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Synthesis and utility of new amine/nucleobase addition products of allenylphosphonates

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Abstract—In the reaction of allenylphosphonates with amines/nucleobases, depending on the amine and the allenylphosphonate, either *Z*- or *E*-vinylphosphonate or allylphosphonate as a single isomer with a β -amino functionality was isolated. A simple route to phosphonates with a β -NH₂ group is developed by direct reaction with ammonia. In reactions with adenine, three different modes of reaction, with one of them involving an unusual cyclisation, are observed. The utility of (enamino)allyl phosphonate products thus obtained in the synthesis of (enamino)-1,3-butadienes via Horner–Wadsworth–Emmons (HWE) reaction is also demonstrated.

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1. Introduction

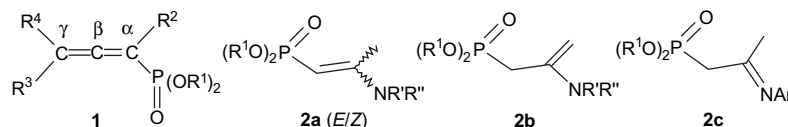
Allenes serve as potential precursors for a variety of molecules of industrial and biological importance.^{1,2} Allenylphosphonates (phosphorylated allenes) **1** constitute a readily accessible family of allenes that can be used as versatile building blocks in organic chemistry.³ One of their simplest reactions is amination leading to vinyl and/or allylphosphonates (**2a–b**); when aromatic amines are used, imine type of products (**2c**) are also possible.⁴ It should be noted that the factors governing different modes of reactivity are not clear, but all of these (**2a–c**) upon reduction can lead to β -aminophosphonates that have a wide range of biological activity.⁵ Compounds of type **2a** are well characterised but those of type **2b** are *not*. These latter compounds should be good precursors for Horner–Wadsworth–Emmons reactions. Among several synthetic routes for these β -aminophosphonates,^{5c,6} one using enamino phosphonates is attractive because of the ease of preparation of the allenylphosphonate precursors. Also, if adenine, guanine, etc., are utilised as the amine components, it should be possible to obtain nucleobase-appended phosphonates that could be of biochemical interest (e.g., chemotherapy).⁷ The reactive site in these nucleobases is another aspect on which details are unclear.

In addition to the above, enamines themselves are valuable intermediates in organic synthesis.⁸ Unlike the thermodynamically unstable primary and secondary enamines, enamino phosphonates are relatively stable.⁹ Thus amination of phosphorylated allenes constitutes a potential entry to stable enamines. Nonphosphorylated allenes undergo amination *mainly under catalytic conditions* to lead to the allylamines;¹⁰ in particular, the phosphine catalysed reaction of azoles with allenes takes place at the terminal carbon.^{10d}

In the above context and in continuation of our work on phosphonate/phosphorane chemistry,¹¹ we have explored the amination reactions of phosphorylated allenes.¹² Our results reveal an interesting array of products, not evident in earlier reports, in this apparently naive reaction. These results are reported here.

2. Results and discussion

In this paper, the following results are discussed in the same order: (i) synthesis and characterisation of (*E*)-(enamino)-vinyl phosphonates **4a–b** and (enamino)allyl phosphonates **5a–d**,¹³ (ii) an extremely simple and straightforward route to the stable (*Z*)- β -enamino phosphonates **6–7**^{6f} and (iii) first



Keywords: Allenylphosphonates; Nucleobase; Enamino phosphonates; HWE reaction; Mitsunobu reaction; X-ray structure.

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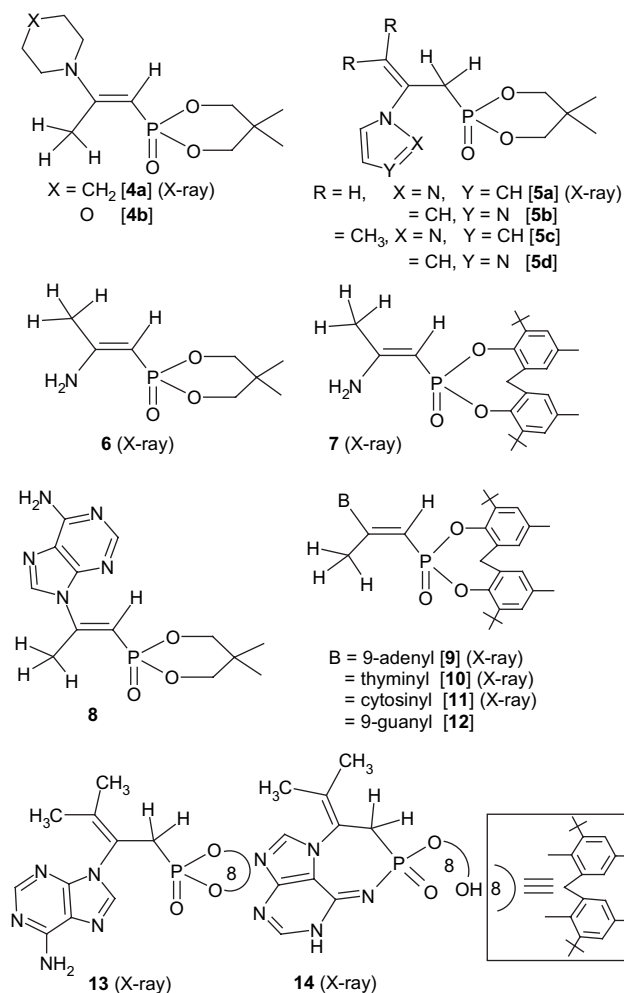


Chart 1.

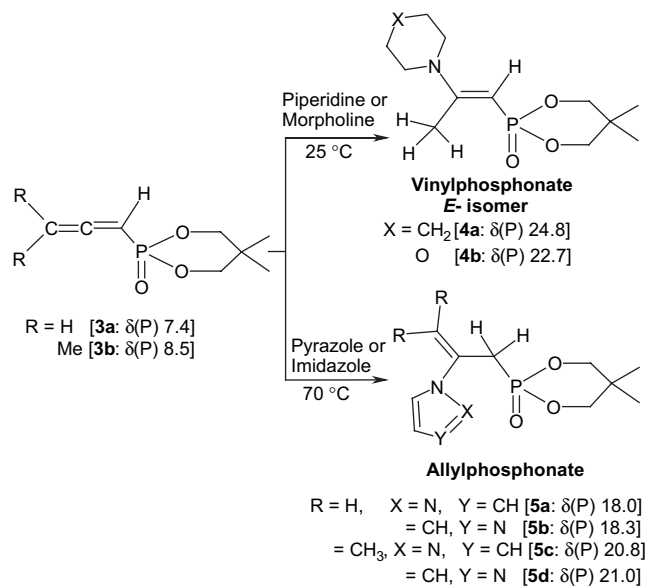
time isolation of nucleobase (adenine, thymine, cytosine and guanine) connected phosphonates **8–13** as *single* isomers,¹⁴ and the unusual cyclisation product **14** with adenine residue. These compounds are shown in Chart 1.

Utility of the addition product of **3c** with *N*-methylethanolamine in the synthesis of adenylylated phosphonates and of compounds **5b** and **5d** in the Horner–Wadsworth–Emmons (HWE) reaction leading to 1,3-butadienes is discussed later.

2.1. Reaction of allenes **3a–b** with secondary amines—formation of (*E*)-(enamino)vinyl phosphonates **4a–b** and (enamino)allyl phosphonates **5a–d**

These reactions were conducted in methyl cyanide at 25 or 70 °C (Scheme 1). The yields are summarised in Table 1. Although it is reported in the literature that there is an equilibrium between the (enamino)vinyl phosphonate and the corresponding (enamino)allyl phosphonate as shown in Scheme 2,^{3a} we did not find any evidence for the thermal conversion of **4a** (Chart 1, see Supplementary data for X-ray structure) to its (enamino)allyl form or of **5a** (Chart 1, see Supplementary data for X-ray structure) to its (enamino)vinyl form. Even in the reaction mixture, only one compound, either **4** or **5**, was observed (³¹P NMR) at 25 °C in both the cases. The amine adds to the central carbon in the reactions shown in Scheme 1. In contrast, it is important to note that phosphine catalysed addition of azoles to activated allenes takes place at the terminal carbon (Scheme 3).^{10d} The *E* stereochemistry for **4a** observed here is different from *Z* stereochemistry observed for (Me)(NEt₂)C=C(F)[P(O)(OEt)]₂.^{4b}

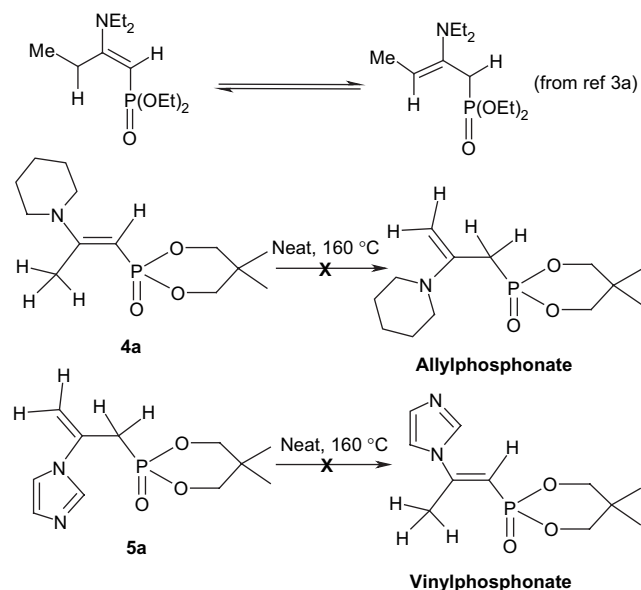
A preliminary theoretical study at B3LYP/6-31G* level using Gaussian '03 program package (see Supplementary



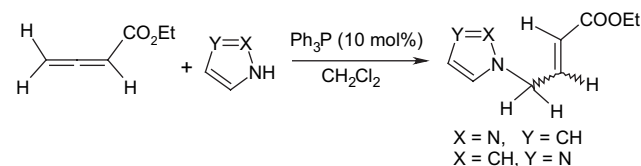
Scheme 1.

