Preparation of *N*-(alk-1-enyl) nucleobase compounds by Horner and Horner–Wadsworth–Emmons reactions

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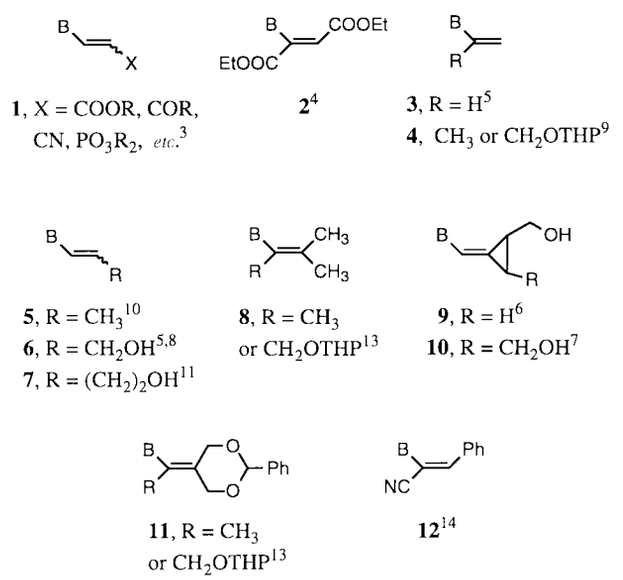
A series of new N^9-(alk-1-enyl)adenines and N^1-(alk-1-enyl)thymines has been prepared by Horner reactions of the new phosphine oxides N^9-(diphenylphosphorylmethyl)adenine and N^1-(diphenylphosphorylmethyl)thymine derivatives **13a–c**, or Horner–Wadsworth–Emmons reactions of the corresponding new phosphonates **14a–b**, with benzaldehyde and various ketones. Yields were highest for the Horner reactions (10–79%), and were limited by steric hindrance, enolization of the ketones, and decomposition of some of the N^1-(alk-1-enyl)thymines in the presence of excess base (NaH). Butanal gave mixtures of products under Horner conditions, probably because aldol reactions intervened.

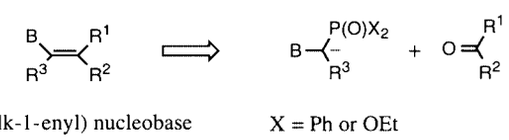
Introduction

N^9-Alkyl derivatives of the purine nucleobases adenine and guanine, and N^1-alkyl derivatives of the pyrimidine nucleobases cytosine, thymine and uracil, are well known and have been extensively investigated for their biological activity, *e.g.* as antiviral compounds.[1] The corresponding alk-1-enyl compounds, which are enamines, have, apart from Zemlicka's allenol derivatives,[2] been much less studied, probably because general preparative methods are lacking. Known methods (Scheme 1) to



Scheme 1 Known *N*-(alk-1-enyl) nucleobases.

prepare such compounds are: (i) The Michael addition of a nucleobase to activated alkynes, which furnishes disubstituted alkenyl nucleobases **1**,[3] or trisubstituted analogs **2**.[4] (ii) Alkylation of nucleobases with 1,2-dihaloalkanes followed by elimination, which has led to vinyl nucleobases **3**[5] and the alk-1-enyl nucleobases **6**,[5] **9**[6] and **10**.[7] Similar base-induced eliminations of a 2-mesyl[8] or a 1-nitro group[9] have led to the alkenyl nucleobases **6** and **4**, respectively. (iii) Base catalysed rearrangement of alk-2-enyl nucleobases to give the alk-1-enyl nucleobases **5**[10] and **7**[11] as well as a few buta-1,3-dienyl nucleobases.[12] (iv) A few tetrasubstituted alkenyl nucleobases **8** and **11** (B = 9-adenyl) have been obtained by double $S_{RN}1$ substitutions followed by Grob-type eliminations.[13] (v) A trisubstituted alk-1-enyl adenine derivative **12** has recently been made by aldol type condensation of a cyanomethyl adenine with benzaldehyde.[14] We are interested in general methods to prepare di-, tri- and tetrasubstituted alkenes with a nucleobase as one of the substituents, and present here our results from a study of Horner and Horner–Wadsworth–Emmons (HWE) reactions to generate the alkenes (Scheme 2). To the best of our knowledge such



Scheme 2 Horner and HWE routes to *N*-(alk-1-enyl) nucleobases.

reactions have not been used before for the preparation of *N*-(alk-1-enyl) nucleobases. The present work has been limited to adenine and thymine as representative examples of the nucleobases, and to compounds with R^3 = H.

Results and discussion

Preparation of Horner and HWE reagents

The necessary Horner and HWE reagents shown in Scheme 2 can be obtained by alkylation of adenine and thymine. The nucleobases are poor nucleophiles, and nucleophilic substitution α to a phosphine oxide or a phosphonate is difficult, but with R^3 = H and 4-nitrobenzenesulfonate as the leaving group the new phosphine oxides **13** and phosphonates **14** could be prepared in 44–70% yields, as shown (Scheme 3). The anion of adenine, generated with sodium hydride, was mainly alkylated at *N*-9 (as shown by the characteristic shifts of C-4 and C-5 in the ^{13}C NMR[15]), and the minor *N*-7 isomer could be removed by column chromatography after *N*-6 protection with a dibutylformamidine group, to give **13a** and **14a**. 3-Benzoylthymine could be alkylated in DMF in the presence of excess potassium carbonate to give **13b** and **14b**, although the benzoyl group was not totally stable under these conditions. A more stable

