Synthesis and Molecular Structure of New Unsaturated Analogues of Nucleotides Containing Six-Membered Rings

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The reaction of 1-(chloromethyl)-3-(diethoxyphosphonyl)-allenes **15** and **16** with purine and pyrimidine bases in the presence of cesium carbonate afforded new acyclic analogs of nucleotides containing a 1,2-alkadienic skeleton (**17**–**24**). Intramolecular cyclization of the alkoxides tethered to the allenyl moiety yielded dihydropyrans **33**–**38** and dihydrofurans **39** and **40**. Dealkylation of the dihydropyrans led to the corresponding phosphonic acids. The molecular structures of new nucleotide analogs **33** and **36** were determined by single-crystal X-ray analyses.

Introduction

Since the discovery of human immunodeficiency virus (HIV) as the causative agent[1,2] of acquired immunodeficiency syndrome (AIDS), there has been a considerable effort in the search for new compounds which could inhibit the replication of HIV. In the attempts to develop effective, selective, and nontoxic antiviral agents, a variety of strategies have been devised to design nucleotide and nucleoside analogs. Irrespective of the synthetic method, these analogs are the result of modification of natural nucleosides, usually of their carbohydrate moiety. Replacement of the carbohydrate moiety by a cyclic or acyclic unsaturated fragment has been demonstrated to be an effective approach for the creation of antiviral and antitumor agents. This diverse class of compounds includes the antibiotics decoyinine (angustmycin A; **1**)[3] and neplanocin A (**2**),[4] the AIDS drug stavudine (**3**),[5] the anti-HIV agents carbovir (**4**)[6a] and BCA {9-[4,5-bis(hydroxymethyl)(cyclopent-2-en-yl]-9*H*-adenine} (**5**),[6b] and the antitumor agent DMDC (2′-deoxy-2′-methylenecytidine) (**6**).[7] Potent antiviral activity has also been found for the methylenecyclopropanes **7**[8] and allene **8**[9] (Figure 1) with a double bond attached directly to a heterocyclic base. Thus, unsaturated analogs of nucleosides are the focus of much attention as antiviral and antitumor agents.[10] Recently, we reported the synthesis of acyclic analogs of nucleotides containing a 1,2-alkadiene moiety.[11]

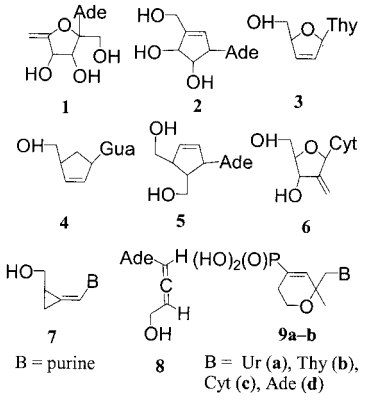

Figure 1. Unsaturated analogs of nucleotides

In order to clarify the relation between the carbon skeleton in cyclic analogs of nucleotides and their physiological activities we designed an efficient methodology for the preparation of a new type of phosphonate analogs of nucleotides **9a**−**d**. Herein we report the simple and convenient method of synthesis of new unsaturated analogs of nucleotides in which the furanose ring has been replaced by a six-membered ring containing an endocyclic double bond.

Results and Discussion

Allenes have been widely used as building blocks in organic chemistry for the construction of five- and six-membered carbocyclic and heterocyclic ring systems.[12] An im-

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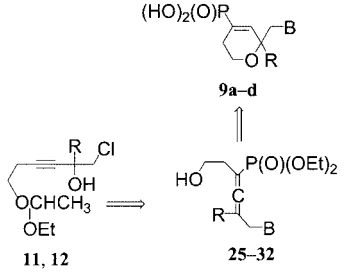
pressive number of heterocyclic systems have been prepared from allenic starting materials or via allenes as unstable intermediates. Previously, we have demonstrated that phosphonoallenes are useful substrates for constructing cyclic and acyclic organophosphorus compounds[13] as they react with halogens,[14] proton acids,[15] sulfenyl chlorides,[16] selenyl chlorides,[17] potassium dichloroiodate ($KICl_2$),[18] and *N*,*N*-diethylbenzeneselenylamide (in the presence of pyridine/SO_3)[19] to form unsaturated heterocyclic compounds[20] due to the participation of the phosphoryl oxygen atom as an internal nucleophile in the final step of the addition.

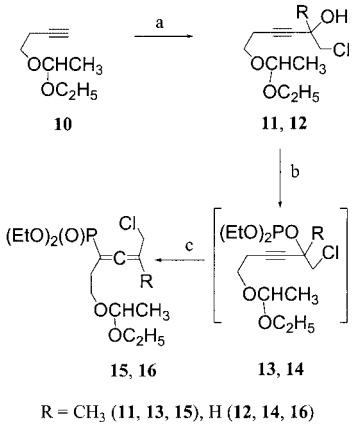
Our research interests now involve the development of new synthetic strategies for the synthesis of physiologically active compounds through the chemical transformation of phosphonoallenes. In a preliminary publication we reported the synthesis of the unsaturated nucleotide analogs **9a**−**d**.[21] Here we provide details of our approach for the construction of unsaturated analogs of nucleotides containing six-membered rings.

Our general retrosynthetic analysis, illustrated for the synthesis of target compounds **9a**−**d,** is given in Scheme 1. It revealed that the cyclic analogs of nucleotides might be constructed by a simple and efficient three-step procedure involving preparation of alkynols **11** and **12**, their transformation to phosphonoallenes **25**−**32**, and cyclization of **25**−**32** to give the final dihydropyrans **9a**−**d**.



Scheme 1. Retrosynthetic analysis of **9a**−**d**

Scheme 2 outlines the synthesis of 1-(chloromethyl)-3-(diethoxyphosphonyl)allenes **15** and **16**. Both of them were synthesized from the same commercially available substrate — 3-butyn-1-ol (**10**). This alcohol was first protected as its ethyl vinyl ether and then transformed into alcohols **11** and **12** by coupling of chloroacetone or chloroacetaldehyde, respectively, with the magnesium salt of protected **10** according to a standard procedure.[22] Chloro alcohols **11** and **12** were isolated by column chromatography in high chemical yields. Subsequent treatment of **11** and **12** with diethyl chlorophosphite in diethyl ether in the presence of triethylamine led to the unstable phosphites **13** and **14**, which rearranged to the allenes **15** and **16**, respectively, in a Horner−Mark [2,3]-sigmatropic rearrangement.[23] Compounds **15** and **16** are stable enough to be handled at ambient temperature. They were isolated by column chromatography on silica gel as colorless oils. According to ^{31}P NMR spectroscopic data, allenes **15** and **16** were obtained as mixtures of two diastereomers (in a 1:1−1:2 ratio) resulting from the chirality of the allenic group.



Scheme 2. Synthesis of **15** and **16**; reagents and conditions: a) (i) EtMgBr, 0 °C, Et_2O, reflux, 2.5 h; (ii) 0 °C, $ClCH_2C(O)R$, reflux, 30 min; b) Et_3N, Et_2O, −15 °C, $ClP(OEt)_2$, 2 h; c) Et_2O, room temp., 24 h

The structural identity of allenes **15** and **16** was established from their ^1H, ^{13}C, and ^{31}P NMR spectroscopic data. The chemical shift of the phosphorus nucleus is characteristic for compounds with a four-coordinate phosphorus atom linked to an sp^2-hybridized carbon atom.[13b] The extreme low-field position of the signal of the central carbon atom of the allenic system ($\delta \approx 210$ ppm relative to tetramethylsilane), with a $J_{C,P}$ coupling constant of 5.0−5.5 Hz, allows the immediate identification of the allenic moiety by ^{13}C NMR spectroscopy.[24] The chemical shift of the signals of the central allenic carbon atom for chloromethylallenes **15** and **16** is $\delta = 206.9$ and 208.6 ppm, respectively.

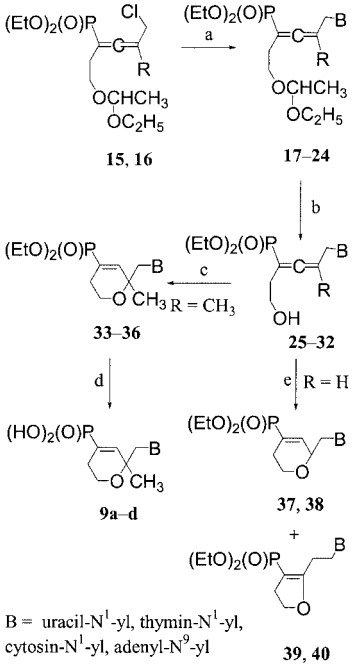
Next we studied the condensation of chloromethylallenes **15** and **16** with some purine and pyrimidine bases. Several kinds of alkylation of alkyl halides by purine and pyrimidine heterocyclic bases have been described previously, including alkylation in the presence of sodium hydride, potassium carbonate, or cesium carbonate. However, the use of sodium or potassium salts of purine and pyrimidine is restricted by their limited solubility in DMF, therefore we decided to use cesium carbonate. The mixture of heterocyclic base and cesium carbonate in DMF reacted smoothly with chloromethylallenes **15** and **16** to afford the acyclic nucleotide analogs **17**−**24**. Inspection of the ^{31}P NMR spectrum of the crude products showed only a minor (3−5%) impurity of the N^3-isomer. A high selectivity for the alkylation of purine and pyrimidine heterocycles has already been reported in earlier publications.[25] The alkylation reaction in the presence of cesium carbonate is faster than the same process mediated by potassium carbonate and reaches an equilibrium after 2.5 h at 50−60 °C. Diesters **17**−**24** were isolated in good yield by column chromatography on silica gel as mixtures of two diastereomers.

Treatment of a methanol solution of compounds **17**−**24** in the presence of *p*-toluenesulfonic acid afforded unprotected allenic alcohols **25**−**32**. The reaction was complete within 1 h at the room temperature. Compounds **25**−**32** were obtained in quantitative yield after evaporation of the solvent and column chromatography of the residue on silica gel.

With these compounds in hand, we wished to study the intramolecular cyclization of tethered alkoxides to the allenyl moiety of compounds **25**−**32**. Several examples of cyclizations of allenic alcohols to 2,5-dihydrofurans[26] or furans[27] have been described in the literature. However, relatively little work has been performed on the synthesis and study of intramolecular cyclization of phosphonoallenic carbinols.[12b,28] Recently, we have described an easy synthesis of 4-(diethylphosphono)-2,5-dihydrofurans from diethylphosphono-substituted α-allenic carbinols.[29] The cyclization of γ,γ-disubstituted phosphonoallenic alcohols **25**−**28** was performed by treatment with a catalytic amount of silver nitrate in THF/water (20:0.5) to afford 3,6-dihydropyrans **33**−**36** within 6 h at 50−52 °C. The reactions were monitored by TLC and ^{1}H NMR spectroscopy. Analysis of the ^{1}H NMR spectrum of the crude material showed a high degree of conversion of **25**−**28** to dihydropyrans **33**−**36**. In contrast to allenes **25**−**28**, compounds **29** and **30** (R = H) formed both dihydropyrans (**37**, **38**) and dihydrofurans (**39**, **40**) under similar reaction conditions.

The structures of phosphonates **33**−**40** were confirmed by NMR spectroscopy. The most useful were the ^{13}C NMR spectra and, especially, the DEPT experiments. They corroborated that compounds **33**−**40** contain one (**37**, **40**), two (**33**, **35**, **36**, **38**, **40**), or three (**34**) different kinds of methyl groups, and four (**33**−**38**) or five (**39**, **40**) different kinds of methylene groups. Moreover, the DEPT experiments indicated the presence of two (**34**), three (**33**, **35**, **36**, **38**), or four (**37**) CH groups. The quaternary carbon atom carrying the phosphonate moiety has the largest $J_{C,P}$ coupling constant ($J_{C,P}$ = 183−185 Hz for **33**−**38** and $J_{C,P}$ = 216 Hz for **39** and **40**).