Table 1. Details on the reaction of phosphorylated allenes with amines/nucleoside bases

Entry	Allenylphosphonate	Amine, reaction conditions	Products	Yield (%)
1	3a	Piperidine, CH ₃ CN, rt	4a	100 (quantitative)
2	3a	Morpholine, CH ₃ CN, rt	4b	100 (quantitative)
3	3a	Pyrazole, CH ₃ CN, 70 °C	5a	80
4	3a	Imidazole, CH ₃ CN, 70 °C	5b	86
5	3b	Pyrazole, CH ₃ CN, 70 °C	5c	54
6	3b	Imidazole, CH ₃ CN, 70 °C	5d	62
7	3a	Ammonia, CH ₃ CN, rt	6	100 (quantitative)
8	3c	Ammonia, CH ₃ CN, rt	7	100 (quantitative)
9	3a	Adenine, DMF, K ₂ CO ₃ , rt	8	52
10	3c	Adenine, DMF, K ₂ CO ₃ , rt	9	70
11	3c	Thymine, DMF, K ₂ CO ₃ , rt	10	65
12	3c	Cytosine, DMF, K ₂ CO ₃ , rt	11	56
13	3c	Guanine, DMF, K ₂ CO ₃ , rt	12	68
14	3d	Adenine, DMF, K ₂ CO ₃ , rt	13+14	44+25
15	3c	<i>N</i> -methylethanolamine, CH ₃ CN, rt	16	100 (quantitative)



Scheme 2.

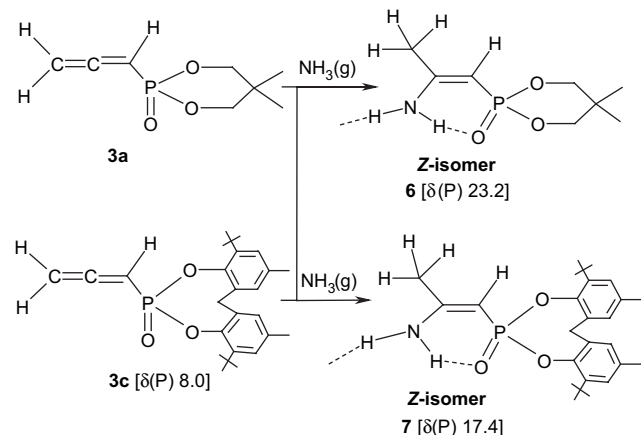


Scheme 3.

data for details) for **4a** and **5a** suggested that enamino(vinyl) form (type **4**) is more stable in the gas phase. However, it should be pointed out that gas phase stability could be different from that of the observed stability in solution/solid state. The main difference between compounds **4a** and **5a** is the presence of a saturated ring in the former and an unsaturated ring in the latter; to what extent this feature affects the stability of the vinyl and allyl forms is still not clear.

2.2. Reaction of allenes **3a** and **3c** with ammonia—formation of (*Z*)-(enamino)vinyl phosphonates **6–7**

Compound **6** or **7** (quantitative yields) could be readily obtained after passing dry ammonia into a methyl cyanide solution of allene **3a** or **3c**, respectively (Scheme 4). For both



Scheme 4.

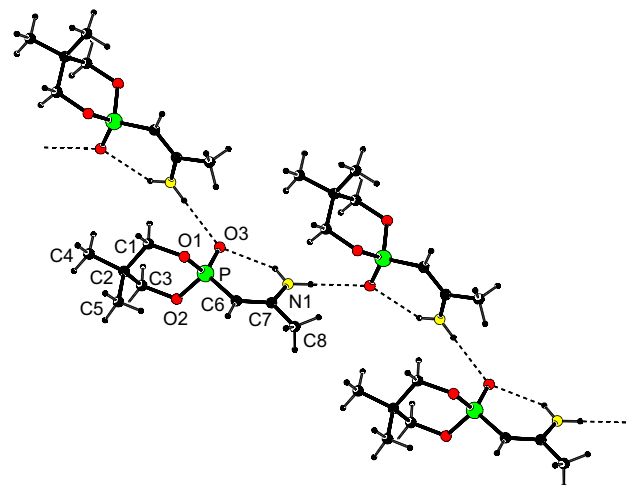
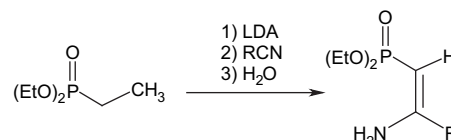


Figure 1. A PLATON drawing of **6** showing hydrogen bonding. P–C(6) 1.718(6) Å. Hydrogen bond parameters: N(1)–H(1)⋯O(3) 0.92(6), 2.23(5), 2.950(7) Å, 135(5)°; N(1)–H(2)⋯O(3′) 0.86(6), 2.34(6), 3.157(7) Å 160(6)°; N(1)–H(1)⋯O(1′) [not shown in the picture] 0.92(6), 2.70(6), 3.319(7) Å, 126(4)°.

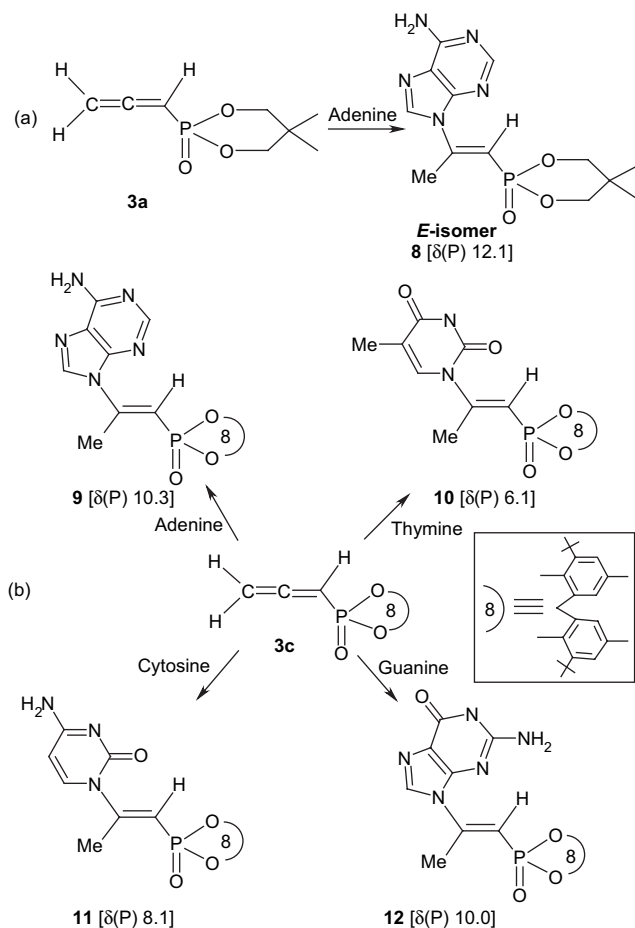
of these, the *Z* form (Fig. 1 for **6** and Supplementary data for the X-ray structure of **7**), and not the *E* form observed in **4a–b**, is favoured because of intramolecular hydrogen bonding involving the phosphoryl oxygen. Although intermolecular hydrogen bonding is also present, formation of hydrogen-bonded six-membered ring appears to have driven the structure towards the *Z* configuration in **6** and **7**. Previous reports have also suggested that the intramolecular hydrogen bonding leads to the *Z* form, but structural proof was not available.^{6f} Our route also offers a viable alternative to the literature method (cf. Scheme 5) because of the ease of synthesis. The potentially reactive β -NH₂ group of **6–7** makes them attractive precursors for further investigations.^{6c,6f}



Scheme 5.

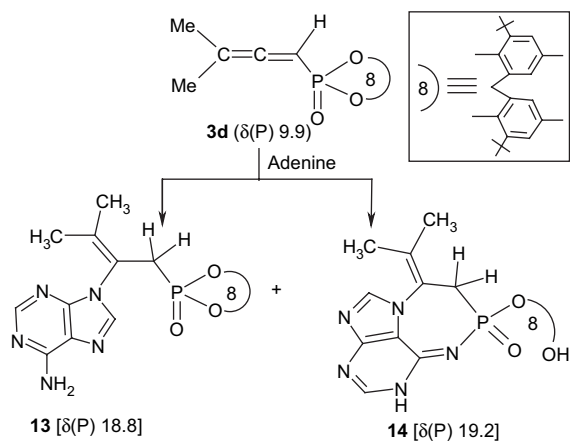
2.3. Reaction of allenylphosphonates with nucleobases—adenyl, thyminy, cytosinyl and guanyl phosphonates **8–13** and the unusual cyclisation product **14**

Reaction of allenes **3a** and **3c** with adenine in DMF at 25 °C afforded only the *E* isomer of the expected (enamino)vinyl phosphonates **8** and **9** (Scheme 6, see Supplementary data for X-ray structure). Details of the reaction conditions, yields, etc., are given in Scheme 6 and Table 1. Analogous reaction of **3c** with thymine, cytosine and guanine led to the (enamino)vinyl phosphonates **10–12** (Scheme 6, see Supplementary data for the X-ray structures).¹⁵ To our knowledge, this is the first authentic report on the isolation of nucleobase-appended (enamino)vinyl phosphonates from the reaction of allenylphosphonates. Column chromatography was employed to separate the products from the unreacted allene/nucleobase. The other by-products were mainly the isomeric alkyne or the β -ketophosphonate formed due to hydrolysis of the allene.