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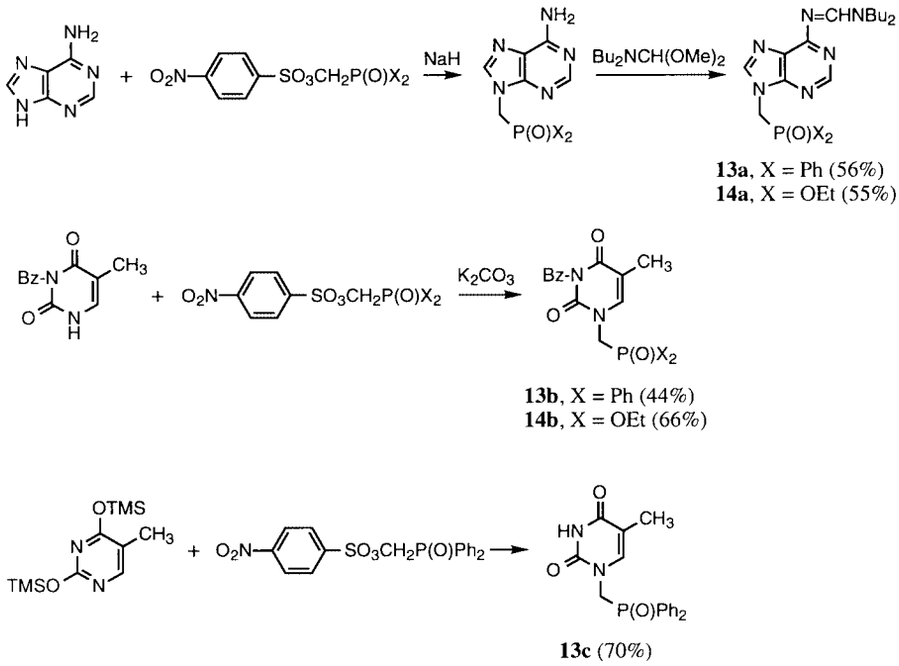
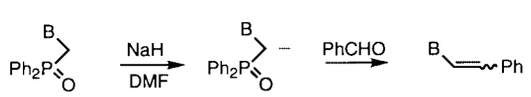


Scheme 3 Preparation of 9-adenyl- and 1-thymidyl-methylphosphine oxides **13** and methylphosphonates **14**.

protecting group such as the benzyloxymethyl (BOM) group was deemed unsuitable because it is removed by hydrogenation, which would probably reduce the *N*-(alk-1-enyl) nucleobase product. The unprotected thymine derivative **13c** was obtained from bis(trimethylsilyl)thymine, which was alkylated preferentially at the *N*-1 position (as shown by strong NOE effects between H-6 and CH_2). Alkylation of underivatised thymine under various conditions gave mostly dialkylated products.

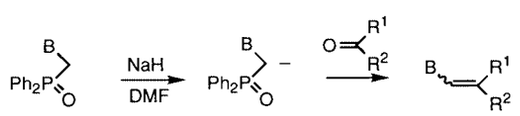
Horner reactions

The Horner reagents **13a–c** were treated with 1 equiv. of NaH (2 equiv. in the case of **13c**) in DMF for 1–2 h at 0 °C to give yellow or green anions. Addition of benzaldehyde as an example of a non-enolizable oxo compound and stirring at rt gave slowly the new alkenes **15a–c** as a mixture of *E* and *Z* isomers (Scheme 4). For the adenine derivative **13a** the product



Scheme 4 Horner reactions with benzaldehyde.

15a could be isolated after 1 day at rt in 65% yield as a 2:7 mixture of *E*- and *Z*-**15a**. The benzoyl protected thymine derivative **13b** gave a 55% isolated yield of **15b** (*E*:*Z* 1:5) after 1 day, but the yield decreased and the *E*:*Z* ratio increased when the reaction time was prolonged in the presence of excess of NaH. Since the yield of the *E* isomer stayed approximately constant this indicates that the *Z* isomer is unstable under the reaction conditions. The unprotected thymine derivative **13c**, transformed to the dianion with NaH, was converted to the alkene product **15c** (*E*:*Z* 1:2) in a yield similar to **15b** after 1 day. Reactions between the anions of **13a–c** and enolizable aliphatic aldehydes gave low yields of mixtures of *N*-(alk-1-enyl) nucleobases, probably because aldol condensations of the aldehydes competed effectively with the Horner reaction. Thus butanal and **13a–c** gave mixtures of products from which no pure *N*-(pent-1-enyl) nucleobases could be isolated. According to ^{1}H NMR on purified fractions some of the desired products were formed, but the main products were derived from the aldol dimer of butanal, 2-ethylhex-2-enal. In the case of **13c** the low yield of products was demonstrated by the fact that the starting material **13c** was isolated from the reaction mixture in 80% yield. With ketones the Horner anions derived from **13a–c** gave the new trisubstituted alkenes **16** in variable yields (Scheme 5).

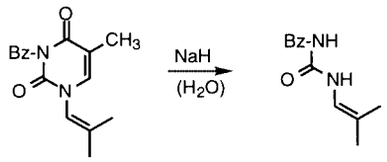


13a–c

B = A^dbf, **16aa**, R^1=R^2=Me (79%)
16ab, R^1=R^2=Pr (49%)
16ac, R^1,R^2 =(CH2)4 (66%)
16ad, R^1,R^2 =(CH2)5 (74%)
16ae, R^1 =Bu^t, R^2 =Me (34%)
16af, R^1 =PhOCH2, R^2 =Me (48%)
B = T^bz, **16ba**, R^1=R^2=Me (34%)
16bb, R^1=R^2=Pr (10%)
B = T, **16ca**, R^1=R^2=Me (40%)
16cb, R^1=R^2=Pr (44%)
16cc, R^1,R^2 =(CH2)5 (68%)

Scheme 5 Horner reactions with ketones.

The reactions were run at rt until TLC indicated that **13a–c** were absent or the amount did not decrease further (3 h to 5 days). The adenine derivative **13a** gave the highest yield (79%) with acetone and 34–74% with higher substituted ketones. No reaction was observed with the crowded di-*tert*-butyl ketone, or with the easily enolizable dibenzyl ketone; however the fairly easily enolizable cyclopentanone gave 66% of the Horner product **16ac**. The benzoyl protected thymine derivative **13b** with acetone and 1 equiv. of NaH gave 34% of **16ba**, but with excess of NaH the product was unstable. We were able to isolate a ring-opened product **17** from a reaction with excess NaH (Scheme 6). The formation of **17** may be explained by a Michael addition of H^-, or more probably OH^- from adventitious water, at C-6 of the thymine ring, followed by elimination of N-1 and hydrolysis at C-4; the alk-1-enyl substituent is expected to facilitate elimination of the N-1 group by resonance stabilisation, and the benzoyl group should facilitate hydrolysis at C-4. A similar reaction could explain the decomposition of the *Z*-**15b** isomer described above. With the more hindered heptan-4-one, **13b** gave a lower yield (10%) of the alkene



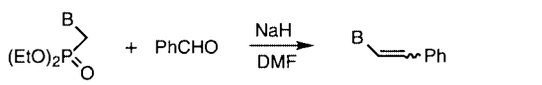
16ba **17**

Scheme 6 Ring-opened product **17** from the decomposition of **16ba**.

product **16bb**. The unprotected thymine derivative **13c** gave 40% of the alkene derivative **16ca** with acetone. No ring-opened product seemed to form in this case, but the reaction mixture turned brown, and a mixture of unidentified polar by-products was formed. With heptan-4-one, **13c** gave 44% of the alkene **16cb**, and with cyclohexanone 68% of the alkene **16cc**. The yields were higher than those obtained from the benzoyl protected **13b**, probably because **13b** suffered partial loss of the benzoyl protecting group during the reactions, and because of ring-opening reactions.