Next, we turned our attention to the deesterification of the phosphonate groups. Bromotrimethylsilane (TMSBr) has frequently been used as an efficient reagent for dealkylation of dialkyl phosphonate esters to generate the corresponding phosphonic acids.[30] Treatment of the diethyl esters **33**−**36** with 5 equiv. of TMSBr in acetonitrile at room temperature for 12 h under nitrogen furnished the phosphonic acids **9a**−**d** in good yields (Scheme 3). The high purity free phosphonic acids **9a**−**d** were obtained by recrystallization from dry methanol. Note that phosphonic acids **9c** and **9d** are very hygroscopic.



Scheme 3. Synthesis of **9a**−**9d**; reagents and conditions: a) 2 equiv. purine or pyrimidine base, 2 equiv. Cs_2CO_3, 50−60 °C, 2.5 h, DMF; b) *p*-$CH_3C_6H_4SO_2OH$, CH_3OH, room temp., 1 h; c) 0.1 equiv. $AgNO_3$, THF/water (20:0.5), reflux, 6 h; d) 5 equiv. $BrSi(CH_3)_3$, CH_3CN, room temp., 12 h; e) 0.1 equiv. $AgNO_3$, THF/water (20:0.5), reflux, 12 h

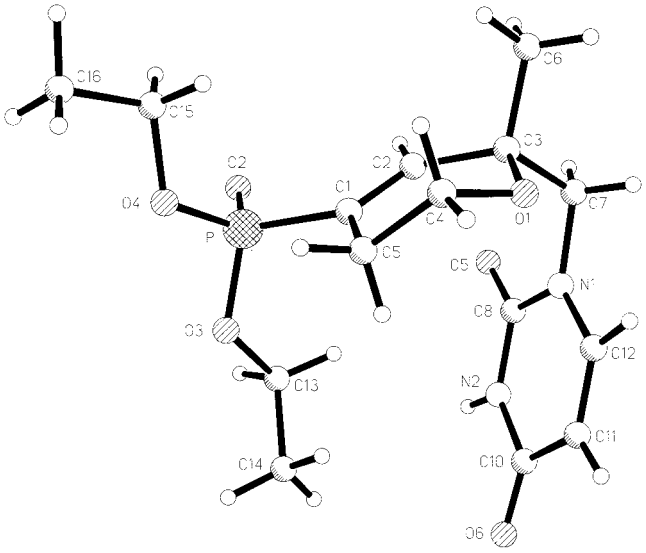


Figure 2. X-ray structure of phosphonate **33**

Single-Crystal X-ray Diffraction Analyses of 33 and 36

Colorless crystals of **33** and **36** suitable for X-ray diffraction analysis were grown by slow cooling of their saturated solutions in $CHCl_3$.[31]

The dihydropyran ring in compound **33** (Figure 2) has a sofa conformation: atoms C1, C2, C3, C5, and O1 are coplanar within 0.05 Å; atom C4 deviates from this plane by 0.66 Å and the pyrimidine ring is strictly planar. The ethoxy groups at the phosphorus atom adopt a *trans* configuration. The molecular packing is governed by intermolecular hydrogen bonds with the participation of a water molecule. The role of the latter is to connect the organic molecules in the crystal structure. The geometrical parameters of the H-bonds are as follows: O1w−H1w = 0.80 Å, H1w···O5(*x*,*y*,*z*) = 2.20 Å, O1w···O5 = 2.944 Å, OHO angle = 154°; O1w−H2w = 0.87 Å, H2w···O2(*x*,*y*,*z*) = 1.89 Å, O1w···O2 = 2.753 Å, OHO angle = 173°.

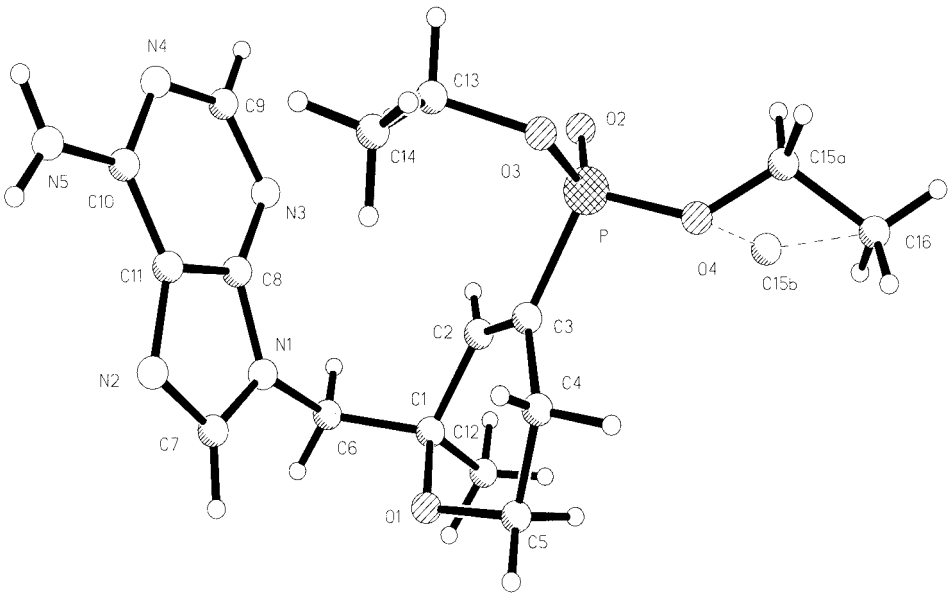


Figure 3. X-ray structure of phosphonate **36**

In the structure of **36** (Figure 3) the six-membered heterocycle has a twist conformation: atoms C1−C4 are coplanar within 0.05 Å, whereas atoms O1 and C5 deviate from this plane in opposite directions by 0.19 and 0.49 Å, respectively. The adenine moiety is planar. One of the two ethoxy groups is statistically ordered (see Figure 3), and the other one adopts a gauche conformation. The molecular packing is determined by rather strong intermolecular NH···N hydrogen bonds between the amino group and adenine nitrogen atoms. The parameters are as follows: N5−H51$_n$ = 0.83 Å, H51$_n$···N2 = 2.25 Å, N5···N2 = 3.063 Å, NHN angle = 168° (symmetry operation: $-x$, $-y$, $z - 1/2$); N5−H52$_n$ = 0.90 Å, H52$_n$···N4 = 2.12 Å, N5···N4 = 2.999 Å, NHN angle = 165° (symmetry operation: $-x$, $-y$, $z + 1/2$).

Conclusion

In summary, a convenient and efficient synthesis of a series of new purine- and pyrimidine-containing nucleotide analogs containing six-membered rings, starting from readily available phosphonoallenes, has been described. Further studies on this potentially important synthetic methodology are currently in progress. The detailed biological evaluation of these analogs and applications of phosphonoallenes to the synthesis of interesting phosphonic acid derivatives will be reported elsewhere.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded with Bruker CXP-200 and Bruker DPX-200 spectrometers at 200 MHz. Chemical shifts for ^{1}H NMR are reported in ppm relative to tetramethylsilane as internal standard. ^{31}P NMR spectra were recorded with a Bruker DPX-200 spectrometer at 81.01 MHz using an external capillary with 85% H_3PO_4 as reference. ^{13}C NMR spectra were recorded with a Bruker DPX-200 spectrometer at 50.3 MHz. Signal multiplicities were determined with DEPT techniques. Chemical shifts refer to tetramethylsilane or to residual solvent signals. Column chromatography was performed with Fluka Silica gel 100 (0.035−0.070 mm). All reactions were monitored by thin-layer chromatography on Fluka Silica Gel 60 F-254/TLC-cards (20 × 20 × 0.2 cm) with detection by spraying with $KMnO_4$ solution. All reagents were of commercial quality or were purified before use. Organic solvents were purified and dried according to established procedures by distillation under argon from an appropriate drying agent. Reagents and organic solvents were purchased from Aldrich Chemical Co. or Fluka.

1-Chloro-6-(1-ethoxyethoxy)-2-methyl-3-hexyn-2-ol (11): 4-(1-Ethoxyethoxy)-1-butyne (**10**; 8.5 g, 0.06 mol) was added dropwise to a solution of EtMgBr [prepared from 1.2 g (0.05 mol) of magnesium turnings and 6.5 g (0.06 mol) of ethyl bromide in 50 mL of THF] at 0 °C over 20 min. The mixture was stirred at room temperature for 2.5 h, at 34 °C for 1 h, and then cooled in an ice bath. Chloroacetone (5.1 g, 0.055 mol) in Et_2O (10 mL) was added dropwise over 10 min and the mixture was heated at 34 °C for 0.5 h. The mixture was cooled and satd. aq. NH_4Cl was added to dissolve the solid components. The two layers were separated and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic fractions were dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The crude product was chromatographed ($CHCl_3$/MeOH, 10:1) to give **11** (5.8 g, 52.7%) as a colorless oil. TLC: R_f = 0.65 ($CHCl_3$/MeOH, 10:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.69 (q, $J_{H,H}$ = 5.4 Hz, 1 H, CH), 3.70−3.36 (m, 6 H, 2 × OCH_2 + CH_2Cl), 2.93 (br. s, 1 H, OH), 2.44 (t, $J_{H,H}$ = 7.0 Hz, 2 H, =C-CH_2), 1.49 (s, 3 H, CH_3), 1.27 (d, $J_{H,H}$ = 5.4 Hz, 3 H, CH-*CH_3*), 1.16 (t, $J_{H,H}$ = 7.0 Hz, 3 H, *CH_3*CH_2O) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 99.3 (CH), 81.9 (C=), 81.84 (C=), 67.3 (C-OH), 62.8 (CH_2O), 60.7 (CH_2O), 54.00 (CH_2Cl), 26.9 (CH_3), 20.0 (CH_2), 19.6 (CH_3), 15.1 (CH_3) ppm. $C_{11}H_{19}ClO_3$ (234.72): calcd. C 56.29, H 8.16; found C 56.12, H 8.09.

1-Chloro-6-(1-ethoxyethoxy)-3-hexyn-2-ol (12): Compound **12** was prepared from chloroacetaldehyde[32] and **10** by the method de-

scribed for **11**. Yield: 63%. TLC: R_f = 0.60 ($CHCl_3$/MeOH, 10:1). ^1H NMR (200 MHz, $CDCl_3$): δ = 4.8 (q, $J_{H,H}$ = 5.4 Hz, 1 H, CH), 4.49 (br. t, 1 H, CH), 3.65−3.39 (m, 6 H, 2 × OCH_2 + CH_2Cl), 3.18 (br. s, 1 H, OH), 2.44 (dt, $J_{H,H}$ = 6.8, $J_{H,H}$ = 2.0 Hz, 2 H, =C-CH_2), 1.25 (d, $J_{H,H}$ = 5.6 Hz, 3 H, CH_3), 1.14 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2O) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 99.4 (CH), 83.8 (C=), 78.5 (C=), 62.6 (CH_2O), 62.4 (HC-OH), 60.8 (CH_2O), 48.8 (CH_2Cl), 20.1 (CH_2), 19.5 (CH_3), 15.0 (CH_3) ppm. $C_{10}H_{17}ClO_3$ (220.69): calcd. C 54.50, H 7.82; found C 54.42, H 7.76.