Scheme 6.

In contrast to the formation of vinyl phosphonates **8–9** in the reaction of adenine with $=\text{CH}_2$ terminal allenes **3a** and **3c**, the allylphosphonate **13** (see Supplementary data for X-ray structure) and the novel cyclised product **14** (Scheme 7, Fig. 2) are obtained from the reaction of the $=\text{CMe}_2$ terminal allene **3d** with adenine. Compounds **13** and **14** could be readily separated from the same reaction mixture of the allene **3d** with adenine. The reactive centre in each of the nucleobases used in the present study (except in **14**) is



Scheme 7.

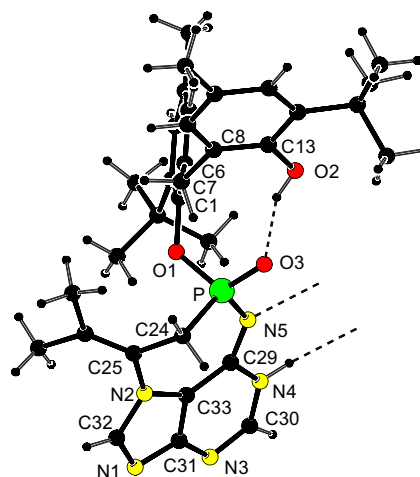
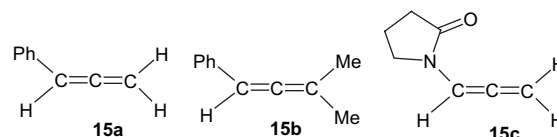
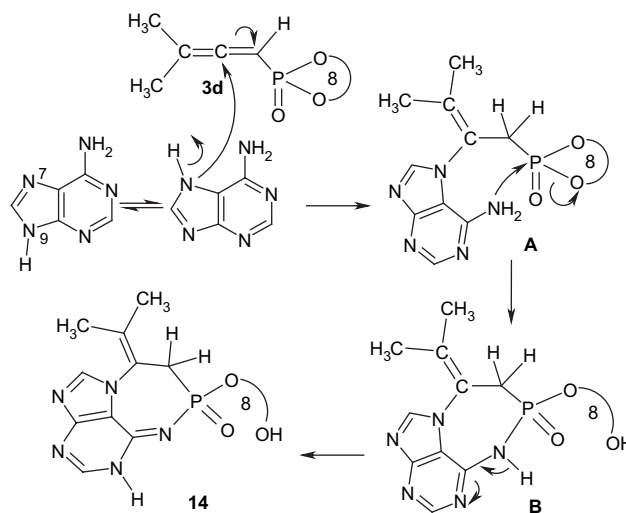


Figure 2. A PLATON drawing of **14**. Hatched lines represent hydrogen bonds. Selected distances: PN(5) 1.617(2), P–C(24) 1.798(2), N(5)–C(29) 1.315, N(2)–C(25) 1.436(3), N(4)–C(29) 1.374(3) Å.

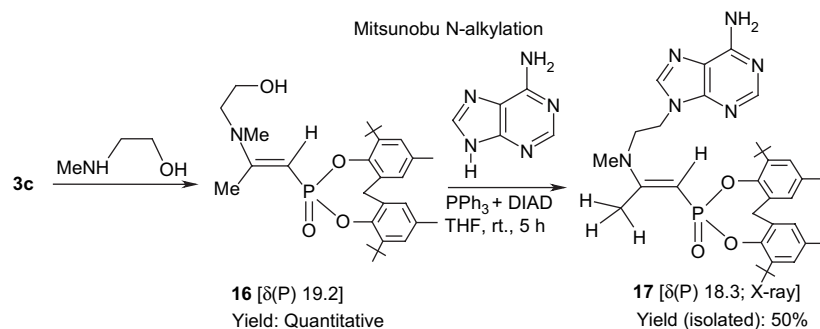
similar to that found in analogous reactions with terminal phosphorylated acetylenes, thus suggesting that they are the preferred sites of action.^{7d} Under these conditions, traditional allenes **15a–c** did not react with adenine.



A plausible pathway for the formation of the unusual ring compound **14** is depicted in Scheme 8.¹⁶ Here species **A** is the N(7) analogue of compound **13** [which is the N(9) derivative]. It should be noted that attack from N(7) of adenine is rather rare. Cyclisation involving the attack of the adenine–NH₂ at phosphorus leading to the seven-membered ring probably occurs via a pentacoordinated transition state, and to our knowledge, does not have precedence.



Scheme 8.



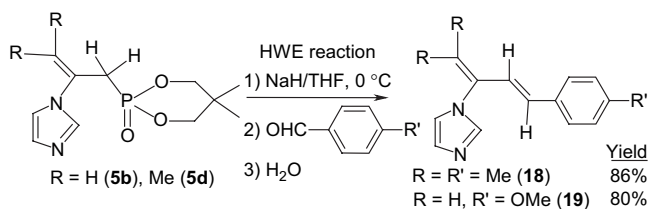
Scheme 9.

2.4. Reaction of *N*-methylethanolamine with **3c**—use of the residual –OH group in the Mitsunobu coupling to adenine

Since secondary amines like piperidine and morpholine gave the vinyl phosphonates **4a–b**, we were interested in utilising this feature for inserting functionalised amines. As an example, by using *N*-methylethanolamine, we obtained product **16** in which the –OH group is intact. This residual –OH group undergoes facile Mitsunobu coupling with adenine to give the *N*-alkylated product **17** (Scheme 9), thus offering adenylation functionality at the ω -position of the phosphonate (see Supplementary data for X-ray structure).

2.5. Horner–Wadsworth–Emmons reaction of **5b** and **5d** with aldehydes

It can be noted that compounds **5a–d** possess a P–CH₂ group ideally suited for Horner–Wadsworth–Emmons reaction. Thus we have utilised **5b** and **5d** for the synthesis of substituted butadienes **18–19** (Scheme 10). To our knowledge, no other simpler route to such interesting butadienes with an enamine functionality is available in the literature.



Scheme 10.

3. Conclusion

In summary, the amination of allenylphosphonates, including those with nucleobases, takes place readily even in the absence of a transition metal catalyst leading to a single isomer of (enamino)vinyl or (enamino)allyl phosphonate while the allenes **15a–c** remained unreactive towards nitrogen nucleophiles. Unlike the equilibrium between the vinyl and allyl forms suggested in previous studies, only one form in each case was stable in the solution (³¹P NMR evidence) as well as the solid state (X-ray). A very simple route to synthetically valuable β -NH₂ substituted phosphonates has been reported. New nucleobase-substituted

phosphonates including a novel cyclisation product involving adenine, that could have potential biological activities, are highlighted. Utility of the products in HWE reaction as well as in the synthesis of remotely functionalized phosphonates via Mitsunobu *N*-alkylation is demonstrated.

4. Experimental

4.1. General

Chemicals were purified when required according to standard procedures.^{17a} All reactions, unless stated otherwise, were performed in a dry nitrogen atmosphere. ¹H, ¹³C and ³¹P{H} NMR spectra were recorded using a 200 or a 400 MHz spectrometer in CDCl₃ (unless stated otherwise) with shifts referenced to SiMe₄ ($\delta=0$) or 85% H₃PO₄ ($\delta=0$). Infrared spectra were recorded on an FT/IR spectrometer. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. Microanalyses were performed using a CHNS analyser. Mass spectra were recorded using a GCMS-QP2010 and LCMS 2010A.