HWE reactions

Horner–Wadsworth–Emmons anions without resonance stabilizing substituents are generally not stable at ambient temperature,[16] but alkenes can be prepared from a mixture of unstablized phosphonates and oxo compounds upon addition of a strong base, and these reactions are usually faster than the corresponding Horner reactions. This was also the case for the phosphonates **14a** and **14b** (Scheme 7). The adenine derivative



14a–b **15a**, B = A^{dbf} (39%)
15b, B = T^{bz} (55%)

Scheme 7 HWE reactions with benzaldehyde.

14a and benzaldehyde in DMF with NaH gave after 2 h at 0 °C **15a** in 39% isolated yield as a 1 : 4 mixture of *E* and *Z* isomers. Longer reaction times at rt did not increase the yield. The thymine derivative **14b** with benzaldehyde and excess NaH in DMF gave after 1 h at rt **15b** (*E*:*Z* 1 : 3) in an isolated yield of 55%. The yield decreased and the *E*:*Z* ratio increased at longer reaction times, as was the case for the Horner reaction. With ketones the yields were lower for the HWE reactions than for the Horner reactions, most likely because the anions could not be preformed and the more strongly basic conditions favoured aldol condensations. Thus **14a** with acetone gave 18% of **16aa**, and with heptan-4-one only 2% of **16ab**. From **14b** and acetone only a 7% yield of **16ba** could be isolated.

Conclusion

A series of new N^9-(alk-1-enyl)adenines and N^1-(alk-1-enyl)-thymines has been prepared by Horner reactions of the phosphine oxides **13a–c** or Horner–Wadsworth–Emmons reactions of the phosphonates **14a–b** with benzaldehyde and various ketones. Yields were highest for the Horner reactions, where the adenine derivative **13a** gave 65–79% with benzaldehyde and unhindered ketones. Lower yields were obtained with sterically hindered ketones, although *tert*-butyl methyl ketone still gave a 34% yield of **16ae**, and yields were generally lower for the thymine derivatives than for the adenine derivatives, in part due to the N^1-(alk-1-enyl)thymines being unstable in the presence of strong base. Aliphatic aldehydes containing α-hydrogen atoms gave mixtures of products under Horner conditions, probably because competitive aldol reactions were faster, and enolate anion formation seems also a limiting factor for obtaining high yields from enolizable ketones, since the anions derived from **13** and **14** are strong bases. Despite these limitations the routes described here are complementary to previous known methods to prepare *N*-(alk-1-enyl) nucleobases, and open up a general route to trisubstituted alkenyl nucleobases.

Experimental

N,*N*-Dibutylformamide dimethyl acetal,[17] 3-benzoylthymine,[18] and (4-nitrophenylsulfonyloxymethyl)diphenylphosphine oxide[19] were prepared according to the literature. NaH was 55–60% in mineral oil from Aldrich. Diethyl phosphite was purum from Fluka. Aldehydes and ketones were 97–99% pure from Aldrich, Fluka, or Merck. Solvents were HPLC grade from LABSCAN, of which DMF and pyridine were dried over molecular sieves (Grace 4 Å) to a water content below 30 ppm, measured on a Metrom 652 KF-Coulometer. TLC was run on Merck 5554 silica 60 aluminium sheets, column chromatography on Merck 9385 silica 60 (0.040–0.063 mm). NMR spectra (reference tetramethylsilane for δ_H and δ_C, external 85% H_3PO_4 for δ_P, *J* values are given in Hz) were run on a Varian Mercury 300 MHz spectrometer, and FAB MS data obtained on a JEOL HX 110/110 Mass Spectrometer.

Diethyl (4-nitrophenylsulfonyloxymethyl)phosphonate

This compound was prepared in the same way as the published 4-chloro analogue.[20] The crude product from evaporation of the diethyl ether phase was recrystallized from EtOAc–hexane 1 : 1 v/v to give pure diethyl (4-nitrophenylsulfonyloxymethyl)-phosphonate (21.2 g, 60%) as light yellow crystals, mp 65.5–67 °C. NMR ($CDCl_3$): δ_P 14.7. δ_H 8.44 (2H, m, Ar), 8.15 (2H, m, Ar), 4.32 (2H, d, *J* 9.6, CH_2P), 4.17 (4H, dq, *J* 7.1 and 7.1, Et), 1.34 (6H, t, *J* 7.1, Et). δ_C 150.78, 140.53, 129.32, 124.37, 63.44 (d, *J* 6), 62.15 (d, *J* 169), 16.36 (d, *J* 6). FAB$^+$ MS: 354.0 (M + H$^+$ calc. 354.0) (Found: C, 37.5; H, 4.4; N, 3.95. Calc. for $C_{11}H_{16}NO_8PS$: C, 37.4; H, 4.6; N, 4.0%).

N^6-(Dibutylaminomethylene)-9-(diphenylphosphorylmethyl)-adenine (13a)