Diethyl 4-Chloro-1-[2-(1-ethoxyethoxy)ethyl]-4-methyl-1,2-butadienylphosphonate (15): NEt_3 (1.62 g, 0.016 mol) was added to a solution of alcohol **11** (2.24 g, 0.014 mol) in Et_2O (100 mL) under N_2 and the mixture was cooled to −15 °C. A solution of diethyl chlorophosphite (2.22 g, 0.0142 mol) in Et_2O (10 mL) was added dropwise and the mixture was stirred at −15 °C for 1 h and at room temp. for 24 h. The solid was removed by filtration and the solvent was evaporated under reduced pressure. The crude product was chromatographed ($CHCl_3$/MeOH, 10:0.3) to give **15** (3.18 g, 68%) as a colorless oil. R_f = 0.8 ($CHCl_3$/MeOH, 10:0.8). ^1H NMR ($CDCl_3$): δ = 4.71 (q, $J_{H,H}$ = 5.4 Hz, 1 H, CH-O), 4.22−4.03 (m, 6 H, 2 × POCH_2CH_3 + CH_2Cl), 3.73 (m, 2 H, OCH_2), 3.52 (m, 2 H, OCH_2), 2.49 (dt, $J_{H,H}$ = 6.5, $J_{H,P}$ = 12.0 Hz, 2 H, OCH_2CH_2), 1.91 (d, $J_{H,H}$ = 6.7 Hz, 3 H, =C-CH_3), 1.26 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × $POCH_2CH_3$), 1.24 (d, $J_{H,H}$ = 5.4 Hz, 3 H, CH-CH_3), 1.14 (t, $J_{H,H}$ = 6.9 Hz, 3 H, OCH_2CH_3) (a mixture of diastereomers) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.9 (d, $J_{C,P}$ = 4.7 Hz, =C=), 99.6 (O-CH), 99.54 (O-CH), 99.52 [d, $J_{C,P}$ = 16.1 Hz, =$C(CH_3)CH_2Cl$], 99.51 [d, $J_{C,P}$ = 16.1 Hz, =$C(CH_3)CH_2Cl$], 91.9 (d, $J_{C,P}$ = 188.9 Hz, PC=), 91.8 (d, $J_{C,P}$ = 188.9 Hz, PC=), 63.3 (d, $J_{C,P}$ = 7.4 Hz, CH_2O), 63.2 (d, $J_{C,P}$ = 7.2 Hz, CH_2O), 62.4 (d, $J_{C,P}$ = 6.2 Hz, CH_2OP), 62.3 (d, $J_{C,P}$ = 6.1 Hz, CH_2OP), 62.6 (CH_2O), 46.5 (d, $J_{C,P}$ = 6.9 Hz, CH_2Cl),), 46.5 (d, $J_{C,P}$ = 6.8 Hz, CH_2Cl), 29.1 (d, $J_{C,P}$ = 7.3 Hz, CH_2), 19.8 (CH_3), 16.2 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.7 (d, $J_{C,P}$ = 6.4 Hz, =CCH_3), 15.2 (CH_3) (a mixture of diastereomers) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.83, 17.81 (a mixture of diastereomers) ppm. $C_{15}H_{28}ClO_5P$ (354.81): calcd. C 50.78, H 7.95, P 8.73; found C 50.70, H 7.92, P 8.59.

Diethyl 4-Chloro-1-[2-(1-ethoxyethoxy)ethyl]-1,2-butadienylphosphonate (16): Compound **16** was prepared from **12** by the method described for **15**. Yield: 54%. TLC: R_f = 0.76 ($CHCl_3$/MeOH, 10:0.8). ^1H NMR ($CDCl_3$): δ = 5.58 [m, 1 H, =CH(CH_2)], 4.62 (q, $J_{H,H}$ = 5.3 Hz, 1 H, CH-O), 4.16−3.98 (m, 6 H, 2 × POCH_2CH_3 + CH_2Cl), 3.73−3.36 (m, 4 H, 2OCH_2), 3.52 (m, 2 H, OCH_2), 2.42 (ddt, $J_{H,H}$ = 6.5, $J_{H,P}$ = 12.0, $J_{H,H}$ = 6.5 Hz, 2 H, OCH_2CH_2), 1.27 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × $POCH_2CH_3$), 1.24 (d, $J_{H,H}$ = 5.3 Hz, 3 H, CH-CH_3), 1.14 (t, $J_{H,H}$ = 6.9 Hz, 3 H, OCH_2CH_3) (a mixture of diastereomers) ppm. ^{13}C NMR ($CDCl_3$): δ = 208.6 (d, $J_{C,P}$ = 5.0 Hz, =C=), 208.5 (d, $J_{C,P}$ = 5.0 Hz, =C=), 99.6 (O-CH), 94.1 (d, $J_{C,P}$ = 188.6 Hz, PC=), 94.0 (d, $J_{C,P}$ = 187.6 Hz, PC=), 91.5 (d, $J_{C,P}$ = 16.1 Hz, =CHCH$_2$Cl), 91.4 (d, $J_{C,P}$ = 16.1 Hz, =CHCH$_2$Cl), 63.3 (d, $J_{C,P}$ = 7.0 Hz, CH_2O), 62.9 (d, $J_{C,P}$ = 7.5 Hz, CH_2O), 62.5 (d, $J_{C,P}$ = 6.5 Hz, CH_2OP), 62.5 (d, $J_{C,P}$ = 6.5 Hz, CH_2OP), 60.70, 60.66 (CH_2O), 40.9 (d, $J_{C,P}$ = 7.5 Hz, CH_2Cl),) 28.9 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 19.7 (CH_3), 16.1 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.1 (CH_3) (a mixture of diastereomers) ppm. ^{31}P NMR ($CDCl_3$): δ = 14.63, 17.81 ppm. $C_{14}H_{26}ClO_5P$ (340.78): calcd. C 49.34, H 7.69, P 9.09; found C 49.47, H 7.78, P 9.20.

General Procedure for the Preparation of Allenes 17−24. Diethyl 4-[2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1-[2-(1-ethoxyethoxy)ethyl]-4-methyl-1,2-butadienylphosphonate (17): A mixture of adenine (0.54 g, 0.004 mol) and cesium carbonate (1.3 g, 0.004 mol) in DMF (30 mL) was stirred at 80 °C for 0.5 h with exclusion of moisture. After the addition of **15** (0.56 g, 0.002 mol), the mixture was heated at 50−60 °C whilst stirring for an additional 2.5 h, until the starting compound **15** had disappeared (TLC). The suspension was filtered and the filtrate taken to dryness in vacuo. The residue was extracted with a boiling mixture of $CHCl_3$ and MeOH (10:2; three 30-mL portions) and filtered. The solvents were evaporated in vacuo and the residue was chromatographed on a column with silica gel ($CHCl_3$/MeOH, 10:1.2) to give **17** (0.36 g, 48%) as a colorless oil. TLC: R_f = 0.68 ($CHCl_3$/MeOH, 10:1.3). ^1H NMR ($CDCl_3$): δ = 10.11 (br. s, 1 H, NH), 7.48 (d, $J_{H,H}$ = 7.8 Hz, 1 H, =CH uracil), 5.66 (d, $J_{H,H}$ = 7.8 Hz, 1 H, =CH uracil), 4.59 (q, $J_{H,P}$ = 5.2 Hz, 1 H, O-CH), 4.31 (d, $J_{H,P}$ = 5.4 Hz, 2 H, CH_2N), 4.09−3.94 (m, 4 H, 2 × CH_3CH_2OP), 3.55 (m, 2 H, OCH_2), 3.41 (m, 2 H, OCH_2), 2.32 (dt, $J_{H,H}$ = 6.4, $J_{H,P}$ = 11.4 Hz, 2 H, CH_2-C=), 1.70 (d, $J_{H,P}$ = 6.7 Hz, 3 H, CH_3-C=), 1.25 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP), 1.22 (d, $J_{H,H}$ = 5.2 Hz, 3 H, CH_3CHO), 1.13 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 207.4 (d, $J_{C,P}$ = 5.3 Hz, =C=), 207.2 (d, $J_{C,P}$ = 5.4 Hz, =C=), 163.8 (C=O), 151.0 (C=O), 144.1 (s, =CH uracil), 102.3 (=CH uracil), 99.6 (OCH), 99.5 (OCH), 98.6 (d, $J_{C,P}$ = 16.6 Hz, C=C-CH_3), 98.5 (d, $J_{C,P}$ = 16.6 Hz, C=C-CH_3), 93.6 (d, $J_{C,P}$ = 188.6 Hz, P-C=), 93.5 (d, $J_{C,P}$ = 189.1 Hz, P-C=), 63.1 (d, $J_{C,P}$ = 6.6 Hz, CH_2O), 63.0 (d, $J_{C,P}$ = 6.6 Hz, CH_2O), 62.17 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.1 (d, $J_{C,P}$ = 5.9 Hz, CH_3CH_2OP), 60.8 (CH_2O), 48.65 (d, $J_{C,P}$ = 6.6 Hz, CH_2N), 29.0 (d, $J_{C,P}$ = 6.7 Hz, CH_2), 28.9 (d, $J_{C,P}$ = 6.6 Hz, CH_2), 19.8 (CH_3), 19.7 (CH_3), 16.1 (d, $J_{C,P}$ = 6.3 Hz, 2 × CH_3CH_2OP), 15.2 (d, $J_{C,P}$ = 6.6 Hz, =CCH_3), 15.1 (OCH_2CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.61, 18.15 ppm. $C_{19}H_{31}N_2O_7P$ (430.43): calcd. C 52.02, H 7.26, N 6.51, P 7.20; found C 53.12, H 7.24, N 6.43, P 7.08.

Diethyl 1-[2-(1-Ethoxyethoxy)ethyl]-4-methyl-4-[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1,2-butadienylphosphonate (18): TLC: R_f = 0.47 ($CHCl_3$/MeOH, 10:1.0). ^1H NMR ($CDCl_3$): δ = 9.71 (br. s, 1 H, NH), 7.25 (s, 1 H, =CH thymine), 4.60 (q, $J_{H,P}$ = 5.0 Hz, 1 H, O-CH), 4.27 (d, $J_{H,P}$ = 5.6 Hz, 2 H, CH_2N), 4.09−3.95 (m, 4 H, 2 × CH_3CH_2OP), 3.58 (m, 2 H, OCH_2CH_3), 3.42 (q, $J_{H,H}$ = 7.1 Hz, 2 H OCH_2CH_2), 2.32 (dt, $J_{H,H}$ = 6.1, $J_{H,P}$ = 11.6 Hz, 2 H, CH_2-C=), 1.86 (s, 3 H, CH_3 thymine), 1.70 (d, $J_{H,P}$ = 6.8 Hz, 3 H, CH_3-C=), 1.25 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP), 1.21 (d, $J_{H,H}$ = 5.0 Hz, 3 H, CH_3CHO), 1.13 (t, $J_{H,H}$ = 7.1 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 207.3 (d, $J_{C,P}$ = 5.8 Hz, =C=), 207.2 (d, $J_{C,P}$ = 5.6 Hz, =C=), 164.6 (C=O), 151.0 (C=O), 140.0 (=CH thymine), 110.8 (=CH thymine), 99.6 (OCH), 99.5 (OCH), 98.8 (d, $J_{C,P}$ = 16.5 Hz, =C-CH_3), 98.7 (d, $J_{C,P}$ = 16.4 Hz, =C-CH_3), 93.5 (d, $J_{C,P}$ = 188.8 Hz, P-C=), 93.4 (d, $J_{C,P}$ = 188.8 Hz, P-C=), 63.10 (d, $J_{C,P}$ = 7.4 Hz, CH_2O), 63.08 (d, $J_{C,P}$ = 6.8 Hz, CH_2O), 62.2 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.1 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2OP), 60.8 (CH_2O), 48.5 (d, $J_{C,P}$ = 6.9 Hz, CH_2N), 29.0 (d, $J_{C,P}$ = 7.0 Hz, CH_2), 19.8 (CH_3), 19.75 (CH_3), 16.2 (d, $J_{C,P}$ = 6.3 Hz, 2 × CH_3CH_2OP), 15.4 (d, $J_{C,P}$ = 6.5 Hz, =CCH_3), 15.1 (OCH_2CH_3), 12.1 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.27, 18.26 ppm. $C_{20}H_{33}N_2O_7P$ (444.46): calcd. C 54.05, H 7.48, N 6.30, P 6.97; found C 54.19, H 7.46, N 6.21, P 6.81.