Precursors 5,5-dimethyl-2-propa-1,2-dienyl-[1,3,2]dioxaphosphinane 2-oxide (**3a**) [δ_{P} 7.4] and 5,5-dimethyl-2-(3-methyl-buta-1,2-dienyl)-[1,3,2]dioxaphosphinane 2-oxide (**3b**) [δ_{P} 8.5] were prepared using a literature procedure;^{12a} an analogous procedure was adapted for 4,8-di-*tert*-butyl-2,10-dimethyl-6-propa-1,2-dienyl-12*H*-5,7-dioxo-6-phospha-dibenzo[*a,d*]cyclooctene 6-oxide (**3c**) [δ_{P} 8.0] and 4,8-di-*tert*-butyl-2,10-dimethyl-6-(3-methyl-buta-1,2-dienyl)-12*H*-5,7-dioxo-6-phospha-dibenzo[*a,d*]cyclooctene 6-oxide (**3d**) [δ_{P} 9.9].^{12b} Compounds propa-1,2-dienyl-benzene (**15a**), (3-methyl-buta-1,2-dienyl)-benzene (**15b**) and 1-propa-1,2-dienyl-pyrrolidin-2-one (**15c**) were prepared by known methods.^{17b–c}

4.1.1. 1-[2-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-yl)-1-methyl-vinyl]-piperidine (4a**).** To a solution of allenylphosphonate **3a** (1.0 mmol) in dry methyl cyanide (10 mL), the amine (piperidine or morpholine) (1.0 mmol) was added via syringe at room temperature and the mixture was stirred for 4 h; the solution was concentrated in vacuo (to ca. 2.5 mL) and kept for crystallisation. Crystals were obtained after 24 h at 25 °C. Yield 0.27 g (100%); colourless needles; mp 74–76 °C [Found: C, 57.05; H, 8.69; N, 5.06. C₁₃H₂₄N₂O₃P requires C, 57.13; H, 8.85; N, 5.12]; ν_{max} (KBr) 1576, 1441, 1416, 1236, 1057, 1011 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 4.23 (dd, $J_{\text{H-H}}=4.7$ Hz,

$J_{H-P}=15.7$ Hz, 2H, OCH_AH_B), 4.00 (d, $J_{H-P}=8.8$ Hz, 1H, PCH), 3.72 (dd, $J_{H-H}=4.7$ Hz, $J_{H-P}=15.7$ Hz, 2H, OCH_AH_B), 3.25 (br, 4H, $N(CH_2CH_2CH_2CH_2CH_2-)$), 2.29 (d, $J_{H-P}=1.4$ Hz, 3H, $C(N(CH_2)_4-CH_3)$), 1.59 (br, 6H, $C(NCH_2CH_2CH_2CH_2CH_2-)$), 1.14, 0.96 (2s, 6H, $C(CH_3)_2$); δ_C (100 MHz, $CDCl_3$) 162.0 (d, $J_{C-P}=21.7$ Hz), 74.6, 74.5, 73.3 (d, $J_{C-P}=217.4$ Hz), 47.2, 32.3 (d, $J_{C-P}=5.1$ Hz), 25.2, 24.1, 21.9, 21.4, 18.1 (d, $J_{C-P}=4.8$ Hz); δ_P (80 MHz, $CDCl_3$) 24.8. X-ray structure was determined for this sample.

4.1.2. 4-[2-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-yl)-1-methyl-vinyl]-morpholine (4b). Yield 0.27 g (100%); white solid; mp 100–102 °C [Found: C, 52.27; H, 8.01; N, 5.08. $C_{12}H_{22}NO_4P$ requires C, 52.31; H, 8.06; N, 5.09]; ν_{max} (KBr) 1584, 1453, 1400, 1233, 1055, 997 cm^{-1} ; δ_H (200 MHz, $CDCl_3$) 4.09 (dd, $J_{H-H}\sim 2.0$ Hz, $J_{H-P}=10.8$ Hz, 1H, OCH_AH_B), 4.00 (d, $J_{H-P}=8.8$ Hz, 1H, PCH), 3.63 (m, 6H, $N(CH_2CH_2OCH_2CH_2-)$), 3.13 (t, $J_{H-H}=5.0$ Hz, 4H, $N(CH_2CH_2OCH_2CH_2-)$), 2.20 (d, $J_{H-P}=2.0$ Hz, 3H, $N(CH_2CH_2OCH_2CH_2-CH_3)$), 1.04, 0.90 (2s, 6H, $C(CH_3)_2$); δ_C (50 MHz, $CDCl_3$) 162.6 (d, $J_{C-P}=20.5$ Hz), 76.7 (d, $J_{C-P}=214.0$ Hz), 74.7, 66.2, 46.2, 32.4 (d, $J_{C-P}=4.4$ Hz), 21.9, 21.4, 17.6 (d, $J_{C-P}=3.8$ Hz); δ_P (80 MHz, $CDCl_3$) 22.7.

4.1.3. 1-[1-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-ylmethyl)-vinyl]-1H-pyrazole (5a). To a solution of allenylphosphonate **3a** (1.88 g, 10.0 mmol) in dry methyl cyanide (20 mL), pyrazole (0.68 g, 10.0 mmol) was added and the reaction mixture heated under reflux (70 °C) for 14 h with continuous stirring. The solvent was removed under reduced pressure and the solid obtained was purified by column chromatography (silica gel, hexane–ethyl acetate). The product was crystallised from dichloromethane–hexane mixture (1:1). Yield 2.02 g (80%); colourless rectangular plates; mp 79–81 °C [Found: C, 51.46; H, 6.76; N, 10.73. $C_{11}H_{17}N_2O_3P$ requires C, 51.56; H, 6.69; N, 10.83]; ν_{max} (KBr) 1649, 1478, 1262, 1053, 1005 cm^{-1} ; δ_H (200 MHz, $CDCl_3$) 7.76 (d, $J_{H-H}=2.0$ Hz, 1H, pyrazolyl-*H*), 7.56 (br s, 1H, pyrazolyl-*H*), 6.32 (d, $J_{H-H}=2.0$ Hz, 1H, pyrazolyl-*H*), 5.36, 5.07 (2d, $J_{H-H}=4.8$ Hz, 2H, $=CH_2$), 3.75–4.02 (m, 4H, OCH_2), 3.45 (d, $J_{H-P}=21.3$ Hz, 2H, PCH₂), 1.04, 0.91 (2s, 6H, $C(CH_3)_2$); δ_C (50 MHz, $CDCl_3$) 142.0, 136.3 (d, $J_{C-P}=10.4$ Hz), 127.4, 107.3, 103.8 (d, $J_{C-P}=9.7$ Hz), 75.7, 75.6, 32.1 (d, $J_{C-P}=5.5$ Hz), 28.2 (d, $J_{C-P}=133.1$ Hz), 21.4, 20.7; δ_P (80 MHz, $CDCl_3$) 18.0. X-ray structure was determined for this sample.

4.1.4. 1-[1-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-ylmethyl)-vinyl]-1H-imidazole (5b). The procedure was the same as that for **5a** using imidazole instead of pyrazole. Yield 1.58 g (86%); pale yellow solid; mp 69–71 °C [Found: C, 51.56; H, 6.72; N, 10.78. $C_{11}H_{17}O_3N_2P$ requires C, 51.56; H, 6.69; N, 10.83]; ν_{max} (KBr) 1647, 1489, 1269, 1059 cm^{-1} ; δ_H (400 MHz, $CDCl_3$) 7.78, 7.21, 7.11 (3 br s, 3H, imidazolyl-*H*), 5.34, 5.22 (2d, $J_{H-H}=5.2$ Hz, 2H, $C=CH_2$), 4.26 (dd, $J_{H-H}=4.8$ Hz, $J_{H-P}=11.1$ Hz, 2H, OCH_AH_B), 3.75 (dd, $J_{H-H}=4.8$ Hz, $J_{H-P}=12.1$ Hz, 2H, OCH_AH_B), 3.18 (d, $J_{H-P}=20.0$ Hz, 2H, PCH₂), 1.07, 0.98 (2s, 6H, $C(CH_3)_2$); δ_C (100 MHz, $CDCl_3$) 135.6, 133.3 (d, $J_{C-P}=10.0$ Hz), 130.0, 117.4, 108.2 (d, $J_{C-P}=9.7$ Hz), 75.5, 75.3, 32.5, 31.0 (d, $J_{C-P}=137.0$ Hz), 21.4, 21.2; δ_P (80 MHz, $CDCl_3$) 18.3.

4.1.5. 1-[1-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-ylmethyl)-2-methyl-propenyl]-1H-pyrazole (5c). This compound was obtained by using 10.5 mmol of the allene **3b** and following the same procedure as that for **5a**. Yield 1.37 g (54%); white solid; mp 102 °C [Found: C, 54.80; H, 7.49; N, 9.74. $C_{13}H_{21}O_3N_2P$ requires C, 54.92; H, 7.44; N, 9.85]; ν_{max} (KBr) 3108, 1721, 1672, 1643, 1510, 1285, 1065 cm^{-1} ; δ_H (400 MHz, $CDCl_3$) 7.47, 7.39, 6.15 (3 br s, 3H, pyrazolyl-*H*), 3.79–3.73 (m, 2H, OCH_AH_B), 3.51–3.48 (m, 2H, OCH_AH_B), 3.17 (d, $J_{H-P}=19.6$ Hz, 2H, PCH₂), 1.83 (d, $J_{H-P}=4.0$ Hz, 3H, $C=C(CH_{3A})_2$), 1.48 (d, $J_{H-P}=5.6$ Hz, 3H, $C=C(CH_{3B})_2$), 0.93, 0.77 (2s, 6H, $C(CH_3)_2$); δ_C (100 MHz, $CDCl_3$) 139.6, 134.0 (d, $J_{C-P}=11.6$ Hz), 132.3, 123.7 (d, $J_{C-P}=13.0$ Hz), 75.7, 75.6, 32.2 (d, $J_{C-P}=6.5$ Hz), 27.7 (d, $J_{C-P}=131.8$ Hz), 21.4, 20.9, 20.4, 20.1; δ_P (160 MHz, $CDCl_3$) 20.8; LCMS: 285 [M+1]⁺.