To a suspension of NaH (5.67 g, 55–60% in mineral oil, 0.13–0.14 mol) in dry DMF (1100 ml) was added adenine (13.5 g, 0.10 mol), and the mixture was stirred at rt under nitrogen for 3 h. A solution of (4-nitrophenylsulfonyloxymethyl)diphenyl-phosphine oxide (41.3 g, 0.10 mol) dissolved in DMF (250 ml) was added dropwise, and the mixture stirred at rt under nitrogen for 4 days. Ethanol (980 ml) was added and the solvents removed *in vacuo*. The residue was refluxed with water (600 ml), kept at 10 °C overnight and filtered. The residue (27.9 g), a 1 : 3 mixture of 7- and 9-(diphenylphosphorylmethyl)adenine (judged by NMR), was suspended under nitrogen in DMF (275 ml). *N*,*N*-Dibutylformamide dimethyl acetal (31.5 ml, 0.16 mol) was added in one portion and the solution was stirred for 3 days followed by evaporation *in vacuo*. The residue was purified by column chromatography on silica, eluted with EtOAc–Et_3N–MeOH 92 : 5 : 3 v/v/v, to give pure **13a** (27.4 g, 56%), R_f = 0.33, mp 130–131.5 °C. NMR (DMSO-d_6): δ_P 25.8. δ_H 8.89 (1H, s, CH=N), 8.32 (1H, s, adenine), 8.05 (1H, s, adenine), 7.87 (4H, m, phenyl), 7.57 (6H, m, phenyl), 5.41 (2H, d, *J* 5.8, CH_2P), 3.56 (2H, t, *J* 7.4, Bu), 3.42 (2H, t, *J* 7.0, Bu), 1.58 (4H, m, Bu), 1.31 (4H, m, Bu), 0.91 (6H, m, Bu). δ_C 158.8, 157.4, 151.4, 151.1, 142.0, 132.1, 130.9, 130.7, 130.6, 129.5, 128.6, 128.4, 124.0, 50.7, 44.2, 42.0 (d, *J* 72), 30.3, 28.5, 19.5, 19.0, 13.6, 13.5. FAB$^+$ MS: 489.0 (M + H$^+$ calc. 489.3) (Found: C, 66.3; H, 6.8; N, 17.1. Calc. for $C_{27}H_{33}N_6OP$: C, 66.4; H, 6.8; N, 17.2%).

3-Benzoyl-1-(diphenylphosphorylmethyl)thymine (13b)

To a solution of 3-benzoylthymine (1.98 g, 8.6 mmol) and (4-nitrophenylsulfonyloxymethyl)diphenylphosphine oxide (3.94 g, 9.4 mmol) in dry DMF (30 ml) was added solid K_2CO_3

(2.4 g, 17 mmol), and the mixture stirred at 55 °C under nitrogen for 2 days. The solvent was removed *in vacuo*, and the residue was partitioned between CH_2Cl_2 (200 ml) and sat. aq. NH_4Cl (100 ml). The organic phase was extracted with water (100 ml), brine (50 ml), dried over Na_2SO_4, and the solvent removed *in vacuo* to give the crude product (4.06 g). Flash chromatography on silica, with CH_2Cl_2–MeOH 98 : 2 v/v followed by CH_2Cl_2–MeOH 95 : 5 v/v as eluent, gave a nearly pure product (2.60 g), which was recrystallized from ethanol–water to give pure **13b** (1.68 g, 44%) as colourless crystals, mp 228–230 °C. NMR (DMSO-d_6): δ_P 26.7. δ_H 7.88–7.52 (16H, m, Ar + H6), 4.92 (2H, d, *J* 4.4, CH_2P), 1.82 (3H, s, CH_3). δ_C 168.9, 162.3, 148.8, 142.2, 135.3, 132.4, 131.2, 130.9, 130.8, 130.7, 129.9, 129.3, 128.8, 128.6, 108.4, 45.5 (d, *J* 73), 11.8. FAB^+ MS: 445.1 (M + H^+ calc. 445.1) (Found: C, 67.4; H, 4.5; N, 6.2. Calc. for $C_{25}H_{21}N_2O_4P$: C, 67.6; H, 4.8; N, 6.3%).

1-(Diphenylphosphorylmethyl)thymine (13c)

Bis(trimethylsilyl)acetamide (35 ml, 140 mmol) was added under nitrogen to a suspension of thymine (7.57 g, 60 mmol) in acetonitrile (40 ml), to give a clear solution after 5 min. (4-Nitrophenylsulfonyloxymethyl)diphenylphosphine oxide (8.35 g, 20 mmol) was then added, and the mixture heated at reflux under nitrogen for 4 days. The suspension was cooled to 0 °C and water (100 ml) and 2 M aq. NH_3 (10 ml) were added, followed by 4 M aq. acetic acid to pH *ca.* 5 (2 ml). After standing overnight the resulting precipitate was filtered off, washed with water and dissolved in 1 M aq. NaOH (100 ml). Small amounts of non-acidic impurities were extracted with dichloromethane (2 × 30 ml), and the aqueous phase filtered and diluted with water (600 ml). The product was precipitated by decreasing the pH to *ca.* 9.6 by slow addition of 1 M aq. NH_4Cl (100 ml). The nearly pure product (5.50 g, 81%) was recrystallised once from pyridine (220 ml) to give pure **13c** as colourless crystals (4.75 g, 70%), mp > 250 °C. NMR (DMSO-d_6): δ_P 26.8. δ_H 11.25 (1H, s, NH), 7.85–7.55 (10H, m, Ar), 7.45 (1H, s, H6), 4.83 (2H, d, *J* 4.7, CH_2), 1.71 (3H, s, CH_3). The compound had too low a solubility for ^{13}C NMR. FAB^+ MS: 341.3 (M + H^+ calc. 341.1) (Found: C, 63.4; H, 5.0; N, 8.4. Calc. for $C_{18}H_{17}N_2O_3P$: C, 63.5; H, 5.0, N, 8.2%).

N^6-(Dibutylaminomethylene)-9-(diethoxyphosphorylmethyl)-adenine (14a)

To a suspension of NaH (0.96 g, 55–60% in mineral oil, 22–24 mmol) in dry DMF (60 ml) was added adenine (2.70 g, 20 mmol), and the mixture was stirred at rt under nitrogen for 3 h. A solution of diethyl (4-nitrophenylsulfonyloxymethyl)-phosphonate (7.07 g, 20 mmol) in dry DMF (20 ml) was added, and the mixture stirred at rt under nitrogen for 3 days. After removal of DMF *in vacuo* the solid residue (11.2 g) was Soxhlet-extracted with ethyl acetate (400 ml) overnight, and crude 9-(diethoxyphosphorylmethyl)adenine (6.7 g, contains *ca.* 1.3 g of sodium 4-nitrobenzenesulfonate, and *ca.* 85% of the 9-isomer and 6% of the 7-isomer according to ^{31}P NMR) isolated by evaporation of the ethyl acetate suspension. To a suspension of crude 9-(diethoxyphosphorylmethyl)adenine (6.35 g) in dry DMF (50 ml) was added *N*,*N*-dibutylformamide dimethyl acetal (6.9 g, 33 mmol), and the mixture stirred under nitrogen at rt for 2 days. Evaporation *in vacuo* gave a red–brown oil which was purified by column chromatography on silica, eluted with EtOAc–MeOH–Et_3N 90 : 5 : 5 v/v/v, to give pure **14a** (4.40 g, 55%) as a yellow oil. NMR ($CDCl_3$): δ_P 18.8. δ_H 9.02 (1H, s, CH=N), 8.57 (1H, s, adenine), 8.07 (1H, s, adenine), 4.62 (2H, d, *J* 12.0, CH_2P), 4.11 (4H, dq, *J* 7.0 and 8.2, Et), 3.72 (2H, t, *J* 7.6, Bu), 3.40 (2H, t, *J* 7.2, Bu), 1.66 (4H, m, Bu), 1.39 (4H, m, Bu), 1.24 (6H, t, *J* 7.0, Et), 0.95 (6H, m, Bu). δ_C 160.1, 158.3, 152.9, 151.7, 141.5, 125.2, 63.2 (d, *J* 6), 5.19, 45.2, 38.4 (d, *J* 157), 31.0, 29.3, 20.2, 19.8, 16.3 (d, *J* 6), 13.9, 13.7. FAB^+ MS: 425.2 (M + H^+ calc. 425.2) (Found: C, 53.6; H, 8.1; N, 19.6. Calc. for $C_{19}H_{33}N_6O_3P$: C, 53.8; H, 7.8; N, 19.8%).