Diethyl 4-[4-Amino-2-oxo-1(2*H*)-pyrimidinyl]-1-[2-(1-ethoxyethoxy)ethyl]-4-methyl-1,2-butadienylphosphonate (19): TLC: R_f = 0.5 ($CHCl_3$/MeOH, 10:1.5). ^1H NMR ($CDCl_3$): δ = 7.80 (br. s, 1 H, NH), 7.44 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 6.61 (br. s, 1 H, NH), 5.88 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 4.61, 4.50 (q, $J_{H,P}$ = 4.8 Hz, 1 H, O-CH), 4.49−4.22 (m, 2 H, CH_2N), 4.00 (dq,

$J_{H,H}$ = 7.0, $J_{H,P}$ = 7.0 Hz, 4 H, 2 × CH_3CH_2OP), 3.67−3.37 (m, 4 H, OCH_2CH_2 + OCH_2CH_3), 2.30 (dt, $J_{H,H}$ = 6.2, $J_{H,P}$ = 11.6 Hz, 2 H, CH_2-C=), 1.68 (d, $J_{H,P}$ = 6.7 Hz, 3 H, CH_3-C=), 1.25 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2OP), 1.24 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2OP), 1.21 (d, $J_{H,H}$ = 4.8 Hz, 3 H, CH_3CHO), 1.13 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 207.6 (d, $J_{C,P}$ = 6.0 Hz, =C=), 207.5 (d, $J_{C,P}$ = 5.5 Hz, =C=), 165.9 (s, C=O), 156.5 (C-NH_2), 144.7 (=CH cytosine), 99.7 (OCH), 99.6 (OCH), 99.6 (d, $J_{C,P}$ = 16.5 Hz, C=*C*-CH_3), 99.5 (d, $J_{C,P}$ = 16.6 Hz, C=*C*-CH_3), 95.1 (=CH cytosine), 92.4 (d, $J_{C,P}$ = 188.8 Hz, P-C=), 92.3 (d, $J_{C,P}$ = 188.9 Hz, P-C=), 63.4 (d, $J_{C,P}$ = 6.5 Hz, CH_2O), 63.3 (d, $J_{C,P}$ = 6.6 Hz, CH_2O), 62.1 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.0 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 60.9 (CH_3CH_2O), 60.8 (CH_3CH_2O), 49.7 (d, $J_{C,P}$ = 6.5 Hz, CH_2N), 29.0 (d, $J_{C,P}$ = 7.0 Hz, CH_2), 28.9 (d, $J_{C,P}$ = 7.0 Hz, CH_2), 19.8 (CH_3), 19.7 (CH_3), 16.1 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.4 (d, $J_{C,P}$ = 6.5 Hz, =CCH_3), 15.1 (OCH_2CH_3), 15.13 (OCH_2CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.69, 18.67 ppm. $C_{19}H_{32}N_3O_6P$ (429.45): calcd. C 53.14, H 7.51, N 9.78, P 7.21; found C 53.02, H 7.47, N 9.69, P 7.15.

Diethyl 4-(6-Amino-9*H*-purin-9-yl)-1-[2-(1-ethoxyethoxy)ethyl]-4-methyl-1,2-butadienylphosphonate 20: TLC: R_f = 0.5 ($CHCl_3$/MeOH, 10:1.8). ^1H NMR ($CDCl_3$): δ = 8.28 (s, 1 H, =CH, adenine), 8.00 (s, 1 H, =CH, adenine), 6.37 (br. s, 2 H, NH_2), 4.73 (d, $J_{H,P}$ = 6.0 Hz, 2 H, CH_2N), 4.54 (q, $J_{H,H}$ = 5.0 Hz, 1 H, O-CH), 4.02−3.88 (m, 4 H, 2 × CH_3CH_2OP), 3.57−3.26 (m, 4 H, OCH_2CH_3 + OCH_2CH_2), 2.22 (dt, $J_{H,H}$ = 6.2, $J_{H,P}$ = 11.9 Hz, 2 H, CH_2-C=), 1.73 (d, $J_{H,P}$ = 6.8 Hz, 3 H, CH_3-C=), 1.24 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP), 1.22 (d, $J_{H,H}$ = 5.0 Hz, 3 H, CH_3CHO), 1.11 (t, $J_{H,H}$ = 7.0 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.8 (d, $J_{C,P}$ = 5.4 Hz, =C=), 206.7 (d, $J_{C,P}$ = 5.3 Hz, =C=), 155.6 (=C, adenine), 152.9 (=CH, adenine), 149.9 (=C, adenine), 140.8 (=CH, adenine), 118.9 (=C, adenine), 99.6 (OCH), 99.54 (OCH), 99.2 (d, $J_{C,P}$ = 16.4 Hz, =*C*-CH_3), 99.1 (d, $J_{C,P}$ = 16.4 Hz, =*C*-CH_3), 93.8 (d, $J_{C,P}$ = 188.2 Hz, P-C=), 93.6 (d, $J_{C,P}$ = 188.2 Hz, P-C=), 63.2 (d, $J_{C,P}$ = 7.1 Hz, CH_2O), 63.0 (d, $J_{C,P}$ = 5.8 Hz, CH_2O), 62.2 (d, $J_{C,P}$ = 5.8 Hz, CH_3CH_2OP), 62.0 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2OP), 60.8 (CH_2O), 45.1 (d, $J_{C,P}$ = 6.6 Hz, CH_2N), 29.0 (d, $J_{C,P}$ = 7.0 Hz, CH_2), 28.9 (d, $J_{C,P}$ = 7.0 Hz, CH_2), 19.8 (CH_3), 19.8 (CH_3), 16.2 (d, $J_{C,P}$ = 6.4 Hz, 2 × CH_3CH_2OP), 15.7 (d, $J_{C,P}$ = 6.6 Hz, =CCH_3), 15.1 (OCH_2CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.98, 17.97 ppm. $C_{20}H_{32}N_5O_5P$ (453.47): calcd. C 52.97, H 7.11, N 15.44, P 6.83; found C 52.91, H 7.15, N 15.32, P 6.70.

Diethyl 4-[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1-[2-(1-ethoxyethoxy)ethyl]-1,2-butadienylphosphonate (21): TLC: R_f = 0.65 ($CHCl_3$/MeOH, 10:1.4). ^1H NMR ($CDCl_3$): δ = 9.36 (br. s, 1 H, NH), 7.48 (d, $J_{H,H}$ = 7.9 Hz, 1 H, =CH uracil), 5.70 (dd, $J_{H,H}$ = 7.9, $J_{H,P}$ = 1.8 Hz, 1 H =CH uracil), 5.49 (m, 1 H, =CH), 4.60 (q, $J_{H,P}$ = 5.3 Hz, 1 H, O-CH), 4.42 (m, 2 H, CH_2N), 4.10−3.96 (m, 4 H, 2 × CH_3CH_2OP), 3.68−3.39 (m, 4 H, 2 OCH_2), 2.38 (ddt, $J_{H,H}$ = 2.7, $J_{H,H}$ = 6.6, $J_{H,P}$ = 11.8 Hz, 2 H, CH_2-C=), 1.29 (t, $J_{H,H}$ = 7.2 Hz, 6 H, 2 × CH_3CH_2OP), 1.25 (d, $J_{H,H}$ = 5.2 Hz, 3 H, CH_3CHO), 1.16 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 209.4 (d, $J_{C,P}$ = 6.0 Hz, =C=), 209.3 (d, $J_{C,P}$ = 5.5 Hz, =C=), 163.5 (C=O), 150.6 (C=O), 144.2 (s, =CH uracil), 102.5 (=CH uracil), 99.8 (OCH), 99.7 (OCH), 94.95 (d, $J_{C,P}$ = 187.6 Hz, P-C=), 94.90 (d, $J_{C,P}$ = 187.6 Hz, P-C=), 89.1 (d, $J_{C,P}$ = 16.1 Hz, C=*C*-H), 89.0 (d, $J_{C,P}$ = 15.6 Hz, C=*C*-H), 63.0 (d, $J_{C,P}$ = 6.5 Hz, CH_2O), 62.5 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 62.4 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 61.1 (CH_2O), 61.00 (CH_2O), 45.2 (d, $J_{C,P}$ = 6.5 Hz, CH_2N), 28.9 (d, $J_{C,P}$ = 5.0 Hz, CH_2), 28.8 (d, $J_{C,P}$ = 5.0 Hz, CH_2), 20.0 (CH_3), 19.8 (CH_3), 16.2 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.2 (OCH_2CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.42, 17.40 ppm. $C_{18}H_{29}N_2O_7P$ (416.41): calcd. C 51.92, H 7.02, N 6.73, P 7.43; found C 52.15, H 7.08, N 6.69, P 7.53.

Diethyl 1-[2-(1-Ethoxyethoxy)ethyl]-4-[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1,2-butadienylphosphonate (22): TLC: R_f = 0.26 ($CHCl_3$/MeOH, 10:0.4). ^1H NMR ($CDCl_3$): δ = 9.81 (br. s, 1 H, NH), 7.20 (d, $J_{H,P}$ = 1.3 Hz, 1 H =CH thymine), 5.44 (m, 1 H, =CH), 4.58 (q, $J_{H,P}$ = 5.3 Hz, 1 H, O-CH), 4.30 (m, 2 H, CH_2N), 4.11−3.96 (m, 4 H, 2 × CH_3CH_2OP), 3.66−3.33 (m, 4 H, 2 OCH_2), 2.32 (ddt, $J_{H,H}$ = 2.7, $J_{H,H}$ = 6.8, $J_{H,P}$ = 11.8 Hz, 2 H, CH_2-C=), 1.88 (s, 3 H, CH_3 thymine), 1.23 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP), 1.18 (d, $J_{H,H}$ = 5.3 Hz, 3 H, CH_3CHO), 1.10 (t, $J_{H,H}$ = 7.1 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 209.2 (d, $J_{C,P}$ = 5.5 Hz, =C=), 209.1 (d, $J_{C,P}$ = 5.5 Hz, =C=), 164.3 (C=O), 151.0 (C=O), 139.9 (=CH thymine), 110.8 (=CH thymine), 99.5 (OCH), 99.5 (OCH), 94.5 (d, $J_{C,P}$ = 187.6 Hz, P-C=), 94.4 (d, $J_{C,P}$ = 187.6 Hz, P-C=), 89.2 (d, $J_{C,P}$ = 16.1 Hz, =*C*-H), 89.1 (d, $J_{C,P}$ = 16.1 Hz, =*C*-H), 62.8 (d, $J_{C,P}$ = 6.9 Hz, CH_2O), 62.7 (d, $J_{C,P}$ = 7.0 Hz, CH_2O), 62.3 (d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2OP), 62.2 (d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2OP), 60.9 (CH_2O), 60.8 (CH_2O), 44.8 (d, $J_{C,P}$ = 6.5 Hz, CH_2N), 28.7 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 28.6 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 19.7 (CH_3), 19.6 (CH_3), 16.1 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.0 (CH_3), 12.0 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.52 ppm. $C_{19}H_{31}N_2O_7P$ (430.43): calcd. C 53.02, H 7.26, N 6.51, P 7.20; found C 53.12, H 7.28, N 6.58, P 7.31.