4.1.6. 1-[1-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-ylmethyl)-2-methyl-propenyl]-1H-imidazole (5d). This compound was obtained by using 10.5 mmol of the allene **3b** and following the same procedure as that for **5a**. Yield 1.58 g (62%); light brown solid; mp 78 °C [Found: C, 54.88; H, 7.38; N, 9.84. $C_{13}H_{21}O_3N_2P$ requires C, 54.92; H, 7.44; N, 9.85]; ν_{max} (KBr) 3106, 1684, 1489, 1263, 1063, 820 cm^{-1} ; δ_H (400 MHz, $CDCl_3$) 7.49, 7.26, 6.95 (3 br s, 3H, imidazolyl-*H*), 4.15–4.10 (m, 2H, OCH_AH_B), 3.67–3.60 (m, 2H, OCH_AH_B), 3.02 (d, $J_{H-P}=21.0$ Hz, 2H, PCH₂), 1.95 (d, $J_{H-P}=4.6$ Hz, 3H, $C=C(CH_{3A})_2$), 1.54 (d, $J_{H-P}=6.1$ Hz, 3H, $C=C(CH_{3B})_2$), 0.99, 1.02 (2s, 6H, $C(CH_3)_2$); δ_C (50 MHz, $CDCl_3$) 137.6, 136.4 (d, $J_{C-P}=10.9$ Hz), 128.9, 119.3, 119.8, 75.3, 75.1, 32.5 (d, $J_{C-P}=6.0$ Hz), 30.1 (d, $J_{C-P}=135.8$ Hz), 21.3, 20.5, 20.0; δ_P (80 MHz, $CDCl_3$) 21.0.

4.1.7. 2-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-yl)-1-methyl-vinylamine (6). To a solution of allenylphosphonate **3a** (1.0 mmol) in 5 mL dry methyl cyanide, an excess of a saturated solution of ammonia in dry methyl cyanide (20 mL) was added slowly at 0 °C with continuous stirring. After 15 min the reaction was brought to room temperature, continued the stirring for about 1 h. After removal of the solvent under reduced pressure, 3 mL of dry toluene was added to get the crystals at 0 °C after one day. However, direct passing of ammonia gas to the phosphorylated allene in toluene did not give the product.

Yield 0.20 g (100%); colourless needles; mp 82–84 °C [Found: C, 46.80; H, 7.87; N, 6.76. $C_8H_{16}O_3NP$ requires C, 46.83; H, 7.86; N, 6.83]; ν_{max} (KBr) 3409, 3322, 3239, 3202, 1647, 1576, 1429, 1219, 1059 cm^{-1} ; δ_H (400 MHz, $CDCl_3$) 6.00 (br s, 2H, NH_2), 4.24–4.28 (dd, $J_{H-H}\sim 2.3$ Hz, $J_{H-P}\sim 9.4$ Hz, 2H, OCH_2), 3.66–3.78 (m, 3H, OCH_2 +PCH), 1.93 (s, 3H, CH_3), 1.17, 0.88 (2s, 6H, $C(CH_3)_2$); δ_C (50 MHz, $CDCl_3$) 163.0 (d, $J_{C-P}=6.1$ Hz), 74.2, 74.1, 69.9 (d, $J_{C-P}=201.3$ Hz), 31.8 (d, $J_{C-P}=5.0$ Hz), 23.9 (d, $J_{C-P}=21.5$ Hz), 21.7, 21.0; δ_P (160 MHz, $CDCl_3$) 23.2. X-ray structure was determined for this sample.

4.1.8. 2-(4,8-Di-*tert*-butyl-2,10-dimethyl-6-oxo-12H-5,7-dioxa-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinylamine (7). The procedure was the same as that for **6** using **3c** and the same molar quantities. Yield 0.44 g (100%); colourless rectangular blocks; mp 130–132 °C [Found: C, 70.63; H, 8.12; N, 3.28. $C_{26}H_{36}O_3NP$ requires

C, 70.72; H, 8.22; N, 3.19]; ν_{\max} (KBr) 3420, 3326, 3239, 3204, 1640, 1582, 1439, 1217, 1138 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 6.98–7.06 (2 br s, 4H, Ar-*H*), 4.40 (br s, 1H, ArCH_AH_X), 4.08 (d, $J_{\text{H-P}}=14.8$ Hz, 1H, *PCH*), 3.79 (d, $J_{\text{H-H}}=13.6$ Hz, 1H, ArCH_AH_X), 2.27 (s, 6H, ArCH_3), 1.97 (s, 3H, CH_3), 1.38 (s, 18H, *t*-Bu-*H*); δ_{C} (50 MHz, CDCl_3) 160.7 (d, $J_{\text{C-P}}=6.0$ Hz), 147.2, 147.0, 140.8, 140.6, 133.5, 131.6, 129.4, 126.9, 73.7 (d, $J_{\text{C-P}}=208.6$ Hz), 36.1, 34.8, 30.8, 24.3 (d, $J_{\text{C-P}}=23.0$ Hz), 21.0; δ_{P} (160 MHz, CDCl_3) 17.4; GC-MS: 441 $[\text{M}]^+$. X-ray structure was determined for this sample.

4.2. Synthesis of nucleobase-appended phosphonates 8–14: representative procedure for 9

Method A: A mixture of adenine (0.191 g, 1.4 mmol), potassium *tert*-butoxide (0.157 g, 1.4 mmol) and catalytic amount of 18-crown-6 in dry methyl cyanide (80 mL) was stirred at room temperature for 30 min. Phosphorylated allene **3c** (0.191 g, 1.2 mmol) was then added all at once under a nitrogen atmosphere and the mixture stirred for overnight. The insolubles were filtered off and the solvent from the filtrate removed under reduced pressure. The residue was chromatographed on a silica gel column using ethyl acetate–hexane mixture as the eluent.

Method B: A mixture of adenine (0.191 g, 1.4 mmol) and potassium carbonate (0.195 g, 1.4 mmol) in dry DMF (70 mL) was stirred at room temperature for 15 min. Phosphorylated allene **3c** (0.50 g, 1.2 mmol) was then added all at once under a nitrogen atmosphere with stirring. Progress of the reaction was monitored by TLC. The solid was filtered off and the solvent was removed by vacuum distillation. The residue was chromatographed on a silica gel with ethyl acetate–hexane mixture.

Method B gave better yields than method A (using **3c**); this is what is given below and in Table 1. Crystals (compounds **9**, **10**, **11** and **13**) suitable for X-ray crystallography were obtained from methanol–methyl cyanide (~1:2) mixture.

4.2.1. 9-[2-(5,5-Dimethyl-2-oxo-2 λ^5 -[1,3,2]dioxaphosphinan-2-yl)-1-methyl-vinyl]-9*H*-purin-6-ylamine (8**).** Yield 0.20 g (52%); white solid; mp 270 °C [Found: C, 48.24; H, 5.51; N, 21.60. $\text{C}_{13}\text{H}_{18}\text{O}_3\text{N}_5\text{P}$ requires C, 48.30; H, 5.61; N, 21.66]; ν_{\max} (KBr) 3304, 3152, 1671, 1642, 1605, 1564, 1476, 1238, 1057 cm^{-1} ; δ_{H} (400 MHz, $\text{DMSO-}d_6$) 8.40, 8.25 (2s, 2H, adenyl-*H*), 8.09 (br s, 2H, NH_2), 7.15 (d, $J_{\text{H-P}}=12.0$ Hz, 1H, *PCH*), 3.98–4.11 (multiplet, 4H, OCH_2), 2.72 (s, 3H, CH_3), 1.21, 0.96 (2s, 6H, $\text{C}(\text{CH}_3)_2$); Solubility was too low to record the ^{13}C NMR; δ_{P} (160 MHz, $\text{DMSO-}d_6$) 12.1. Crystals were obtained from dimethyl sulfoxide (not suitable for X-ray crystallography).

4.2.2. 9-[2-(4,8-Di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinyl]-9*H*-purin-6-ylamine (9**).** Yield 0.47 g (70%); colourless needles; mp 248–250 °C [Found: C, 66.58; H, 6.85; N, 12.65. $\text{C}_{31}\text{H}_{38}\text{O}_3\text{N}_5\text{P}$ requires C, 66.53; H, 6.84; N, 12.52]; ν_{\max} (KBr) 3308, 3144, 1682, 1605, 1561, 1458, 1213, 1136 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 8.42 and 8.10 (2s, 2H, adenyl-*H*), 7.72 (d, $J_{\text{H-P}}=12.0$ Hz, 1H, *PCH*), 7.05 (s, 4H, Ar-*H*), 5.80 (br s, 2H, NH_2), 3.90–4.10

(br s, 2H, ArCH_2), 2.94 (d, $J_{\text{H-P}}=2.9$ Hz, 3H, CH_3), 2.29 (s, 6H, ArCH_3), 1.38 (s, 18H, *t*-Bu-*H*); δ_{C} (50 MHz, CDCl_3) 156.0, 153.7, 150.6, 147.5 (d, $J_{\text{C-P}}=22.5$ Hz), 146.1, 140.7, 140.6, 138.1, 134.4, 131.8, 129.5, 127.3, 120.8, 107.2 (d, $J_{\text{C-P}}=209.8$ Hz), 35.6, 34.8, 30.9, 21.0, 18.6; δ_{P} (160 MHz, CDCl_3) 10.3. X-ray structure was determined for this sample.