3-Benzoyl-1-(diethoxyphosphorylmethyl)thymine (14b)

To a solution of 3-benzoylthymine (2.00 g, 8.7 mmol) and diethyl (4-nitrophenylsulfonyloxymethyl)phosphonate (3.40 g, 9.6 mmol) in dry DMF (20 ml) was added solid K_2CO_3 (2.4 g, 17 mmol), and the mixture stirred at 60 °C under nitrogen for 7 h. The solvent was removed *in vacuo*, and the residue was partitioned between CH_2Cl_2 (200 ml) and sat. aq. NH_4Cl (100 ml). The organic phase was extracted with water (100 ml), brine (50 ml), dried over Na_2SO_4, and the solvent removed *in vacuo* to give the crude product (3.12 g) as an oil. Flash chromatography on silica, with CH_2Cl_2–MeOH 98 : 2 v/v as eluent, gave pure **14b** (2.19 g, 66%) as a colourless oil. NMR ($CDCl_3$): δ_P 19.3. δ_H 7.87–7.39 (5H, m, phenyl), 7.18 (1H, q, *J* 1, thymine), 4.05–4.15 (6H, m, CH_2P and Et), 1.91 (3H, d, *J* 1, thymine), 1.25 (6H, t, *J* 7, Et). δ_C 168.8, 163.0, 149.7, 140.0, 135.3, 131.6, 130.6, 129.3, 111.5, 63.5 (*J* 6), 42.1 (*J* 156), 16.6 (*J* 6), 12.6. FAB^+ MS: 381.1 (M + H^+ calc. 381.1) (Found: C, 53.5; H, 5.6; N, 7.4. Calc. for $C_{17}H_{21}N_2O_6P$: C, 53.7; H, 5.6; N, 7.4%).

Horner reactions with benzaldehyde

***N^6*-(Dibutylaminomethylene)-9-(2-phenylethenyl)adenine (15a).** Compound **13a** (0.49 g, 1 mmol) was evaporated *in vacuo* from pyridine (10 ml), dissolved under N_2 in dry DMF (10 ml), and cooled to 0 °C. Sodium hydride (55% suspension in mineral oil, 0.045 g, 1 mmol) was added in one portion and the mixture stirred for 2 h at 0 °C. Benzaldehyde (0.14 ml, 1.4 mmol) was added, and the mixture was allowed to warm up slowly to room temperature and stirred for 1 day at rt. Water (10 ml) was added at 5 °C, and the solution extracted with diethyl ether (7 × 10 ml). The combined organic layers were dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by column chromatography on silica, eluted with heptane–EtOAc–Et_3N, 58 : 38 : 4 v/v/v, to give **15a** (0.25 g, 65%) as an oily mixture of *E* and *Z* isomers (*E* : *Z* 2 : 7 according to ^1H NMR). The isomers were not separated. The *E* isomer: NMR ($CDCl_3$): δ_H 8.93 (1H, s, CH=N), 8.54 (1H, s, adenine), 8.13 (1H, s, adenine), 7.61 (1H, d, *J* 14.7, HC=C), 7.22 (6H, m, phenyl + C=CH), 3.62 (2H, m, Bu), 3.30 (2H, m, Bu), 1.54 (4H, m, Bu), 1.30 (4H, m, Bu), 0.85 (6H, m, Bu). The *Z* isomer: NMR ($CDCl_3$): δ 8.91 (1H, s, CH=N), 8.51 (1H, s, adenine), 7.60 (1H, s, adenine), 7.22 (5H, m, phenyl), 6.95 (1H, d, *J* 9.2, HC=C), 6.49 (1H, d, *J* 9.2, HC=C), 3.62 (2H, m, Bu), 3.30 (2H, m, Bu), 1.54 (4H, m, Bu), 1.30 (4H, m, Bu), 0.85 (6H, m, Bu). FAB^+ MS: 377.2 (M + H^+ calc. 377.2) (Found: C, 69.6; H, 7.7; N, 21.7. Calc. for $C_{22}H_{28}N_6$: C, 70.2; H, 7.5; N, 22.3%).

3-Benzoyl-1-(2-phenylethenyl)thymine (15b). Compound **13b** (0.44 g, 1 mmol) was evaporated from dry pyridine (10 ml), dissolved in dry DMF (15 ml), and NaH (55% suspension in mineral oil, 0.045 g, 1 mmol) added under N_2. After 2 h benzaldehyde (0.106 g, 0.102 ml, 1 mmol) was added, and the mixture stirred at rt for 20 h. Then additional benzaldehyde (0.050 ml, 0.5 mmol) and NaH (0.020 g, 0.5 mmol) were added, and the mixture stirred for 3 h at rt. Water (60 ml) was added, and the suspension extracted with ethyl acetate (3 × 40 ml), the ethyl acetate solution dried ($MgSO_4$) and evaporated *in vacuo*, and the residue purified by column chromatography on silica, eluted with hexane–ethyl acetate 2 : 1 v/v, to give **15b** (0.185 g, 55%) as a semisolid mixture of *E* and *Z* isomers (*E* : *Z* 1 : 5 according to ^1H NMR). The isomers were not separated. NMR ($CDCl_3$): *E* isomer: δ_H 7.25–8.00 (12H, m, phenyl + H-6 + NCH=C), 6.62 (1H, d, *J* 14.7, C=CHPh), 2.07 (3H, d, *J* 1.2, Me). *Z* isomer: δ_H 7.25–8.00 (10H, m, phenyl), 6.91 (1H, q, *J* 1.2, H-6), 6.72 (1H, d, *J* 9.0, NCH=C), 6.49 (1H, d, *J* 9.0, C=CHPh), 1.77 (3H, d, *J* 12, Me). FAB^+ MS: 333.1 (M + H^+ calc. 333.1)

(Found: C, 71.6; H, 4.8; N, 8.5. Calc. for $C_{20}H_{16}N_2O_3$: C, 72.3; H, 4.85; N, 8.4%).