Diethyl 4-[4-Amino-2-oxo-1(2*H*)-pyrimidinyl]-1-[2-(1-ethoxyethoxy)-ethyl]-1,2-butadienylphosphonate (23): TLC: R_f = 0.5 ($CHCl_3$/MeOH, 10:1.5). ^1H NMR ($CDCl_3$): δ = 7.80 (br. s, 1 H, NH), 7.35 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 6.90 (br. s, 1 H, NH), 5.92 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 5.56 (m, 1 H, =CH), 4.62, (q, $J_{H,P}$ = 5.4 Hz, 1 H, O-CH), 4.39 (m, 2 H, CH_2N), 4.03 (m, 4 H, 2 × CH_3CH_2OP), 3.71−3.35 (m, 4 H, OCH_2CH_2 + OCH_2CH_3), 2.36 (ddt, $J_{H,H}$ = 2.6, $J_{H,H}$ = 6.6, $J_{H,P}$ = 11.8 Hz, 2 H, CH_2-C=), 1.27 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 CH_3CH_2OP), 1.23 (d, $J_{H,H}$ = 5.2 Hz, 3 H, CH_3CHO), 1.15 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 209.1 (d, $J_{C,P}$ = 6.0 Hz, =C=), 209.0 (d, $J_{C,P}$ = 5.5 Hz, =C=), 166.0 (C=O), 156.2 (C-NH_2), 144.4 (=CH cytosine), 99.6 (OCH), 99.5 (OCH), 95.3 (=CH cytosine), 93.5 (d, $J_{C,P}$ = 185.6 Hz, P-C=), 93.4 (d, $J_{C,P}$ = 185.0 Hz, P-C=), 89.9 (d, $J_{C,P}$ = 16.0 Hz, C=*C*-H), 89.8 (d, $J_{C,P}$ = 15.6 Hz, C=*C*-H), 63.0 (d, $J_{C,P}$ = 7.0 Hz, CH_2O), 62.9 (d, $J_{C,P}$ = 7.0 Hz, CH_2O), 62.3 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.2 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 60.9 (CH_2O), 60.8 (CH_2O), 46.6 (d, $J_{C,P}$ = 7.0 Hz, CH_2N), 28.7 (d, $J_{C,P}$ = 4.6 Hz, CH_2), 19.8 (CH_3), 19.7 (CH_3), 16.0 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.4 (CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.49, 17.47 ppm. $C_{18}H_{30}N_3O_6P$ (415.42): calcd. C 52.04, H 7.28, N 10.12, P 7.46; found C 53.22, H 7.34, N 9.94, P 7.28.

Diethyl 4-(6-Amino-9*H*-purin-9-yl)-1-[2-(1-ethoxyethoxy)ethyl]-1,2-butadienylphosphonate (24): TLC: R_f = 0.62 ($CHCl_3$/MeOH, 10:1.2). ^1H NMR ($CDCl_3$): δ = 8.28 (s, 1 H, =CH, adenine), 8.01 (s, 1 H, =CH, adenine), 6.77 (br. s, 2 H, NH_2), 5.67 (m, 1 H, =CH), 4.82 (t, $J_{H,H}$ = 6.2 Hz, 2 H, CH_2N), 4.55 (q, $J_{H,H}$ = 4.9 Hz, 1 H, O-CH), 4.06−3.88 (m, 4 H, 2 × CH_3CH_2OP), 3.62−3.30 (m, 4 H, OCH_2CH_3 + OCH_2CH_2), 2.28 (ddt, $J_{H,H}$ = 2.3, $J_{H,H}$ = 7.0, $J_{H,P}$ = 11.7 Hz, 2 H, CH_2-C=), 1.23 (t, $J_{H,H}$ = 7.1 Hz, 3 H, CH_3CH_2OP), 1.21 (t, $J_{H,H}$ = 7.1 Hz, 3 H, CH_3CH_2OP), 1.19 (d, $J_{H,H}$ = 5.5 Hz, 3 H, CH_3CHO), 1.12 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2O), 1.11 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2O) ppm. ^{13}C

NMR ($CDCl_3$): δ = 208.7 (d, $J_{C,P}$ = 5.5 Hz, =C=), 208.6 (d, $J_{C,P}$ = 5.5 Hz, =C=), 155.7 (=C, adenine), 152.7 (=CH, adenine), 149.4 (=C, adenine), 140.3 (=CH, adenine), 118.9 (=C, adenine), 99.6 (OCH), 94.9 (d, $J_{C,P}$ = 187.1 Hz, P-C=), 94.8 (d, $J_{C,P}$ = 187.1 Hz, P-C=), 89.6 (d, $J_{C,P}$ = 16.1 Hz, =*C*-H), 89.5 (d, $J_{C,P}$ = 16.1 Hz, =*C*-H), 62.5 (d, $J_{C,P}$ = 7.0 Hz, CH_2O), 62.7 (d, $J_{C,P}$ = 7.0 Hz, CH_2O), 62.3 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2OP), 62.1 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 60.8 (CH_2O), 60.7 (CH_2O), 40.7 (d, $J_{C,P}$ = 7.0 Hz, CH_2N), 28.6 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 28.5 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 19.6 (CH_3), 19.6 (CH_3), 16.0 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 15.9 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 15.0 (OCH_2CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.23, 17.22 ppm. $C_{19}H_{30}N_5O_5P$ (439.45): calcd. C 51.93, H 6.88, N 15.94, P 7.05; found C 52.11, H 6.75, N 15.79, P 7.20.

General Procedure for the Preparation of Allenes 25−32. Diethyl 4-[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1-(2-hydroxyethyl)-4-methyl-1,2-butadienylphosphonate (25): *p*-Toluenesulfonic acid (0.05 g) was added to a solution of phosphonate **17** (0.86 g, 0.002 mol) in CH_3OH (10 mL). The solution was stirred at room temperature for 1 h and the solvent evaporated in vacuo. The crude product was chromatographed on a column with silica gel ($CHCl_3$/MeOH, 10:1.2) to give product **25** (0.65 g, 90.3%) as a colorless oil. TLC: R_f = 0.52 ($CHCl_3$/MeOH, 10:1.3). ^1H NMR ($CDCl_3$): δ = 10.00 (br. s, 1 H, NH), 7.43 (d, $J_{H,H}$ = 8.0 Hz, 1 H, =CH uracil), 5.73 (d, $J_{H,H}$ = 8.0 Hz, 1 H, =CH uracil), 4.47 and 4.25 (ABX, $J_{H,H}$ = 15.4, $J_{H,P}$ = 6.9, $J_{H,P}$ = 6.7 Hz, 2 H, CH_2N), 4.18−4.03 (m, 4 H, 2 × CH_3CH_2OP), 3.72 (t, $J_{H,H}$ = 5.4 Hz, 2 H, $HOCH_2$), 3.20 (br. s, 1 H, OH), 2.37 (dt, $J_{H,H}$ = 6.1, $J_{H,P}$ = 11.4 Hz, 2 H, CH_2-C=), 1.81 (d, $J_{H,P}$ = 6.8 Hz, 3 H, CH_3-C=), 1.33 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.6 (d, $J_{C,P}$ = 5.2 Hz, =C=), 163.8 (C=O), 151.15 (C=O), 144.5 (=CH uracil), 102.4 (=CH uracil), 99.0 (d, $J_{C,P}$ = 16.6 Hz, C=*C*-CH_3), 94.5 (d, $J_{C,P}$ = 188.1 Hz, P-C=), 62.4 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2OP), 60.5 (d, $J_{C,P}$ = 6.4 Hz, CH_2OH), 49.2 (d, $J_{C,P}$ = 6.6 Hz, CH_2N), 32.0 (d, $J_{C,P}$ = 6.8 Hz, CH_2), 16.2 (d, $J_{C,P}$ = 6.3 Hz, 2 × CH_3CH_2OP), 15.5 (d, $J_{C,P}$ = 6.6 Hz, =CCH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.57 ppm. $C_{15}H_{23}N_2O_6P$ (358.33): calcd. C 50.28, H 6.47, N 7.82, P 8.64; found C 50.17, H 6.45, N 7.70, P 8.71.

Diethyl 1-(2-Hydroxyethyl)-4-methyl-4-[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1,2-butadienylphosphonate (26): TLC: R_f = 0.48 ($CHCl_3$/MeOH, 10:1.3). ^1H NMR ($CDCl_3$): δ = 9.95 (br. s, 1 H, NH), 7.12 (s, 1 H, =CH thymine), 4.39 and 4.12 (ABX, $J_{H,H}$ = 15.4, $J_{H,P}$ = 6.9, $J_{H,P}$ = 6.8 Hz, 2 H, CH_2N), 4.10−3.94 (m, 4 H, 2 × CH_3CH_2OP), 3.64 (t, $J_{H,H}$ = 5.6 Hz, 2 H, $HOCH_2$), 3.23 (br. s, 1 H, OH), 2.29 (dt, $J_{H,H}$ = 6.0, $J_{H,P}$ = 11.8 Hz, 2 H, CH_2-C=), 1.98 (s, 3 H, CH_3, thymine), 1.73 (d, $J_{H,P}$ = 6.7 Hz, 3 H, CH_3-C=), 1.26 (t, $J_{H,H}$ = 6.9 Hz, 3 H, CH_3CH_2OP), 1.24 (t, $J_{H,H}$ = 6.8 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.5 (d, $J_{C,P}$ = 5.2 Hz, =C=), 164.3 (C=O), 151.3 (C=O), 140.4 (=CH thymine), 110.9 (=*C*-CH_3 thymine), 99.0 (d, $J_{C,P}$ = 16.6 Hz, C=*C*-CH_3), 94.3 (d, $J_{C,P}$ = 187.8 Hz, P-C=), 62.3 (d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2OP), 62.3 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2OP), 60.5 (d, $J_{C,P}$ = 6.3 Hz, CH_2OH), 49.0 (d, $J_{C,P}$ = 6.6 Hz, CH_2N), 32.0 (d, $J_{C,P}$ = 6.8 Hz, CH_2), 16.2 (d, $J_{C,P}$ = 6.3 Hz, 2 × CH_3CH_2OP), 15.6 (d, $J_{C,P}$ = 6.7 Hz, =CCH_3), 12.1 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.66 ppm. $C_{16}H_{25}N_2O_6P$ (372.35): calcd. C 51.61, H 6.77, N 7.52, P 8.32; found C 51.55, H 6.74, N 7.43, P 8.20.

Diethyl 4-[4-Amino-2-oxo-1(2*H*)-pyrimidinyl]-1-(2-hydroxyethyl)-4-methyl-1,2-butadienylphosphonate (27): TLC: R_f = 0.29 ($CHCl_3$/MeOH, 10:1.5). ^1H NMR ($CDCl_3$): δ = 7.75 (br. s, 1 H, NH), 7.32 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 7.15 (br. s, 1 H, NH), 5.91 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 4.40 and 4.16 (ABX, $J_{H,H}$ = 16.8, $J_{H,P}$ = 7.0 Hz, 2 H, N-CH_2), 4.08−3.80 (m, 4 H, 2 × CH_3CH_2OP), 3.59 (t, $J_{H,H}$ = 5.2 Hz, 2 H, $HOCH_2$), 2.28 (dt, $J_{H,H}$ = 6.0, $J_{H,P}$ = 10.4 Hz, 2 H, CH_2-C=), 1.66 (d, $J_{H,P}$ = 6.7 Hz, 3 H, CH_3-C=), 1.22 (t, $J_{H,H}$ = 7.2 Hz, 3 H, CH_3CH_2OP), 1.21 (t, $J_{H,H}$ = 7.2 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.5 (d, $J_{C,P}$ = 5.0 Hz, =C=), 166.3 (C=O), 156.8 (C-NH_2), 145.2 (=CH cytosine), 99.7 (d, $J_{C,P}$ = 17.1 Hz, C=*C*-CH_3), 95.5 (=CH cytosine), 93.4 (d, $J_{C,P}$ = 187.1 Hz, P-C=), 62.3 (d, $J_{C,P}$ = 6.0 Hz, CH_2OP), 62.1 (d, $J_{C,P}$ = 6.0 Hz, CH_2OP), 59.9 (d, $J_{C,P}$ = 7.5 Hz, CH_2OH), 50.6 (CH_2N), 31.8 (d, $J_{C,P}$ = 7.0 Hz, CH_2), 16.1 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.7 (d, $J_{C,P}$ = 6.5 Hz, =CCH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.64, 18.67 ppm. $C_{15}H_{24}N_3O_5P$ (357.34): calcd. C 50.42 H, 6.77, N 11.76, P 8.67; found C 50.30, H 6.72, N 11.84, P 8.60.