4.2.3. 1-[2-(4,8-Di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinyl]-5-methyl-1*H*-pyrimidine-2,4-dione (10**).** Yield 0.42 g (65%); colourless needles; mp 220 °C [Found: C, 67.53; H, 7.12; N, 5.19. $\text{C}_{31}\text{H}_{39}\text{O}_5\text{N}_2\text{P}$ requires C, 67.62; H, 7.14; N, 5.10]; ν_{\max} (KBr) 3567 (br), 3206, 3075, 1699, 1458, 1260, 931 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 8.20 (br s, 1H, thyminy-NH), 7.06 (br s, 4H, Ar-*H*), 6.91 (s, 1H, thyminy-NH), 6.01 (d, $J_{\text{H-P}}=10.4$ Hz, 1H, *PCH*), 4.06 (br s, 2H, ArCH_2), 2.64 (d, $J_{\text{H-P}}=3.2$ Hz, 3H, CH_3), 2.29 (s, 6H, ArCH_3), 1.97 (s, 3H, thyminy- CH_3), 1.40 (s, 18H, *t*-Bu-*H*); δ_{C} (50 MHz, CDCl_3) 163.9, 148.7, 140.6, 134.8, 138.6, 131.8, 129.5, 127.5, 111.7, 115.9 (d, $J_{\text{C-P}}=202.5$ Hz), 35.3, 34.9, 30.9, 29.7, 19.9; δ_{P} (80 MHz, CDCl_3) 6.1. X-ray structure was determined for this sample.

4.2.4. 4-Amino-1-[2-(4,8-di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinyl]-1*H*-pyrimidin-2-one (11**).** Yield 0.36 g (56%); colourless thick rectangular blocks; mp 200–205 °C [Found: C, 67.15; H, 7.15; N, 7.85. $\text{C}_{30}\text{H}_{38}\text{O}_4\text{N}_3\text{P}$ requires C, 67.26; H, 7.15; N, 7.85]; ν_{\max} (KBr) 3370, 1651, 1508, 1385, 1211 cm^{-1} ; δ_{H} (400 MHz, CDCl_3 ; $\text{DMSO-}d_6$) 7.20 (d, $J_{\text{H-P}}=10.0$ Hz, 1H, *PCH*), 7.09 (s, 4H, Ar-*H*), 6.06 (d, $J_{\text{H-H}}=6.6$ Hz, 1H, cytosinyl-*H*), 5.82 (d, $J_{\text{H-H}}=6.4$ Hz, 1H, cytosinyl-*H*), 4.07 (br s, 2H, ArCH_2), 2.63 (s, 3H, CH_3), 2.30 (s, 6H, ArCH_3), 1.40 (s, 18H, *t*-Bu-*H*); ^{13}C NMR spectrum was not clear due to lower solubility; δ_{P} (160 MHz, CDCl_3) 8.1. X-ray structure was determined for this sample.

4.2.5. 2-Amino-9-[2-(4,8-di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinyl]-1,9-dihydro-purin-6-one (12**).** Yield 0.46 g (68%); white solid; mp 268–274 °C [Found: C, 64.68; H, 6.63; N, 12.17. $\text{C}_{31}\text{H}_{38}\text{O}_4\text{N}_5\text{P}$ requires C, 64.68; H, 6.65; N, 12.17]; ν_{\max} (KBr) 3393, 3308, 3196, 1703, 1640, 1599, 1211 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 12.30 (br s, 2H, NH_2), 7.90 (s, 1H, guanyl-*H*), 7.50 (d, $J_{\text{H-P}}=19.5$ Hz, 1H, *PCH*), 7.06 (br s, 4H, Ar-*H*), 6.50 (br s, 1H, NH), 4.07 (br s, 2H, ArCH_2), 2.86 (d, $J_{\text{H-P}}=3.9$ Hz, 3H, CH_3), 2.29 (s, 6H, ArCH_3), 1.29 (s, 18H, *t*-Bu-*H*); δ_{C} (100 MHz, $\text{DMSO-}d_6$) 157.0, 154.3, 151.8, 149.3 (d, $J_{\text{C-P}}=22.0$ Hz), 145.6, 140.9, 136.0, 134.5, 132.9, 129.7, 127.5, 118.6, 103.8 (d, $J_{\text{C-P}}=202.0$ Hz), 34.9, 34.2, 31.2, 21.0, 18.6 (d, $J_{\text{C-P}}=3.7$ Hz); δ_{P} (160 MHz, CDCl_3) 10.0.

4.2.6. 9-[1-(4,8-Di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-methyl]-2-methyl-propenyl]-9*H*-purin-6-ylamine (13**), **CH}_3\text{CN} and **3-*tert*-butyl-5-[3-*tert*-butyl-5-(9-isopropylidene-7-oxo-5,7,8,9-tetrahydro-2,3,5,6,9a-pentaaza-7 λ^5 -phospha-benzof[*c,d*]azulen-7-yloxy)-2-methyl-benzyl]-4-methyl-phenol (**14**).** Two products **13** and **14** were obtained in the reaction of **3d** with adenine following the same****

procedure as that for **9** using the same molar quantities. The reaction mixture showed two peaks at δ 18.8 (ca. 80%) and 19.3 (ca. 20%) in the ^{31}P NMR.

Compound 13: Yield 0.31 g (44%); colourless thin plates; mp 180–182 °C [Found (after drying): C, 67.33; H, 7.26; N, 11.86. $\text{C}_{33}\text{H}_{42}\text{O}_3\text{N}_5\text{P}$ requires C, 67.44; H, 7.20; N, 11.92]; ν_{max} (KBr) 3221, 3113, 3044, 1630, 1588, 1560, 1431, 1174 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 8.35 and 7.93 (2s, 2H, adenylyl-*H*), 6.99 and 6.98 (2s, 4H, Ar-*H*), 5.58 (br s, 2H, NH_2), 3.90 (d and a broad signal, $J_{\text{H-C-P}}=20.8$ Hz, 3H, PCH_2 merged with peak due to 1H of ArCH_AH_B), 3.50 (br, 1H, ArCH_2), 2.24 (s, 6H, ArCH_3), 2.14 (d, $J_{\text{H-P}}=3.5$ Hz, 3H, $\text{C}(\text{CH}_{3A})_2$), 1.64 (s, 3H, $\text{C}(\text{CH}_{3B})_2$), 1.25 (s, 18H, *t*-Bu-*H*); δ_{C} (100 MHz, CDCl_3) 155.5, 153.4, 150.1, 144.6, 144.5, 141.8, 140.9, 138.0, 137.8, 135.0, 132.8, 129.0, 127.6, 119.3, 119.1, 119.0, 34.7, 34.3, 31.3 (d, $J_{\text{C-P}}=146.6$ Hz), 30.8, 21.2, 20.9, 20.3, 20.2; δ_{P} (160 MHz, CDCl_3) 18.8. X-ray structure was determined for this sample.

Compound 14: Yield 0.17 g (25%); colourless diamond-like crystals; mp 196–198 °C [Found: C, 67.48; H, 7.22; N, 11.96. $\text{C}_{33}\text{H}_{42}\text{O}_3\text{N}_5\text{P}$ requires C, 67.44; H, 7.20; N, 11.92]; ν_{max} (KBr) 3335, 3177, 1669, 1595, 1456, 1238, 1196 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 8.01 and 7.93 (2s, 2H, adenylyl-*H*), 7.26, 7.04, 6.93 (3s, 4H, Ar-*H*), 6.72, 6.48 (2 br s, 2H, $\text{NH}+\text{OH}$), 4.90 (br s, 1H, ArCH_AH_X), 3.67 (d, $J_{\text{H-P}}=21.2$ Hz, 2H, PCH), 3.20 (br s, 1H, ArCH_AH_X), 2.27 and 2.16 (2s, 6H, ArCH_3), 2.02 (d, $J_{\text{H-P}}=4.8$ Hz, 3H, $=\text{C}(\text{CH}_{3A})_2$), 1.83 (d, $J_{\text{H-P}}=6.0$ Hz, 3H, $=\text{C}(\text{CH}_{3B})_2$), 1.41, 1.20 (2s, 18H, *t*-Bu-*H*); δ_{C} (100 MHz, CDCl_3) 155.6, 145.6, 141.6, 135.2, 132.8, 128.0, 127.6, 126.3, 119.0, 34.8, 34.6 (d, $J_{\text{C-P}}=167.3$ Hz), 34.5, 31.5, 29.8, 21.2, 21.0, 20.9; δ_{P} (160 MHz, CDCl_3) 19.2. X-ray structure was determined for this sample.

4.2.7. 2-([2-(4,8-Di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinyl]-methyl-amino)-ethanol (16). The procedure is similar to that of **4a** using the same molar quantities. Yield 0.49 g (100%); white solid; mp 198–202 °C [Found: C, 69.76; H, 8.19; N, 2.82. $\text{C}_{29}\text{H}_{42}\text{O}_4\text{NP}$ requires C, 69.71; H, 8.21; N, 2.80]; ν_{max} (KBr) 3457, 1570, 1456, 1238, 1132, 1032 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 7.01 (s, 4H, Ar-*H*), 4.30 (d, $J_{\text{H-P}}=8.8$ Hz, 1H, PCH), 3.96 (br s, 2H, ArCH_2), 3.73 (t, $J_{\text{H-H}}=7.1$ Hz, 2H, CH_2OH), 3.42 (t, $J_{\text{H-H}}=7.1$ Hz, 2H, NCH_2), 2.95 (s, 3H, CH_3), 2.44 (s, 3H, NCH_3), 2.27 (s, 6H, ArCH_3), 1.75 (br s, 1H, OH), 1.39 (s, 18H, *t*-Bu-*H*); δ_{C} (50 MHz, CDCl_3) 160.3 (d, $J_{\text{C-P}}=23.5$ Hz), 146.5, 140.8, 134.5, 133.5, 132.3, 129.3, 127.6, 126.9, 82.5 (d, $J_{\text{C-P}}=226.0$ Hz), 64.1, 60.1, 53.6, 35.7, 34.8, 30.8, 21.0, 18.2; δ_{P} (160 MHz, CDCl_3) 19.2.