1-(2-Phenylethenyl)thymine (15c). Compound **13c** (0.34 g, 1 mmol) was evaporated from dry pyridine (10 ml), suspended in dry DMF (20 ml), and NaH (55% suspension in mineral oil, 0.100 g, 2.2 mmol) added under N_2. After 2 h benzaldehyde (0.106 g, 0.102 ml, 1 mmol) was added, and the mixture stirred at rt for 20 h. Water (30 ml) was added, and the suspension extracted with ethyl acetate (3 × 50 ml), the ethyl acetate solution dried (Na_2SO_4) and evaporated *in vacuo*, and the residue purified by column chromatography on silica, eluted with heptane–EtOAc–MeOH–Et_3N 50 : 49 : 0.5 : 0.5 v/v/v/v, to give **15c** (0.120 g, 53%) as a solid mixture of *E* and *Z* isomers (*E* : *Z* 1 : 2 according to ^1H NMR). The isomers were not separated. NMR (DMSO-d_6): *E* isomer: δ_H 11.5 (1H, br s, NH), 8.05 (1H, s, H-6), 7.58 (1H, d, *J* 14.8, NCH=C), 7.26–7.49 (5H, m, phenyl), 6.86 (1H, d, *J* 14.8, C=CHPh), 1.87 (3H, s, Me). *Z* isomer: δ_H 11.5 (1H, br s, NH), 7.26–7.49 (5H, m, phenyl), 7.03 (1H, s, H-6), 6.59 (1H, d, *J* 9.1, NCH=C), 6.49 (1H, d, *J* 9.1, C=CHPh), 1.63 (3H, s, Me). FAB^+ MS: 229.2 (M + H^+ calc. 229.3) (Found: C, 67.8; H, 5.3; N, 12.0. Calc. for $C_{13}H_{12}N_2O_2$: C, 68.4; H, 5.3; N, 12.3%).

Horner reactions with ketones

***N*^{6}-(Dibutylaminomethylene)-9-(2-methylprop-1-enyl)adenine (16aa).** Compound **13a** (0.49 g, 1 mmol) was evaporated *in vacuo* from pyridine (10 ml), dissolved under N_2 in dry DMF (10 ml), and cooled to 0 °C. NaH (55% suspension in mineral oil, 0.045 g, 1 mmol) was added in one portion and the mixture stirred for 2 h at 0 °C. Acetone (0.10 ml, 1.4 mmol) was dissolved in dry DMF (4 ml) and added dropwise. The mixture was allowed to warm up slowly to room temperature and stirred for 2 days. Water (10 ml) was added at 5 °C, and the solution extracted with diethyl ether (7 × 10 ml). The combined extracts were dried over Na_2SO_4 and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica, eluted with heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v. Yield: 0.26 g (79%, oil), R_f = 0.11 (heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v). NMR ($CDCl_3$): δ_H 9.03 (1H, s, CH=N), 8.58 (1H, s, adenine), 7.88 (1H, s, adenine), 6.60 (1H, d, *J* 1.4, C=CH), 3.74 (2H, t, *J* 7.6, Bu), 3.42 (2H, t, *J* 7.3, Bu), 1.97 (3H, s, CH_3), 1.73 (3H, d, *J* 1.1, CH_3), 1.68 (4H, m, Bu), 1.40 (4H, m, Bu), 0.96 (6H, t, *J* 7.3, Bu). δ_C 159.4, 157.5, 152.5, 151.3, 141.1, 136.1, 124.7, 114.8, 51.5, 44.8, 30.7, 28.9, 22.4, 19.9, 19.5, 17.8, 13.6, 13.4. FAB^+ MS: 328.5 (M + H^+ calc. 329.2) (Found: C, 65.7; H, 8.7; N, 25.4. Calc. for $C_{18}H_{28}N_6$: C, 65.8; H, 8.6; N, 25.6%).

***N*^{6}-(Dibutylaminomethylene)-9-(2-propylpent-1-enyl)adenine (16ab).** Prepared in the same way as **16aa** from heptan-4-one (0.20 ml), stirred for 2 days. Yield: 0.18 g (49%, oil), R_f = 0.26 (heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v). NMR ($CDCl_3$): δ_H 8.88 (1H, s, CH=N), 8.40 (1H, s, adenine), 7.67 (1H, s, adenine), 6.39 (1H, s, C=CH), 3.55 (2H, t, *J* 7.6, Bu), 3.24 (2H, t, *J* 7.3, Bu), 2.06 (2H, t, *J* 7.3, Pr), 1.85 (2H, t, *J* 7.8, Pr), 1.48 (6H, m, Pr + Bu), 1.23 (6H, m, Pr + Bu), 0.80 (9H, m, Pr + Bu), 0.62 (3H, t, *J* 7.4, Pr). δ_C 158.9, 157.6, 152.0, 151.3, 144.1, 141.3, 124.6, 114.6, 51.5, 44.8, 35.5, 31.2, 30.6, 28.8, 20.5, 20.4, 19.8, 13.6, 13.5, 13.3. FAB^+ MS: 384.6 (M + H^+ calc. 385.3) (Found: C, 68.7; H, 9.8; N, 21.3. Calc. for $C_{22}H_{36}N_6$: C, 68.7; H, 9.4; N, 21.85%).