Diethyl 4-(6-Amino-9*H*-purin-9-yl)-1-(2-hydroxyethyl)-4-methyl-1,2-butadienylphosphonate (28): TLC: R_f = 0.21 ($CHCl_3$/MeOH, 10:1.8). ^1H NMR ($CDCl_3$): δ = 8.25 (s, 1 H, =CH, adenine), 7.91 (s, 1 H, =CH, adenine), 6.33 (br. s, 2 H, NH_2), 4.79 (d, $J_{H,P}$ = 5.6 Hz, 2 H, CH_2N),4.60 (br. s, 1 H, OH), 4.05−3.92 (m, 4 H, 2 × CH_3CH_2OP), 3.67 (t, $J_{H,H}$ = 5.5 Hz, 2 H, $HOCH_2$), 2.30 (dt, $J_{H,H}$ = 5.5, $J_{H,P}$ = 10.9 Hz, 2 H, CH_2-C=), 1.68 (d, $J_{H,P}$ = 6.7 Hz, 3 H, CH_3-C=), 1.26 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.6 (d, $J_{C,P}$ = 4.9 Hz, =C=), 155.7 (=C, adenine), 152.9 (=CH, adenine), 149.5 (=C, adenine), 140.9 (=CH, adenine), 119.3 (=C, adenine), 98.2 (d, $J_{C,P}$ = 16.6 Hz, =*C*-CH_3), 93.9 (d, $J_{C,P}$ = 187.4 Hz, P-C=), 62.4 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.2 (d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2OP), 59.6 (d, $J_{C,P}$ = 6.9 Hz, CH_2OH), 46.2 (d, $J_{C,P}$ = 7.2 Hz, CH_2N), 31.9 (d, $J_{C,P}$ = 6.8 Hz, CH_2), 16.2 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP), 15.4 (d, $J_{C,P}$ = 6.5 Hz, =CCH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.50 ppm. $C_{16}H_{24}N_5O_4P$ (381.37): calcd. C 50.39, H 6.34, N 18.36, P 8.12; found C 50.31, H 6.33, N 18.30, P 8.01.

Diethyl 4-[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1-(2-hydroxyethyl)-1,2-butadienylphosphonate (29): TLC: R_f = 0.51 ($CHCl_3$/MeOH, 10:1.2). ^1H NMR ($CDCl_3$): δ = 10.42 (br. s, 1 H, NH), 7.37 (d, $J_{H,H}$ = 7.8 Hz, 1 H, =CH uracil), 5.61 (d, $J_{H,H}$ = 7.8 Hz, 1 H, =CH uracil), 5.49 (m, 1 H, =CH), 4.49−4.17 (m, 2 H, CH_2N), 4.06−3.92 (m, 4 H, 2 × CH_3CH_2OP), 3.62 (t, $J_{H,H}$ = 6.0 Hz, 2 H, $HOCH_2$), 3.50 (br. s, 1 H, OH), 2.28 (ddt, $J_{H,H}$ = 2.6, $J_{H,H}$ = 5.8, $J_{H,P}$ = 12.2 Hz, 2 H, CH_2-C=), 1.21 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 208.6 (d, $J_{C,P}$ = 5.0 Hz, =C=), 164.0 (C=O), 150.9 (C=O), 144.5 (=CH uracil), 102.2 (=CH uracil), 94.8 (d, $J_{C,P}$ = 187.6 Hz, P-C=), 89.2 (d, $J_{C,P}$ = 16.1 Hz, C=*C*-H), 62.5 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 62.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2OP), 59.8 (d, $J_{C,P}$ = 6.5 Hz, CH_2OH), 45.3 (d, $J_{C,P}$ = 7.0 Hz, CH_2N), 31.4 (d, $J_{C,P}$ = 6.0 Hz, CH_2), 16.0 (d, $J_{C,P}$ = 6.0 Hz, 2 × CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.91 ppm. $C_{14}H_{21}N_2O_6P$ (344.30): calcd. C 48.84, H 6.15, N 8.14, P 9.00; found C 49.00, H 6.23, N 7.99, P 8.91.

Diethyl 1-(2-Hydroxyethyl)-4-[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-1,2-butadienylphosphonate (30): TLC: R_f = 0.57 ($CHCl_3$/MeOH, 10:1.2). ^1H NMR ($CDCl_3$): δ = 10.19 (br. s, 1 H, NH), 7.22 (s, 1 H, =CH thymine), 5.55 (m, 1 H, =CH), 4.56−4.23 (m, 2 H, CH_2N), 4.16−4.00 (m, 4 H, 2 × CH_3CH_2OP), 3.73 (t, $J_{H,H}$ = 5.6 Hz, 2 H, $HOCH_2$), 3.50 (br. s, 1 H, OH), 2.38 (ddt, $J_{H,H}$ = 2.6, $J_{H,H}$ = 6.0, $J_{H,P}$ = 12.0 Hz, 2 H, CH_2-C=), 1.90 (s, 3 H, CH_3, thymine), 1.31 (t, $J_{H,H}$ = 7.4 Hz, 3 H, CH_3CH_2OP), 1.30 (t, $J_{H,H}$ = 7.5 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 208.7 (d, $J_{C,P}$ = 5.5 Hz, =C=), 164.4 (C=O), 151.2 (C=O), 140.2 (=CH thymine), 111.0 (=*C*-CH_3 thymine), 95.1 (d, $J_{C,P}$ = 187.1 Hz, P-C=), 89.4 (d, $J_{C,P}$ = 16.1 Hz, C=*C*-H), 62.5 (d, $J_{C,P}$ =

6.0 Hz, 2 × CH_3CH_2OP), 60.1 (d, $J_{C,P}$ = 6.5 Hz, CH_2OH), 45.2 (d, $J_{C,P}$ = 7.0 Hz, CH_2N), 31.6 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 16.2 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 16.1 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 12.1 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.01 ppm. $C_{15}H_{23}N_2O_6P$ (358.33): calcd. C 50.28, H 6.47, N 7.82, P 8.64; found C 50.42, H 6.54, N 7.66, P 8.54.

Diethyl 4-[4-Amino-2-oxo-1(2*H*)-pyrimidinyl]-1-(2-hydroxyethyl)-1,2-butadienylphosphonate (31): TLC: R_f = 0.35 ($CHCl_3$/MeOH, 10:2.0). ^1H NMR ($CDCl_3$): δ = 7.70 (br. s, 1 H, NH), 7.42 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 7.00 (br. s, 1 H, NH), 5.97 (d, $J_{H,H}$ = 7.2 Hz, 1 H, =CH cytosine), 5.63 (m, 1 H, =CH), 4.78 (br. s, 1 H, OH), 4.64−4.26 (m, 2 H, N-CH_2), 4.15−3.98 (m, 4 H, 2 × CH_3CH_2OP), 3.74 (t, $J_{H,H}$ = 6.0 Hz, 2 H, $HOCH_2$), 2.36 (ddt, $J_{H,H}$ = 2.8, $J_{H,H}$ = 6.0, $J_{H,P}$ = 12.0 Hz, 2 H, CH_2-C=), 1.33 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2OP), 1.32 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 208.6 (d, $J_{C,P}$ = 5.5 Hz, =C=), 166.3 (C=O), 156.6 (C-NH_2), 146.0 (=CH cytosine), 95.6 (=CH cytosine), 94.4 (d, $J_{C,P}$ = 186.6 Hz, P-C=), 90.0 (d, $J_{C,P}$ = 16.1 Hz, C=*C*-H), 62.3 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 59.5 (d, $J_{C,P}$ = 7.0 Hz, CH_2OH), 46.8 (CH_2N), 31.4 (d, $J_{C,P}$ = 5.5 Hz, CH_2), 16.0 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.47, 18.67 ppm. $C_{14}H_{22}N_3O_5P$ (343.32): calcd. C 48.98 H, 6.46, N 12.24, P 9.02; found C 50.20, H 6.60, N 12.08, P 8.88.

Diethyl 4-(6-Amino-9*H*−purin-9-yl)-1-(2-hydroxyethyl)-1,2-butadienylphosphonate (32): TLC: R_f = 0.37 ($CHCl_3$/MeOH, 10:1.2). ^1H NMR ($CDCl_3$): δ = 8.23 (s, 1 H, =CH, adenine), 7.87 (s, 1 H, =CH, adenine), 5.86 (br. s, 2 H, NH_2), 5.56 (m, 1 H, =CH), 5.00−4.76 (m, 2 H, CH_2N), 4.14−3.94 (m, 4 H, 2 × CH_3CH_2OP), 3.86 (t, $J_{H,H}$ = 5.5 Hz, 2 H, $HOCH_2$), 2.36 (ddt, $J_{H,H}$ = 2.5, $J_{H,H}$ = 5.5, $J_{H,P}$ = 12.0 Hz, 2 H, CH_2-C=), 1.80 (br. s, 1 H, OH + H_2O), 1.29 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP) ppm. ^{13}C NMR (CD_3OD): δ = 207.8 (d, $J_{C,P}$ = 5.5 Hz, =C=), 155.2 (=C, adenine), 151.7 (=CH, adenine), 148.6 (=C, adenine), 141.0 (=CH, adenine), 118.4 (=C, adenine), 93.6 (d, $J_{C,P}$ = 188.6 Hz, P-C=), 90.4 (d, $J_{C,P}$ = 16.1 Hz, =*C*-H), 62.2 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 62.0 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP), 58.8 (d, $J_{C,P}$ = 6.5 Hz, CH_2OH), 39.5 (CH_2N), 30.4 (d, $J_{C,P}$ = 6.0 Hz, CH_2), 14.6 (d, $J_{C,P}$ = 6.5 Hz, 2 × CH_3CH_2OP) ppm. ^{31}P NMR (CD_3OD): δ = 25.21 ppm. $C_{15}H_{22}N_5O_4P$ (367.34): calcd. C 49.04, H 6.04, N 19.07, P 8.43; found C 49.22, H 6.16, N 18.89, P 8.29.

General Procedure for the Preparation of Phosphonates 33−36. Diethyl 6-{[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]methyl}-6-methyl-3,6-dihydro-2*H*-pyran-4-ylphosphonate (33): Silver nitrate (0.07 g) was added to a round-bottomed flask equipped with a reflux condenser and a magnetic stirring bar. The flask was flushed with N_2 and a THF/water (20:0.5) mixture (10 mL) was added, followed by **25** (0.72 g, 0.002 mol), and the solution was heated to reflux for 6 h. The reaction was monitored by TLC on silica gel. The solvent was evaporated in vacuo and the residue was chromatographed on a column with silica gel ($CHCl_3$/MeOH, 10:1.0). Yield 60% (0.44 g). TLC: R_f = 0.57 ($CHCl_3$/MeOH, 10:1.0). ^1H NMR ($CDCl_3$): δ = 9.97 (br. s, 1 H, NH), 7.36 (d, $J_{H,H}$ = 7.7 Hz, 1 H, =CH uracil), 6.57 (d, $J_{H,P}$ = 22.0 Hz, 1 H, PC=*CH*) 5.62 (d, $J_{H,H}$ = 7.7 Hz, 1 H, =CH uracil), 4.06−3.80 (m, 6 H, 2 × CH_3CH_2OP + OCH_2CH_2), 3.73−3.63 (m, 2 H, CH_2N), 2.15 (dt, $J_{H,H}$ = 6.0, $J_{H,P}$ = 5.0 Hz, 2 H, CH_2-C=), 1.28 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP), 1.27 (d, $J_{H,P}$ = 1.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.8 (C=O), 151.1 (C=O), 145.7 (=CH uracil), 142.4 (d, $J_{C,P}$ = 7.7 Hz, P-C=*CH*), 128.4 (d, $J_{C,P}$ = 184.9 Hz, P-C=), 100.9 (=CH uracil), 75.2 (d, $J_{C,P}$ = 16.5 Hz, C), 61.9 (d, $J_{C,P}$ = 5.7 Hz, CH_3CH_2OP), 61.9 (d, $J_{C,P}$ = 5.8 Hz, CH_3CH_2OP), 58.9 (d, $J_{C,P}$ = 9.0 Hz, CH_2O), 53.2 (d, $J_{C,P}$ = 2.0 Hz, CH_2N), 24.0 (d, $J_{C,P}$ = 7.7 Hz, =C-CH_2), 21.6 (d, $J_{C,P}$ = 1.6 Hz, CH_3), 16.1 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 16.0 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.28 ppm. $C_{15}H_{23}N_2O_6P$ (358.33): calcd. C 50.28, H 6.47, N 7.82, P 8.64; found C 50.21, H 6.52, N 7.68, P 8.51.