4.2.8. 9-(2-([2-(4,8-Di-*tert*-butyl-2,10-dimethyl-6-oxo-12*H*-5,7-dioxo-6 λ^5 -phospha-dibenzo[*a,d*]cycloocten-6-yl)-1-methyl-vinyl]-methyl-amino)-ethyl)-9*H*-purin-6-ylamine (17). To a stirred solution of **16** (0.632 g, 1.05 mmol), triphenylphosphine (0.332 g, 1.27 mmol) and adenine (0.142 g, 1.05 mmol) in dry THF (25 mL) at room temperature was added diethylzodicarboxylate dropwise (0.256 g, 1.27 mmol). The solution was then stirred at room temperature for 6 h, after which the volatile components were removed under reduced pressure and the residue

was purified by chromatography (silica gel, in hexane–ethyl acetate) to give the pure product as a white solid. Crystals (**17**·2MeOH) were obtained after 48 h at 25 °C from methanol. Yield 0.37 g (50%); colourless plates; mp 248 °C [Found (after drying): C, 66.25; H, 7.34; N, 13.40. $\text{C}_{34}\text{H}_{45}\text{O}_3\text{N}_6\text{P}$ requires C, 66.21; H, 7.35; N, 13.36]; ν_{max} (KBr) 3459, 3297, 3129, 1649, 1574, 1439, 1236, 1128, 1026 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 8.37 and 7.63 (2s, 2H, adenylyl-*H*), 7.02 (br s, 4H, Ar-*H*), 5.72 (br s, 2H, NH_2), 4.32 (br s, 3H, $\text{CH}_2+\text{ArCH}_A\text{H}_X$), 3.99 (br s, 1H, ArCH_AH_X), 3.74 (br s, 2H, NCH_2), 3.57 (d, $J_{\text{H-P}}=23.3$ Hz, 1H, PCH), 2.71 (s, 3H, CH_3), 2.35 (s, 3H, NCH_3), 2.26 (s, 6H, ArCH_3), 1.26–1.43 (multiplet, 18H, *t*-Bu-*H*); δ_{C} (100 MHz, CDCl_3) 159.0 (d, $J_{\text{C-P}}=23.0$ Hz), 155.7, 153.2, 149.9, 140.7, 140.4, 133.7, 132.3, 129.2, 127.8, 127.0, 111.6, 78.9 (d, $J_{\text{C-P}}=231.0$ Hz), 50.9, 41.4, 38.9, 34.8, 31.1, 30.8, 29.5, 21.0; δ_{P} (160 MHz, CDCl_3) δ 18.3; LCMS: 617 $[\text{M}]^+$ (after the loss of methanol solvent). X-ray structure was determined on this sample.

4.2.9. 1-[2-Methyl-1-(2-*p*-tolyl-vinyl)-propenyl]-1*H*-imidazole (18). To a suspension of sodium hydride (0.12 g, 4.8 mmol) in THF (10 mL), phosphonate **5b** (0.32 g, 1.2 mmol) in THF (20 mL) was added at 0 °C and the mixture stirred for 15 min. Then anisaldehyde (0.17 g, 1.2 mmol) in THF (10 mL) was added slowly (5 min), the mixture stirred for 4 h, quenched with water (20 mL) and extracted with ether (3×20 mL). The combined organic layer was washed with water, saturated brine solution, dried (Na_2SO_4) and the solvent evaporated to afford an oily material. This was purified by silica gel column chromatography using hexane–ethyl acetate mixture. Yield 0.23 g (86%); pale yellow liquid [Found: C, 80.52; H, 7.65; N, 11.68. $\text{C}_{16}\text{H}_{18}\text{N}_2$ requires C, 80.63; H, 7.61; N, 11.75]; ν_{max} (neat) 1709, 1640, 1609, 1510, 1248 cm^{-1} ; δ_{H} (200 MHz, CDCl_3) 7.45, 7.21 (2s, 2H, imidazolyl-*H*), 7.19 (s, 2H, Ar-*H*), 7.13 (d, $J_{\text{H-H}}=15.7$ Hz, 1H, $\text{CH}_A=\text{CH}_B$), 7.08 (d, $J_{\text{H-H}}=7.8$ Hz, 2H, Ar-*H*), 6.86 (s, 1H, imidazolyl-*H*), 5.78 (d, $J_{\text{H-H}}=15.7$ Hz, 1H, $\text{CH}_A=\text{CH}_B$), 2.30 (s, 3H, ArCH_3), 2.05 (s, 3H, $\text{C}=\text{C}(\text{CH}_{3A})_2$), 1.57 (s, 3H, $\text{C}=\text{C}(\text{CH}_{3B})_2$); δ_{C} (50 MHz, CDCl_3) 139.0, 134.4, 133.9, 130.3, 129.4, 129.1, 128.6, 126.5, 122.1, 120.5, 21.2, 20.63, 19.7; LCMS: 239 $[\text{M}+1]^+$.

4.2.10. 1-[3-(4-Methoxy-phenyl)-1-methylene-allyl]-1*H*-imidazole (19). The procedure was the same as that for **18** by starting with **5d** and using the same molar quantities. Yield 0.23 g (80%); pale yellow liquid [Found: C, 74.23; H, 6.21; N, 12.23. $\text{C}_{16}\text{H}_{18}\text{ON}_2$ requires C, 74.31; H, 6.24; N, 12.36]; ν_{max} (neat) 3119, 1740, 1682, 1603, 1512, 1254 cm^{-1} ; δ_{H} (200 MHz, CDCl_3) 7.68 (s, 1H, imidazolyl-*H*), 7.33 (d, $J_{\text{H-H}}=8.8$ Hz, 2H, Ar-*H*), 7.15 (s, 1H, imidazolyl-*H*), 7.10 (d, $J_{\text{H-H}}=2.0$ Hz, 1H, imidazolyl-*H*), 6.87 (d, $J_{\text{H-H}}=8.8$ Hz, 2H, Ar-*H*), 6.73 (d, $J_{\text{H-H}}=15.6$ Hz, 1H, $\text{CH}_A=\text{CH}_B$), 6.49 (d, $J_{\text{H-H}}=15.6$ Hz, 1H, $\text{CH}_A=\text{CH}_B$), 5.26, 5.17 (2s, 2H, $\text{C}=\text{CH}_2$), 3.82 (s, 3H, OCH_3); δ_{C} (50 MHz, CDCl_3) 160.3, 142.0, 137.0, 132.6, 129.3, 128.4, 122.1, 119.6, 114.4, 109.9, 55.4; LCMS: 227 $[\text{M}+1]^+$ (another peak at *m/e* 385 probably due to dimer minus imidazole was seen).

X-ray crystallography: Single crystal X-ray data were collected on an Enraf-Nonius MACH3 or on a Bruker

AXS-SMART diffractometer, using Mo K α ($\lambda=0.71073$ Å) radiation. The structures were solved by direct methods and refined by full-matrix least squares method using standard procedures.¹⁸ Absorption corrections were done using SADABS program, wherever applicable. In some cases, the terminal carbon atoms of the *tert*-butyl groups showed high thermal and hence were refined using a suitable disorder model. All nonhydrogen atoms were refined anisotropically; hydrogen atoms were fixed by geometry or located by a Difference Fourier and refined isotropically. Crystal data are available as Supplementary data as well as CIF files. CCDC reference numbers are 605830–605839.

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Supplementary data

Supplementary data (crystal data, PLATON drawings, CIF files and details of theoretical calculations) associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.08.034.