***N*^{6}-(Dibutylaminomethylene)-9-(cyclopentylidenemethyl)-adenine (16ac).** Prepared in the same way as **16aa** from cyclopentanone (0.12 ml), stirred for 3 hours. Yield: 0.23 g (66%, oil), R_f = 0.17 (heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v). NMR ($CDCl_3$): δ_H 8.80 (1H, s, CH=N), 8.34 (1H, s, adenine), 7.80 (1H, s, adenine), 6.64 (1H, quintet, *J* 2.3, C=CH), 3.49 (2H, t, *J* 7.6, Bu), 3.17 (2H, t, *J* 7.3, Bu), 2.30 (2H, m, cyclopentyl), 2.19 (2H, m, cyclopentyl), 1.44 (8H, m, cyclopentyl + Bu), 1.18 (4H, m, Bu), 0.85 (6H, m, Bu). δ_C 159.4, 157.5, 152.2, 150.5, 142.0, 139.9, 124.4, 111.1, 51.2, 44.5, 31.6, 30.3, 29.4, 28.6, 25.6, 25.3, 19.6, 19.1, 13.3, 13.1. FAB^+ MS: 355.0 (M + H^+ calc. 355.3) (Found: C, 67.4; H, 8.8; N, 23.1. Calc. for $C_{20}H_{30}N_6$: C, 67.8; H, 8.5; N, 23.7%).

***N*^{6}-(Dibutylaminomethylene)-9-(cyclohexylidenemethyl)-adenine (16ad).** Prepared in the same way as **16aa** from cyclohexanone (0.15 ml), stirred for 4 days. Yield: 0.27 g (74%, oil), R_f = 0.20 (heptane–EtOAC–Et_3N 58 : 38 : 4 v/v/v). NMR ($CDCl_3$): δ_H 8.77 (1H, s, CH=N), 8.32 (1H, s, adenine), 7.58 (1H, s, adenine), 6.29 (1H, s, C=CH), 3.46 (2H, t, *J* 7.6, Bu), 3.14 (2H, t, *J* 7.3, Bu), 2.06 (2H, t, *J* 5.8, cyclohexyl), 1.88 (2H, t, *J* 5.5, cyclohexyl), 1.38 (10H, m, cyclohexyl + Bu), 1.14 (4H, m, Bu), 0.68 (6H, m, Bu). δ_C 159.1, 157.3, 152.1, 151.2, 142.8, 141.0, 124.5, 111.3, 51.1, 44.5, 32.8, 30.4, 28.6, 27.8, 27.2, 26.6, 25.5, 19.6, 19.1, 13.3, 13.1. FAB^+ MS: 368.5 (M + H^+ calc. 369.3) (Found: C, 68.05; H, 8.9; N, 22.55. Calc. for $C_{21}H_{32}N_6$: C, 68.4; H, 8.75; N, 22.8%).

***N*^{6}-(Dibutylaminomethylene)-9-(2,3,3-trimethylbut-1-enyl)-adenine (16ae).** Prepared in the same way as **16aa** from 2,2-dimethylbutan-3-one (0.17 ml), stirred for 4 days. Yield: 0.13 g (34%, *E* : *Z* 3 : 7) consisting of pure *E* isomer (0.02 g), a mixed fraction (0.07 g), and pure *Z* isomer (0.04 g). The *E* isomer: oil, R_f = 0.21 (heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v). NMR ($CDCl_3$): δ_H 9.00 (1H, s, CH=N), 8.59 (1H, s, adenine), 7.86 (1H, s, adenine), 6.66 (1H, d, *J* 1.4, C=CH), 3.73 (2H, t, *J* 7.7, Bu), 3.41 (2H, t, *J* 7.3, Bu), 1.72 (3H, d, *J* 1.4, CH_3), 1.67 (4H, m, Bu), 1.39 (4H, m, Bu), 1.25 (9H, s, Bu^t), 0.96 (6H, m, Bu). δ_C 159.6, 157.7, 152.6, 151.7, 147.7, 141.7, 125.1, 113.9, 51.8, 45.1, 35.8, 31.0, 29.2, 28.8, 20.2, 19.8, 13.9, 13.7, 13.3. The *Z* isomer: mp 90–92 °C, R_f = 0.16 (heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v). NMR ($CDCl_3$): δ_H 9.01 (1H, s, CH=N), 8.59 (1H, s, adenine), 7.78 (1H, s, adenine), 6.38 (1H, d, *J* 1.4, C=CH), 3.73 (2H, t, *J* 7.7, Bu), 3.40 (2H, t, *J* 7.3, Bu), 1.97 (3H, d, *J* 1.1, CH_3), 1.67 (4H, m, Bu), 1.36 (4H, m, Bu), 0.96 (6H, t, *J* 6.7, Bu), 0.96 (9H, s, Bu^t). δ_C 159.7, 157.8, 152.8, 152.5, 152.0, 142.2, 125.1, 113.9, 51.8, 45.1, 36.0, 31.0, 29.4, 29.2, 20.4, 20.2, 19.7, 13.9, 13.7. FAB^+ MS: 370.5 (M + H^+ calc. 371.3) (Found: C, 67.8; H, 9.3; N, 22.25. Calc. for $C_{21}H_{34}N_6 \cdot 0.1H_2O$: C, 67.7; H, 9.3; N, 22.6%).

***N*^{6}-(Dibutylaminomethylene)-9-(2-methyl-3-phenoxyprop-1-enyl)adenine (16af).** Prepared in the same way as **16aa** from phenoxyacetone (0.19 ml), stirred for 4 days. Yield: 0.20 g (48%, semi-solid mixture of the two isomers, *E* : *Z* 2 : 5), R_f = 0.15 (heptane–EtOAc–Et_3N 58 : 38 : 4 v/v/v). The isomers were not separated. The *E* isomer: NMR ($CDCl_3$): δ_H 8.92 (1H, s, CH=N), 8.49 (1H, s, adenine), 7.89 (1H, s, adenine), 7.83 (1H, s, C=CH), 7.18 (2H, m, phenyl), 6.79 (3H, m, phenyl), 4.38 (2H, s, OCH_2), 3.62 (2H, m, Bu), 3.29 (2H, m, Bu), 2.00 (3H, s, CH_3), 1.54 (4H, m, Bu), 1.28 (4H, m, Bu), 0.84 (6H, m, Bu). The *Z* isomer: NMR ($CDCl_3$): δ_H 8.92 (1H, s, CH=N), 8.49 (1H, s, adenine), 7.90 (1H, s, adenine), 7.18 (2H, m, phenyl), 7.00 (1H, s, C=CH), 6.79 (3H, m, phenyl), 4.53 (2H, s, OCH_2), 3.62 (2H, m, Bu), 3.29 (2H, m, Bu), 1.82 (3H, s, CH_3), 1.54 (4H, m, Bu), 1.28 (4H, m, Bu), 0.84 (6H, m, Bu). FAB^+ MS: 420.6 (M + H^+ calc. 421.3) (Found: C, 68.2; H, 7.5; N, 19.8. Calc. for $C_{24}H_{32}N_6O$: C, 68.5; H, 7.7; N, 20.0%).