Diethyl 6-Methyl-6-{[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]methyl}-3,6-dihydro-2*H*-pyran-4-ylphosphonate (34): TLC: R_f = 0.55 ($CHCl_3$/MeOH, 10:1.0). ^1H NMR ($CDCl_3$): δ = 9.71 (br. s, 1 H, NH), 7.11 (q, $J_{H,H}$ = 1.0 Hz, 1 H, =CH thymine), 6.50 (d, $J_{H,P}$ = 22.0 Hz, 1 H, PC=*CH*) 4.04−3.90 (m, 6 H, 2 × CH_3CH_2OP + OCH_2CH_2), 3.91−3.57 (m, 2 H, CH_2N), 2.09 (dt, $J_{H,H}$ = 6.0, $J_{H,P}$ = 4.7 Hz, 2 H, CH_2-C=), 1.81 (d, $J_{H,H}$ = 1.0 Hz, CH_3, thymine), 1.22 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP), 1.20 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 164.3 (C=O), 151.2 (C=O), 142.6 (d, $J_{C,P}$ = 7.7 Hz, P-C=*CH*), 141.5 (=CH thymine), 128.2 (d, $J_{C,P}$ = 185.0 Hz, P-C=), 109.3 (=*C*-CH_3 thymine), 75.2 (d, $J_{C,P}$ = 16.5 Hz, C), 61.9 (d, $J_{C,P}$ = 5.8 Hz, 2 × CH_3CH_2OP), 58.9 (d, $J_{C,P}$ = 9.0 Hz, CH_2O), 53.0 (d, $J_{C,P}$ = 1.9 Hz, CH_2N), 24.0 (d, $J_{C,P}$ = 7.8 Hz, =C-CH_2), 21.6 (d, $J_{C,P}$ = 1.7 Hz, CH_3), 16.1 (d, $J_{C,P}$ = 6.2 Hz, 2 × CH_3CH_2OP), 12.1 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.37 ppm. $C_{16}H_{25}N_2O_6P$ (372.35): calcd. C 51.61, H 6.77, N 7.52, P 8.32; found C 51.74, H 6.70, N 7.41, P 8.14.

Diethyl 6-{[4-Amino-2-oxo-1(2*H*)-pyrimidinyl]methyl}-6-methyl-3,6-dihydro-2*H*-pyran-4-ylphosphonate (35): TLC: R_f = 0.42 ($CHCl_3$/MeOH, 10:1.5). ^1H NMR ($CDCl_3$): δ = 7.75 (br. s, 2 H, NH_2), 7.37 (d, $J_{H,H}$ = 7.3 Hz, 1 H, =CH cytosine), 6.55 (d, $J_{H,P}$ = 22.3 Hz, 1 H, *CH*=CP), 5.92 (d, $J_{H,H}$ = 7.3 Hz, 1 H, =CH cytosine), 4.35 and 3.49 (AB, $J_{H,H}$ = 14.0 Hz, 2 H, N-CH_2), 3.98 (dq, $J_{H,P}$ = 7.0, $J_{H,P}$ = 7.0 Hz, 4 H, 2 × CH_3CH_2OP), 3.93−3.56 (m, 2 H, OCH_2), 1.99 (m, 2 H, CH_2-C=), 1.24 (t, $J_{H,H}$ = 6.9 Hz, 3 H, CH_3CH_2OP), 1.24 (s, 3 H, CH_3-C), 1.15 (t, $J_{H,H}$ = 7.1 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 165.5 (C=O), 156.4 (C-NH_2), 146.4 (=CH cytosine), 144.1 (d, $J_{C,P}$ = 8.6 Hz, PC=*CH*), 127.3 (d, $J_{C,P}$ = 183.1 Hz, P*C*=CH), 94.7 (=CH cytosine), 75.6 (d, $J_{C,P}$ = 16.6 Hz, C), 62.1 (d, $J_{C,P}$ = 6.0 Hz, CH_2OP), 61.9 (d, $J_{C,P}$ = 5.5 Hz, CH_2OP), 58.8 (d, $J_{C,P}$ = 10.1 Hz, CH_2O), 55.1 (CH_2N), 24.1 (d, $J_{C,P}$ = 7.5 Hz, CH_2), 21.9 (CCH_3), 16.2 (d, $J_{C,P}$ = 6.0 Hz, 2 × CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.10 ppm. $C_{15}H_{24}N_3O_5P$ (357.34): calcd. C 50.42 H, 6.77, N 11.76, P 8.67; found C 50.49, H 6.80, N 11.78, P 8.75.

Diethyl 6-[(6-Amino-9*H*-purin-9-yl)methyl]-6-methyl-3,6-dihydro-2*H*-pyran-4-ylphosphonate (36): TLC: R_f = 0.49 ($CHCl_3$/MeOH, 10:1.5). ^1H NMR ($CDCl_3$): δ = 8.35 (s, 1 H, =CH, adenine), 7.93 (s, 1 H, =CH, adenine), 6.61 (d, $J_{H,P}$ = 21.4 Hz, 1 H, PC=*CH*), 5.82 (br. s, 2 H, NH_2), 4.44 and 4.19 (AB, 2 H, $J_{H,H}$ = 14.2 Hz, CH_2N), 3.94−3.48 (m, 6 H, 2 × CH_3CH_2OP + CH_2CH_2O), 2.06 (m, 2 H, CH_2-C=), 1.33 (s, $J_{H,P}$ = 6.7 Hz, 3 H, CH_3), 1.21 (t, $J_{H,H}$ = 6.90 Hz, 3 H, CH_3CH_2OP), 1.18 (t, $J_{H,H}$ = 6.90 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 155.6 (=C, adenine), 152.5 (=CH, adenine), 149.9 (=C, adenine), 142.8 (d, $J_{C,P}$ = 7.5 Hz, P-C=*CH*), 141.4 (=CH, adenine), 128.1 (d, $J_{C,P}$ = 183.7 Hz, P-C=), 118.3 (=C, adenine), 74.3 (d, $J_{C,P}$ = 16.4 Hz, C), 61.4 (d, $J_{C,P}$ = 4.9 Hz, CH_3CH_2OP), 61.3 (d, $J_{C,P}$ = 4.0 Hz, CH_3CH_2OP), 58.9 (d, $J_{C,P}$ = 9.1 Hz, CH_2CH_2O), 50.1 (CH_2N), 23.6 (d, $J_{C,P}$ = 7.6 Hz, =CH-CH_2), 21.6 (d, $J_{C,P}$ = 1.5 Hz,CH_3), 15.9 (d, $J_{C,P}$ = 6.0 Hz, 2 × CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.02 ppm. $C_{16}H_{24}N_5O_4P$ (381.37): calcd. C 50.39, H 6.34, N 18.36, P 8.12; found C 50.24, H 6.24, N 18.27, P 8.01.

Diethyl 6-{[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]methyl}]-3,6-dihydro-2*H*-pyran-4-ylphosphonate (37): TLC: R_f = 0.4 ($CHCl_3$/

MeOH, 10:1.0). ^{1}H NMR ($CDCl_3$): δ = 8.97 (br. s, 1 H, NH), 7.31 (d, $J_{H,H}$ = 7.8 Hz, 1 H, =CH uracil), 6.65 (d, $J_{H,P}$ = 22.0 Hz, 1 H, PC=*CH*) 5.70 (d, $J_{H,H}$ = 7.8 Hz, 1 H, =CH uracil), 4.52 (m, 1 H, CH), 4.19−4.05 (m, 6 H, 2 × CH_3CH_2OP + OCH_2CH_2), 3.68 (m, 2 H, CH_2N), 2.50−2.11 (m, 2 H, CH_2-C=), 1.37 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2OP), 1.36 (t, $J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 164.1 (C=O), 151.0 (C=O), 145.5 (=CH uracil), 138.5 (d, $J_{C,P}$ = 8.0 Hz, P-C=*CH*), 129.2 (d, $J_{C,P}$ = 185.1 Hz, P-C=), 101.3 (=CH uracil), 72.3 (d, $J_{C,P}$ = 17.0 Hz, CH), 62.6 (d, $J_{C,P}$ = 9.6 Hz, CH_2O), 61.9 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2OP), 50.6 (CH_2N), 24.1 (d, $J_{C,P}$ = 7.5 Hz, =C-CH_2), 16.1 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.35 ppm. $C_{14}H_{21}N_2O_6P$ (344.30): calcd. C 48.84, H 6.15, N 8.14, P 9.00; found C 48.70, H 6.20, N 8.08, P 8.64.

Diethyl 6-{[5-Methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-methyl}-3,6-dihydro-2*H*-pyran-4-ylphosphonate (38): TLC: R_f = 0.58 ($CHCl_3$/MeOH, 10:1.0). ^{1}H NMR ($CDCl_3$): δ = 9.70 (br. s, 1 H, NH thymine), 7.03 (s, 1 H, =CH thymine), 6.56 (d, $J_{H,P}$ = 21.8 Hz, 1 H, PC=*CH*), 4.41 (m, 1 H, CH), 4.09−3.55 (m, 6 H, 2 × CH_3CH_2OP, CH_2O), 3.60−3.49 (m, 2 H, CH_2N), 2.48−1.98 (m, 2 H, CH_2-C=), 1.84 (s, 3 H, CH_3 thymine), 1.26 (t, $J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 164.4 (C=O), 151.1 (C=O), 141.5 (=CH thymine), 138.8 (d, $J_{C,P}$ = 8.0 Hz, P-C=*CH*), 129.2 (d, $J_{C,P}$ = 185.6 Hz, P-C=), 109.8 (=CH thymine), 72.5 (d, $J_{C,P}$ = 16.6 Hz, CH), 62.7 (d, $J_{C,P}$ = 9.1 Hz, CH_2O), 62.0 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2OP), 50.6 (CH_2N), 24.2 (d, $J_{C,P}$ = 7.5 Hz, =C-CH_2), 16.2 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 12.2 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.35 ppm. $C_{15}H_{23}N_2O_6P$ (358.33): calcd. C 50.28, H 6.47, N 7.82, P 8.64; found C 50.11, H 6.50, N 7.72, P 8.50.

Diethyl 2-{[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]ethyl}-4,5-dihydro-3-furanylphosphonate (39): TLC: R_f = 0.51 ($CHCl_3$/MeOH, 10:1.0). ^{1}H NMR ($CDCl_3$): δ = 8.90 (br. s, 1 H, NH), 7.31 (d, $J_{H,H}$ = 7.9 Hz, 1 H, =CH uracil), 5.72 (dd, $J_{H,H}$ = 7.9, $J_{H,P}$ = 2.2 Hz, 1 H, =CH uracil), 4.43 (t, $J_{H,H}$ = 9.6 Hz, 2 H, OCH_2), 4.18−4.10 (m, 4 H, 2 × CH_3CH_2OP), 4.00 (t, $J_{H,H}$ = 6.7 Hz, 2 H, CH_2N), 2.99 (t, $J_{H,H}$ = 6.7 Hz, 2 H, CH_2CH_2N), 2.81 (t, $J_{H,H}$ = 6.7 Hz, 2 H, CH_2-C=), 1.35 (t, $J_{H,H}$ = 7.0 Hz, 6 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 167.8 (d, $J_{C,P}$ = 30.7 Hz, =C-), 163.5 (C=O), 150.5 (C=O), 144.7 (=CH uracil), 101.8 (=CH uracil), 96.3 (d, $J_{C,P}$ = 216.8 Hz, P-C=), 70.5 (d, $J_{C,P}$ = 12.1 Hz, OCH_2), 61.4 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2OP), 46.2 (CH_2N), 31.3 (d, $J_{C,P}$ = 9.6 Hz, CH_2), 26.9 (CH_2), 16.3 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2OP) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.52 ppm. $C_{14}H_{21}N_2O_6P$ (344.30): calcd. C 48.84, H 6.15, N 8.14, P 9.00; found C 49.11, H 6.12, N 7.98, P 9.17.

