** (0.5 g, 1.27 mmol), cinnamaldehyde (0.16 mL, 1.27 mmol) and BTPP (0.38 mL, 1.24 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 0.2 g (40%) of **10be**. According to general procedure B, imine **3b** (2.32 g, 5.8 mmol), cinnamaldehyde (0.8 mL, 6.38 mmol) and Cs_2CO_3 (2.4 g, 7.4 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 1.3 g (60%) of **10be** as a pale yellow oil; ^{1}H NMR (δ) 8.52 (s, 1H, CH═N), 7.20–7.75 (m, 10H, Ph–H, PhCH═C*H*), 6.91 (dd, 1H, $^{3}J_{HP}$=13.8 Hz, $^{3}J_{HH}$=11.1 Hz, CH═CP), 6.81 (d, 1H, $^{3}J_{HH}$=15.6 Hz, PhC*H*═CH), 4.14 (m, 4H, 2×CH_2), 2.37 (s, 3H, PhCH_3), 1.27 (t, 6H, $^{3}J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 161.3 (d, $^{3}J_{CP}$=10.0 Hz, C═N), 142.1 (*C*arom–C), 136.3 (d, $^{1}J_{CP}$=187.6 Hz, C═*C*P), 133.3 (*C*arom–C), 131.3 (C═*C*–Ph), 129.7–127.0 (Carom), 126.4 (d, $^{2}J_{CP}$=23.6 Hz, *C*═CP), 122.3 (d, $^{3}J_{CP}$=16.6 Hz, *C*═C–Ph), 62.5 (CH_2), 21.5

(CH_3), 16.2 (CH_3); ^{31}P NMR (δ) 13.0; IR (NaCl, ν_{max}) 1590 (C=N), 1245 (P=O), 1025 (P–O); EIMS *m/z* 383 (M^+, 31). Anal. Calcd for $C_{22}H_{26}NO_3P$: C, 68.92; H, 6.84; N, 3.65. Found: C, 68.90; H, 6.85; N, 3.70.

(1*E*,3*E*,5*E*)-3-(Diethoxyphosphoryl)-1-(4-methylphenyl)-2-azahepta-1,3,5-triene 10bf. According to general procedure A, imine **3b** (1.22 g, 3.1 mmol), crotonaldehyde (0.25 mL, 3.1 mmol) and BTPP (0.94 mL, 3.1 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 15:1 to yield 0.2 g (40%) of **10bf**. According to general procedure B, imine **3b** (2.9 g, 7.2 mmol), crotonaldehyde (0.6 mL, 7.9 mmol) and Cs_2CO_3 (3 g, 9.4 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 1.6 g (70%) of **10bf** as a pale yellow oil; ^{1}H NMR (δ) 8.47 (s, 1H, CH=N), 7.71 (d, 2H, $^3J_{HH}$=8.1 Hz, Ph–H), 7.21 (d, 2H, $^3J_{HH}$=8.05, Ph–H), 6.74 (dd, 1H, $^3J_{HP}$=18.9 Hz, $^3J_{HH}$=11.0 Hz, CH=CP), 6.74 (dd, 1H, $^3J_{HH}$=23.4 Hz, $^3J_{HH}$=10.5 Hz, C*H*=CHCH$_3$), 6.06 (m, 1H, CH=C*H*CH$_3$), 4.13 (m, 4H, 2×CH_2), 2.36 (s, 3H, $PhCH_3$), 1.82 (d, 3H, $^2J_{HH}$=6.0 Hz, CH=CHC*H*$_3$), 1.30 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 160.8 (d, $^3J_{CP}$=10.2 Hz, C=N), 141.8 (*C*arom–C), 136.7 (d, $^2J_{CP}$=23.1 Hz, *C*=CP), 134.4 (d, $^1J_{CP}$=178.3 Hz, C=*C*P), 133.8 (*C*arom–C), 131.3 (C=*C*–CH_3), 129.7–128.5 (Carom), 126.0 (d, $^3J_{CP}$=16.1 Hz, *C*=C–CH_3), 62.0 (CH_2), 21.5 ($PhCH_3$), 18.8 (C=C–*C*H$_3$), 16.2 (CH_3); ^{31}P NMR (δ) 14.6; IR (NaCl, ν_{max}) 1632 (C=N), 1274 (P=O), 1029 (P–O); EIMS *m/z* 321 (M^+, 14). Anal. Calcd for $C_{17}H_{24}NO_3P$: C, 63.54; H, 7.53; N, 4.36. Found: C, 63.65; H, 7.60; N, 4.40.