References and notes

- Selected recent reviews: (a) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, 28, 199; (b) Zimmer, R.; Dinesh, C. U.; Nandan, E.; Khan, F. A. *Chem. Rev.* **2000**, 100, 3067; (c) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, 34, 535; (d) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, 31, 12; (e) Wei, L.-L.; Xiong, H.; Hsung, R. P. *Acc. Chem. Res.* **2003**, 36, 773; (f) Ma, S. *Acc. Chem. Res.* **2003**, 36, 701; (g) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, 43, 1196; (h) Ma, S. *Chem. Rev.* **2005**, 105, 2829; (i) Hammond, G. B. Functionalized Fluorinated Allenes. In *Fluorine-Containing Synthons*; Soloshonok, V., Ed.; ACS Publications Division and Oxford University Press: Washington, DC, 2005.
- Some recent references: (a) Oh, C. H.; Ahn, T. W.; Raghava Reddy, V. *Chem. Commun.* **2003**, 2622; (b) Fleming, S. A.; Carroll, S. M.; Hirshi, J.; Liu, R.; Pace, J. L.; Redd, J. T. *Tetrahedron Lett.* **2004**, 45, 3341; (c) Hopkins, C. D.; Malinakova, H. C. *Org. Lett.* **2004**, 6, 2221; (d) Silvetri, M. A.; Bromfield, D. C.; Lepore, S. E. *J. Org. Chem.* **2005**, 70, 8239; (e) Fu, C.; Ma, S. *Org. Lett.* **2005**, 7, 1707; (f) Zhu, X.-F.; Henry, C. E.; Wang, J.; Dudding, T.; Kwon, Y. *Org. Lett.* **2005**, 7, 1387; (g) Fu, C.; Chen, G.; Liu, X.; Ma, S. *Tetrahedron* **2005**, 61, 7768; (h) Zhu, X.-F.; Schaffner, A.-P.; Li, R. C.; Kwon, O. *Org. Lett.* **2005**, 7, 2977; (i) Shi, Y.-L.; Shi, M. *Org. Lett.* **2005**, 7, 3057; (j) Woodwar, A. R.; Burks, H. E.; Chan, L. M.; Morken, J. P. *Org. Lett.* **2005**, 7, 5505.
- (a) Schuster, H. F.; Coppola, G. M. *Allenenes in Organic Synthesis*; Wiley: New York, NY, 1984; pp 247–252; (b) Alabugin, I. V.; Brei, V. K. *Russ. Chem. Rev.* **1997**, 66, 205; (c) Patois, C.; Richard, L.; Savignac, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1577.
- (a) Palacios, F.; Aparicio, D.; García, J. *Tetrahedron* **1996**, 52, 9609; (b) Zapata, A. J.; Gu, Y.; Hammond, G. B. *J. Org. Chem.* **2000**, 65, 227; (c) Johnson, J. S.; Bergman, R. G. *J. Am. Chem. Soc.* **2001**, 123, 2923.
- (a) Kukhar, V. P.; Hudson, H. R. *Aminophosphonic and Aminophosphinic Acids—Chemistry and Biological Activity*; Wiley: Chichester, UK, 2000; Chapter 1; (b) Kafarski, P.; Lejczak, B. *Curr. Med. Chem. Anti-Cancer Agents* **2001**, 1, 301; (c) Palacios, F.; Alonso, C.; de los Santos, J. M. *Chem. Rev.* **2005**, 105, 899.
- Selected recent references: (a) Rulev, A. Yu.; Larina, L. I.; Voronkov, M. G. *Russ. J. Gen. Chem.* **2001**, 71, 1891; (b) Panarina, A. E.; Dogadina, A. V.; Zakharov, V. I.; Ionin, B. I. *Tetrahedron Lett.* **2001**, 42, 4365; (c) Palacios, F.; Pascual, S.; Oyarzabal, J.; de Retana, A. M. O. *Org. Lett.* **2002**, 4, 769; (d) Palacios, F.; Aparicio, D.; de Retana, A. M. O.; de los Santos, J. M.; Gil, J. I.; de Munain, R. L. *Tetrahedron: Asymmetry* **2003**, 14, 689; (e) Zhao, Y.; Jiang, N.; Wang, J. *Tetrahedron Lett.* **2003**, 44, 8339; (f) Palacios, F.; de Retana, A. M. O.; Pascual, S.; Oyarzabal, J. *J. Org. Chem.* **2004**, 69, 8767; (g) Xu, C.; Yuan, C. *Eur. J. Org. Chem.* **2004**, 4410.
- For examples of nucleobase appended phosphonates and their biological activity see: (a) Holy, A. Synthesis and Biological Activity of Isopolar Acyclic Nucleotide Analogs. In *Recent Advances in Nucleosides: Chemistry and Chemotherapy*; Chu, C. K., Ed.; Elsevier: Amsterdam, 2002; (b) Zidek, Z.; Potměšil, P.; Kmončieková, E.; Holý, A. *Eur. J. Pharmacol.* **2003**, 475, 149; (c) Pérez-Pérez, M.-J.; Rozenski, J.; Busson, R.; Herdewijn, P. *J. Org. Chem.* **1995**, 60, 1531; (d) Naesens, L.; Lenaerts, L.; Andrei, G.; Snoeck, R.; Van Beers, D.; Holy, A.; Balzarini, J.; De Clercq, E. *Antimicrob. Agents Chemother.* **2005**, 49, 1010; (e) Wu, T.; Froeyen, M.; Kempeneers, V.; Pannecouque, C.; Wang, J.; Busson, R.; De Clercq, E.; Herdewijn, P. *J. Am. Chem. Soc.* **2005**, 127, 5056; (f) De Clercq, E.; Balzarini, A. G.; Leyssen, P.; Naesens, L.; Neyts, J.; Pannecouque, C.; Snoeck, R.; Ying, C.; Hockova, D.; Holy, A. *Nucleosides Nucleotides Nucleic Acids* **2005**, 24, 331; (g) Hocková, D.; Holý, A.; Masojdková, G.; Andrei, R.; Snoeck, E.; De Clercq, E.; Balzarini, J. *J. Med. Chem.* **2003**, 46, 5064; (h) Lazrek, H. B.; Rochdi, A.; Khaider, H.; Barascut, J.-L.; Imbach, J.-L.; Balzarini, J.; Witvrouw, M.; Pannecouque, C.; De Clercq, E. *Tetrahedron* **1998**, 54, 3807.
- The Chemistry of Enamines*; Rappaport, Z., Ed.; Wiley: Chichester, UK, 1994.
- Novak, B. M.; Cafmeyer, J. T. *J. Am. Chem. Soc.* **2001**, 123, 11083.
- Amination of nonphosphorylated allenenes: (a) Shimizu, I.; Tsuji, J. *Chem. Lett.* **1984**, 233; (b) Besson, L.; Goré, J.; Cazes, B. *Tetrahedron Lett.* **1995**, 36, 3857; (c) Al-Masum, M.; Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1997**, 38, 6071; (d) Vineux, D.; Guillouzie, A.-F.; Cristau, H.-J. *Tetrahedron* **2006**, 62, 3710.
- (a) Muthiah, C.; Praveen Kumar, K.; Aruna Mani, C.; Kumara Swamy, K. C. *J. Org. Chem.* **2000**, 65, 3733; (b) Praveen Kumar, K.; Muthiah, C.; Kumaraswamy, S.; Kumara Swamy, K. C. *Tetrahedron Lett.* **2001**, 42, 3219; (c) Muthiah, C.; Senthil Kumar, K.; Vittal, J. J.; Kumara Swamy, K. C. *Synlett* **2002**, 1787; (d) Kumaraswamy, S.; Kommana, P.; Satish Kumar, N.; Kumara Swamy, K. C. *Chem. Commun.* **2002**, 40; (e) Balaraman, E.; Kumara Swamy, K. C. *Synthesis* **2004**, 3037; (f) Kumar, N. S.; Praveen Kumar, K.; Pavan Kumar, K. V. P.; Kommana, P.; Vittal, J. J.; Kumara Swamy, K. C. *J. Org. Chem.* **2004**, 69, 1880; (g) Kumara Swamy, K. C.;

- Kumaraswamy, S.; Senthil Kumar, K.; Muthiah, C. *Tetrahedron Lett.* **2005**, *46*, 3347; (h) Kumara Swamy, K. C.; Praveen Kumar, K.; Bhuvan Kumar, N. *J. Org. Chem.* **2006**, *71*, 1002; (i) Kumara Swamy, K. C.; Satish Kumar, N. *Acc. Chem. Res.* **2006**, *39*, 324.
- Compounds **3a–b** are known; compounds **3c–d** were prepared similarly. See: (a) Patois, C.; Richard, L.; Savignac, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1577; (b) Satish Kumar, N. Ph.D. Thesis, University of Hyderabad, India, 2004.
 - Single crystal X-ray data were collected on a Bruker AXS SMART diffractometer using Mo K α ($\lambda=0.71073$ Å) radiation. The structures were solved and refined by standard methods: (a) Sheldrick, G. M. *SADABS, Siemens Area Detector Absorption Correction*; University of Göttingen: Göttingen, Germany, 1996; (b) Sheldrick, G. M. *SHELXTL NT Crystal Structure Analysis Package, version 5.10*; Bruker AXS, Analytical X-ray System: Madison, WI, 1999.
 - (*Z*)- and (*E*)- α -Alkenyl phosphonates with nucleobases like adenine, guanine, thymine, etc., are prepared by reacting alkynyl phosphonates with nucleobase+KO-*t*-Bu+18-C-6 (Ref. 7h).
 - The allene **3a** also reacts, but **3c** yields more stable products.
 - For possible adenine-N(7)H tautomer depicted in Scheme 3, see: Shaw, G. Purines. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Potts, K. T. (Volume Editor); Pergamon: Oxford, UK, 1984; Vol. 5, Section 4.09, p 520.
 - (a) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: Oxford, UK, 1986; (b) Brandsama, L. Synthesis of Acetylenes. In *Allenenes and Cumulenes: Methods and Techniques*; Elsevier: Oxford, UK, 2004; pp 243; (c) Wei, L.-L.; Xiong, H.; Douglas, J. C.; Hsung, P. R. *Tetrahedron Lett.* **1999**, *40*, 6903.
 - (a) Sheldrick, G. M. *SADABS, Siemens Area Detector Absorption Correction*; University of Göttingen: Göttingen, Germany, 1996; (b) Sheldrick, G. M. *SHELXTL NT Crystal Structure Analysis Package, version 5.10*; Bruker AXS, Analytical X-ray System: Madison, WI, 1999.