Diethyl 2-{[5-Methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-ethyl}-4,5-dihydro-3-furanylphosphonate (40): TLC: R_f = 0.45 ($CHCl_3$/MeOH, 10:1.0). ^{1}H NMR ($CDCl_3$): δ = 9.30 (br. s, 1 H, NH), 7.08 (s, 1 H, =CH thymine), 4.34 (t, $J_{H,H}$ = 9.6 Hz, 2 H, OCH_2), 4.08−3.91 (m, 4 H, 2 × CH_3CH_2OP), 3.89 (t, $J_{H,H}$ = 6.5 Hz, 2 H, CH_2N), 2.90 (t, $J_{H,H}$ = 6.5 Hz, 2 H, CH_2CH_2N), 2.72 (t, $J_{H,H}$ = 9.6 Hz, 2 H, CH_2-C=), 1.99 (s, 3 H, CH_3 thymine), 1.27 (t, $J_{H,H}$ = 7.0 Hz, 6 H, CH_3CH_2OP) ppm. ^{13}C NMR ($CDCl_3$): δ = 168.0 (d, $J_{C,P}$ = 31.19 Hz, =C-), 164.4 (C=O), 150.6 (C=O), 140.6 (=CH thymine), 110.8 (=C thymine), 94.3 (d, $J_{C,P}$ = 216.6 Hz, P-C=), 70.4 (d, $J_{C,P}$ = 11.6 Hz, OCH_2), 61.3 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 45.7 (CH_2N), 31.2 (d, $J_{C,P}$ = 9.1 Hz, CH_2), 26.8 (CH_2), 16.2 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2OP), 12.1 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 18.64 ppm. $C_{15}H_{23}N_2O_6P$ (358.33): calcd. C 50.28, H 6.47, N 7.82, P 8.64; found C 50.02, H 6.59, N 7.90, P 8.88.

General Procedure for the Preparation of Phosphonates 9a−d. 6-{[2,4-Dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]methyl}-6-methyl-3,6-dihydro-2*H*-pyran-4-ylphosphonate (9a): Bromotrimethylsilane (1.5 g, 0.01 mol) was added dropwise, from a syringe, to the diester **33** (0.72 g, 0.002 mol) in 10 mL of CH_3CN at room temperature, and the reaction mixture was stirred in a closed flask overnight. The solvents were removed under reduced pressure and the residual oil was dissolved in CH_3CN (40 mL), treated with water (0.5 mL), and the solution stirred at 40−50 °C for 1 h. The reaction solvents were evaporated in vacuo, and the product was crystallized from hexane to give 0.44 g (72%) of compound **9a**. M.p. 210−212 °C. ^{1}H NMR (CD_3OD): δ = 7.52 (d, $J_{H,H}$ = 7.6 Hz, 1 H, =CH uracil), 6.46 (dt, $J_{H,P}$ = 22.0, $J_{H,P}$ = 1.5 Hz, 1 H, PC=*CH*) 5.52 (d, $J_{H,H}$ = 7.6 Hz, 1 H, =CH uracil), 5.00 (br. s, 2OH + H_2O from solution), 4.08 and 3.77 (AB, $J_{H,H}$ = 14.1 Hz, 2 H, CH_2N), 3.94−3.46 (m, 2 H, CH_2CH_2O), 2.20 (dt, $J_{H,H}$ = 6.0, $J_{H,P}$ = 5.0 Hz, 2 H, CH_2-C=), 1.28 (s, 3 H, CH_3) ppm. ^{13}C NMR (CD_3OD): δ = 164.8 (C=O), 151.1 (C=O), 146.7 (=CH uracil), 139.1 (d, $J_{C,P}$ = 7.5 Hz, P-C=*CH*), 130.5 (d, $J_{C,P}$ = 184.1 Hz, P-C=), 99.3 (=CH uracil), 74.3 (d, $J_{C,P}$ = 16.5 Hz, C), 58.2 (d, $J_{C,P}$ = 8.6 Hz, CH_2O), 52.3 (CH_2N), 23.3 (d, $J_{C,P}$ = 9.1 Hz, =C-CH_2), 20.5 (CH_3) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.28 ppm. $C_{11}H_{15}N_2O_6P$ (302.22): calcd. C 43.72, H 5.00, N 9.27, P 10.25; found C 43.64, H 5.08, N 9.10, P 10.13.

6-Methyl-6-{[5-methyl-2,4-dioxo-3,4-dihydro-1(2*H*)-pyrimidinyl]-methyl}-3,6-dihydro-2*H*-pyran-4-ylphosphonate (9b): M.p. 198−200 °C. ^{1}H NMR (CD_3OD): δ = 7.39 (q, $J_{H,H}$ = 1.0 Hz, 1 H, =CH thymine), 6.48 (dt, $J_{H,P}$ = 21.8, $J_{H,P}$ = 1.7 Hz, 1 H, PC=*CH*) 5.00 (br. s, 2 OH + H_2O from solution), 4.02 and 3.78 (AB, $J_{H,H}$ = 14.2 Hz, 2 H, CH_2N), 3.97−3.45 (m, 2 H, CH_2CH_2O), 2.18 (dt, $J_{H,H}$ = 6.5, $J_{H,P}$ = 5.0 Hz, 2 H, CH_2-C=), 1.86 (d, $J_{H,H}$ = 1.0 Hz, CH_3, thymine), 1.32 (s, 3 H, CH_3) ppm. ^{13}C NMR (CD_3OD): δ = 164.9 (C=O), 151.3 (C=O), 142.4 (=CH thymine), 139.2 (d, $J_{C,P}$ = 7.5 Hz, P-C=*CH*), 130.4 (d, $J_{C,P}$ = 183.6 Hz, P-C=), 108.0 (=*C*-CH_3 thymine), 74.4 (d, $J_{C,P}$ = 16.6 Hz, C), 58.2 (d, $J_{C,P}$ = 9.1 Hz, CH_2O), 52.2 (d, $J_{C,P}$ = 1.7 Hz, CH_2N), 23.4 (d, $J_{C,P}$ = 8.6 Hz, =C-CH_2), 20.5 (d, $J_{C,P}$ = 1.5 Hz, CH_3), 10.3 (CH_3, thymine) ppm. ^{31}P NMR ($CDCl_3$): δ = 17.37 ppm. $C_{12}H_{17}N_2O_6P$ (330.25): calcd. C 43.64, H 5.19, N 12.72, P 9.38; found C 43.50, H 5.29, N 12.64, P 9.24.

6-{[4-Amino-2-oxo-1(2*H*)-pyrimidinyl]methyl}-6-methyl-3,6-dihydro-2*H*-pyran-4-ylphosphonate (9c): M.p. 248−250 °C. ^{1}H NMR (D_2O): δ = 7.71 (d, $J_{H,H}$ = 7.7 Hz, 1 H, =CH cytosine), 6.32 (dt, $J_{H,P}$ = 21.7, $J_{H,H}$ = 1.0 Hz, 1 H, *CH*=CP), 6.04 (d, $J_{H,H}$ = 7.7 Hz, 1 H, =CH cytosine), 4.08 (s, 2OH + NH_2 + H_2O), 4.15 and 3.78 (AB, $J_{H,H}$ = 14.4 Hz, 2 H, N-CH_2), 3.90−3.59 (m, 2 H, OCH_2), 1.99 (dt, $J_{H,P}$ = 6.0, $J_{H,H}$ = 5.1 Hz, 2 H, CH_2-C=), 1.23 (s, 3 H, CH_3-C) ppm. ^{13}C NMR (D_2O): δ = 159.7 (C=O), 150.9 (=CH cytosine), 149.4 (C-NH_2), 139.2 (d, $J_{C,P}$ = 8.0 Hz, PC=*CH*), 131.9 (d, $J_{C,P}$ = 179.6 Hz, P*C*=CH), 94.0 (=CH cytosine), 75.8 (d, $J_{C,P}$ = 16.6 Hz, C), 59.7 (d, $J_{C,P}$ = 9.1 Hz, CH_2O), 54.5 (d, $J_{C,P}$ = 2.0 Hz, CH_2N), 24.1 (d, $J_{C,P}$ = 9.1 Hz, CH_2), 21.5 (d, $J_{C,P}$ = 2.0 Hz, CCH_3) ppm. ^{31}P NMR (D_2O): δ = 14.67 ppm. $C_{11}H_{16}N_3O_5P$ (287.23): calcd. C 46.00 H, 5.61, N 9.75, P 10.78; found C 46.09, H 5.69, N 9.68, P 10.62.

6-[(6-Amino-9*H*-purin-9-yl)methyl]-6-methyl-3,6-dihydro-2*H*-pyran-4-ylphosphonate (9d): M.p. 170−173 °C. ^{1}H NMR (CD_3OD): δ = 8.39 (s, 1 H, =CH, adenine), 8.27 (s, 1 H, =CH, adenine), 6.51 (d, $J_{H,P}$ = 21.8 Hz, 1 H, PC=*CH*), 5.08 (s, 2OH + NH_2 + H_2O), 4.57 and 4.39 (AB, 2 H, $J_{H,H}$ = 14.2 Hz, CH_2N), 3.98−3.86 (m, 1 H, *CH*HO), 3.77−3.65 (m, 1 H, CH*H*O), 2.13−1.76 (m, 2 H, CH_2-C=), 1.36 (s, 3 H, CH_3) ppm. ^{13}C NMR (CD_3OD): δ = 149.4

(=C, adenine), 148.6 (=C, adenine), 144.9 (=CH, adenine), 143.2 (=CH, adenine), 139.3 (d, $J_{C,P}$ = 7.5 Hz, P-C=*CH*), 130.8 (d, $J_{C,P}$ = 183.6 Hz, P-C=), 116.8 (=C, adenine), 73.5 (d, $J_{C,P}$ = 16.6 Hz, C), 58.4 (d, $J_{C,P}$ = 9.1 Hz, CH_2O), 50.1 (CH_2N), 23.6 (d, $J_{C,P}$ = 8.6 Hz, =CH-*CH_2*), 20.3 (d, $J_{C,P}$ = 2.0 Hz,CH_3) ppm. ^{31}P NMR (CD_3OD): δ = 14.63 ppm. $C_{12}H_{16}N_5O_4P$ (325.26): calcd. C 44.31, H 4.96, N 21.53, P 9.52; found C 44.43, H 5.03, N 21.48, P 9.40.

X-ray Crystal Structure Determination of 33: $C_{15}H_{25}N_2O_7P$, M = 376.34, monoclinic, a = 8.719(2), b = 11.030(2), c = 19.187(4) Å, β = 94.44(3)°, V = 1839.7(7) Å^3, T = 293(2) K, space group $P2_1/c$ (no. 14), Z = 4, μ(Mo-K_α) = 0.136 mm^{-1}, 3454 reflections measured, 3227 unique (R_{int} = 0.029) which were used in all calculations. The final $wR(F^2)$ was 0.0796 [$I > 2\sigma(I)$].

X-ray Crystal Structure Determination of 36: $C_{16}H_{24}N_5O_4P$, M = 381.37, orthorhombic, a = 19.368(4), b = 12.863(3), c = 7.747(2) Å, V = 1930.0(8) Å^3, T = 293(2) K, space group $Pna2_1$ (no. 33), Z = 4, μ(Mo-K_α) = 0.131 mm^{-1}, 1828 reflections measured, 1828 unique (R_{int} = 0.0) which were used in all calculations. The final $wR(F^2)$ was 0.0784 [$I > 2\sigma(I)$].

CCDC-244470 (**33**) and -244471 (**36**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk).

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