(1*E*,3*E*,5*E*)-3-(Diethoxyphosphoryl)-6-phenyl-1-(3-pyridyl)-2-azahexa-1,3,5-triene 10eb. According to general procedure B, imine **3e** (1.06 g, 2.7 mmol), cynamaldehyde (0.4 mL, 2.8 mmol) and Cs_2CO_3 (1.1 g, 3.4 mmol) were used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 5:1 to yield 0.6 g (50%) of **10be** as a yellow oil; ^{1}H NMR (δ) 8.99 (s, 1H, Pyr–H), 8.64 (bs, 2H, Pyr–H, CH=N), 8.18 (d, 1H, $^3J_{HH}$=8.0 Hz, Pyr–H), 7.61–7.20 (m, 7H, Ph–H, 1×Pyr–H, CH=C*H*Ph), 7.10–7.00 (m, 1H, C*H*=CHPh), 6.82 (d, 1H, $^3J_{HP}$=15.9 Hz, CH=CP), 4.18 (m, 4H, 2×CH_2), 1.27 (t, 6H, $^3J_{HH}$=7.1 Hz, 2×CH_3); ^{13}C NMR (δ) 158.1 (d, $^3J_{CP}$=10.0 Hz, C=N), 150.3 (Pyr), 149.2 (*C*arom–C), 148.8 (Pyr), 139.1 (*C*arom–C), 137.1 (Pyr), 133.4 (d, $^1J_{CP}$=173.4 Hz, C=*C*P), 129.7–128.3 (Carom), 126.2 (d, $^2J_{CP}$=25.1 Hz, *C*=CP), 124.1 (d, $^3J_{CP}$=18.3 Hz, *C*=C–Ph), 123.1 (Carom–H), 122.3 (Pyr–H), 62.5 (CH_2), 16.2 (CH_3); ^{31}P NMR (δ) 13.4; IR (NaCl, ν_{max}) 1632 (C=N), 1274 (P=O), 1029 (P–O); EIMS *m/z* 370 (M^+, 1). Anal. Calcd for $C_{20}H_{23}N_2O_3P$: C, 64.86; H, 6.26; N, 7.56. Found: C, 64.75; H, 6.30; N, 7.50.

Synthesis of pyridines 12

General procedure: Azatriene (**10be**, **10bf** or **10eb**) was dissolved in 10 mL of dry toluene and the solution was heated at reflux for 5 days. The solvent was removed at reduced pressure and the crude product was purified by flash chromatography eluting with the appropriate solvent to provide the pure compounds.

6-(Diethoxyphosphoryl)-2-(4-methylphenyl)-3-phenylpyridine 12a. According to general procedure, azatriene **10be** (0.4 g, 1.04 mmol) was used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 10:1 to yield 0.2 g (50%) of **12a** as a brown oil; ^{1}H NMR (δ) 7.85 (dd, 1H, $^3J_{HH}$=7.3 Hz, $^3J_{HP}$=6.5 Hz, Pyr–H_5), 7.69 (dd, 1H, $^3J_{HH}$=7.3 Hz, $^4J_{HP}$=6.1 Hz, Pyr–H_4), 6.95–7.25 (m, 9H, Ph–H), 4.14 (m, 4H, 2×CH_2), 2.37 (s, 3H, $PhCH_3$), 1.27 (t, 6H, $^3J_{HH}$=7.1 Hz, 2×CH_3); ^{13}C NMR (δ) 157.6 (d, $^3J_{CP}$=23.1 Hz, C=N), 149.7 (d, $^1J_{CP}$=228.4 Hz, 6-Pyr), 139.2 (*C*arom–C), 138.2 (d, $^3J_{CP}$=12.6 Hz, 4-Pyr), 136.3 (*C*arom–C), 130.9–126.3 (Carom), 126.4 (d, $^2J_{CP}$=25.6 Hz, 5-Pyr), 62.5 (CH_2), 21.5 ($PhCH_3$), 16.2 (CH_3); ^{31}P NMR (δ) 10.8; IR (NaCl, ν_{max}) 3050 (Carom–H), 1255 (P=O), 1023 (P–O); EIMS *m/z* 381 (M^+, 50). Anal. Calcd for $C_{22}H_{24}NO_3P$: C, 69.28; H, 6.34; N, 3.67. Found: C, 69.40; H, 6.40; N, 3.60.

6-(Diethoxyphosphoryl)-3-methyl-2-(4-methylphenyl)-pyridine 12b. According to general procedure, azatriene **10bf** (0.4 g, 1.24 mmol) was used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 5:1 to yield 0.24 g (60%) of **12b** as a brown oil; ^{1}H NMR (δ) 7.72 (dd, 1H, $^3J_{HH}$=7.7 Hz, $^3J_{HP}$=6.3 Hz, Pyr–H_5), 7.60 (dd, 1H, $^3J_{HH}$=7.6 Hz, $^4J_{HP}$=5.7 Hz, Pyr–H_4), 7.38–7.17 (m, 4H, Ph–H), 4.14 (m, 4H, 2×CH_2), 2.35 (s, 3H, Pyr–CH_3), 2.27 (s, 3H, $PhCH_3$), 1.27 (t, 6H, $^3J_{HH}$=7.3 Hz, 2×CH_3); ^{13}C NMR (δ) 157.6 (d, $^3J_{CP}$=23.1 Hz, C=N), 148.4 (d, $^1J_{CP}$=228.6 Hz, 6-Pyr), 138.2 (d, $^3J_{CP}$=12.6 Hz, 4-Pyr), 136.8 (*C*arom–CH_3), 133.8 (*C*arom–CH_3), 131.7–128.3 (Carom), 126.4 (d, $^2J_{CP}$=25.6 Hz, 5-Pyr), 62.8 (CH_2), 21.1 ($PhCH_3$), 20.5 (Pyr–CH_3), 16.2 (CH_3); ^{31}P NMR (δ) 11.4; IR (NaCl, ν_{max}) 3050 (Carom–H), 1261 (P=O), 1043 (P–O); EIMS *m/z* 319 (M^+, 50). Anal. Calcd for $C_{17}H_{22}NO_3P$: C, 63.94; H, 6.94; N, 4.39. Found: C, 64.05; H, 6.90; N, 4.45.

6-(Diethoxyphosphoryl)-3-phenyl-2-(3-pyridyl)pyridine 12c. According to general procedure, azatriene **10eb** (0.3 g, 0.8 mmol) was used. The crude residue was purified by flash chromatography eluting with hexane/ethyl acetate 5:1 to yield 0.15 g (50%) of **12c** as a brown oil; ^{1}H NMR (δ) 8.58 (d, 1H, $^4J_{HH}$=2.3 Hz, Pyr–H), 8.43 (dd, 1H, $^3J_{HH}$=4.8 Hz, $^4J_{HH}$=1.7 Hz, Pyr–H), 7.96 (dd, 1H, $^3J_{HH}$=7.8 Hz, $^3J_{HP}$=6.0 Hz, Pyr–H_5), 7.78 (dd, 1H, $^3J_{HH}$=7.8 Hz, $^4J_{HP}$=5.4 Hz, Pyr–H_4), 7.61 (dd, 1H, $^3J_{HH}$=7.9 Hz, $^4J_{HH}$=1.9 Hz, Pyr–H), 7.59–7.10 (m, 6H, 5×Ph–H, Pyr–H), 4.14 (m, 4H, 2×CH_2), 1.27 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3); ^{13}C NMR (δ) 154.4 (d, $^3J_{CP}$=23.6 Hz, 2-Pyr), 152.3 (*C*arom–C), 150.8 (Carom), 150.3 (d, $^1J_{CP}$=210.1 Hz, 6-Pyr), 150.1 (*C*arom–C), 137.4, 138.1, 149.4 (Carom), 135.8 (*C*arom–C), 129.7–127.3 (Carom), 126.7 (d, $^2J_{CP}$=25.6 Hz, 5-Pyr), 122.6 (Pyr), 63.2 (CH_2), 16.2 (CH_3),; ^{31}P NMR (δ) 10.5; IR (NaCl, ν_{max}) 3100 (Carom–H), 1235 (P=O), 1016 (P–O); EIMS *m/z* 368 (M^+, 1). Anal. Calcd for $C_{20}H_{21}N_2O_3P$: C, 65.21; H, 5.75; N, 7.60. Found: C, 65.10; H, 5.80; N, 7.65.

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