3-Benzoyl-1-(2-methylprop-1-enyl)thymine (16ba). Compound **13b** (0.44 g, 1 mmol) was evaporated from dry pyridine (10 ml), dissolved in dry DMF (10 ml), and NaH (55% suspension in mineral oil, 0.045 g, 1 mmol) added under N_2. After 2 h at rt acetone (0.15 ml, 2 mmol) was added, and the mixture stirred at rt for 4 days. Diethyl ether (60 ml) followed by water (60 ml) were added, the phases were separated, and the water phase (pH adjusted to 7–8) was extracted with diethyl ether (2 × 40 ml). The combined organic phases were washed with

brine, dried ($MgSO_4$) and evaporated *in vacuo*, and the residue purified by column chromatography on silica, eluted with hexane–ethyl acetate 3 : 2 v/v, to give **16ba** (0.096 g, 34%) as colourless crystals, mp 135–136 °C, R_f = 0.44 (hexane–ethyl acetate 2 : 3 v/v). NMR ($CDCl_3$): δ_H 7.92 (2H, dd, *J* 8 and 1, Ph), 7.62 (1H, tt, *J* 8 and 1, Ph), 7.49 (2H, t, *J* 8, Ph), 7.02 (1H, q, *J* 1.2, H-6), 6.15 (1H, septet, *J* 1.5, NCH=C), 1.97 (3H, d, *J* 1.2, T-Me), 1.84 (3H, d, *J* 1.5, E-Me), 1.74 (3H, d, *J* 1.5, Z-Me). FAB^+ MS: 285.2 ($M + H^+$ calc. 285.1) (Found: C, 67.1; H, 5.6; N, 9.9. Calc. for $C_{16}H_{16}N_2O_3$: C, 67.6; H, 5.7; N, 9.85%).

1-Benzoyl-2-(2-methylprop-1-enyl)urea (17). When **13b** (0.44 g, 1 mmol) was reacted with acetone (0.15 ml, 2 mmol) as described above but with excess of NaH (2 mmol), compound **17** (0.060 g, 28%) was isolated after column chromatography as colourless crystals, mp 174–175 °C, R_f = 0.57 (hexane–ethyl acetate 2 : 3 v/v). NMR (DMSO-d_6): δ_H 10.99 (1H, s, NH), 10.34 (1H, d, *J* 10.2, NH), 7.98 (2H, d, *J* 8, Ph), 7.64 (1H, t, *J* 8, Ph), 7.51 (2H, t, *J* 8, Ph), 6.46 (1H, d, *J* 10.2, NCH=C), 1.71 (3H, s, *E*-Me), 1.66 (3H, s, *Z*-Me). FAB^+ MS: 219.1 ($M + H^+$ calc. 219.1) (Found: C, 65.95; H, 6.3; N, 12.7. Calc. for $C_{12}H_{14}N_2O_2$: C, 66.0; H, 6.5; N, 12.8%).

3-Benzoyl-1-(2-propylpent-1-enyl)thymine (16bb). Prepared in the same way as **16ba** from **13b** and heptan-4-one, reaction time 5 days. Yield: 0.035 g (10%), mp 104–105 °C, R_f = 0.64 (hexane–ethyl acetate 2 : 3 v/v). NMR ($CDCl_3$): δ_H 7.93 (2H, d, *J* 8, Ph), 7.64 (1H, t, *J* 8, Ph), 7.48 (2H, t, *J* 8, Ph), 6.99 (1H, q, *J* 1.2, H-6), 6.13 (1H, s, NCH=C), 2.11 (2H, t, 7.6, *E* C=C-CH_2), 2.05 (2H, t, *J* 7.7, *Z* C=C-CH_2), 1.98 (3H, d, *J* 1.2, T-Me), 1.49 (4H, m, 2 × C-CH_2-Me), 0.93 (3H, t, *J* 7.3, Me), 0.92 (3H, t, *J* 7.6, Me). FAB^+ MS: 340.9 ($M + H^+$ calc. 341.2) (Found: C, 70.0; H, 7.1; N, 8.2. Calc. for $C_{20}H_{24}N_2O_3$: C, 70.6; H, 7.1; N, 8.2%).

1-(2-Methylprop-1-enyl)thymine (16ca). Prepared in the same way as **16ba** from **13c**, 2 mmol of NaH, and acetone, reaction time 4 days. Yield: 0.071 g (40%) as colourless crystals, mp 130–131 °C, R_f = 0.21 (hexane–ethyl acetate 2 : 3 v/v). NMR ($CDCl_3$): δ_H 9.04 (1H, s, NH), 6.91 (1H, q, *J* 1.2, H-6), 6.13 (1H, septet, *J* 1.5, NCH=C), 1.92 (3H, d, *J* 1.2, T-Me), 1.83 (3H, d, *J* 1.5, *E*-Me), 1.68 (3H, d, *J* 1.5, *Z*-Me). FAB^+ MS: 181.0 ($M + H^+$ calc. 181.1) (Found: C, 59.4; H, 6.8; N, 15.2. Calc. for $C_9H_{12}N_2O_2$: C, 60.0; H, 6.7; N, 15.55%).

1-(2-Propylpent-1-enyl)thymine (16cb). Prepared in the same way as **16ba** from **13c**, 2 mmol of NaH, and heptan-4-one, reaction time 5 days. Yield: 0.104 g (44%), mp 86–87 °C, R_f = 0.38 (hexane–ethyl acetate 2 : 3 v/v). NMR ($CDCl_3$): δ_H 8.64 (1H, s, NH), 6.82 (1H, q, *J* 1.2, H-6), 6.55 (1H, s, NCH=C), 2.05 (2H, t, *J* 7.5, *E* C=C-CH_2), 1.93 (2H, t, *J* 7.7, *Z* C=C-CH_2), 1.86 (3H, d, *J* 1.2, T-Me), 1.41 (4H, m, 2 × C-CH_2-Me), 0.88 (3H, t, *J* 7.3, Me), 0.82 (3H, t, *J* 7.3, Me). FAB^+ MS: 237.0 ($M + H^+$ calc. 237.2) (Found: C, 65.8; H, 8.5; N, 11.9. Calc. for $C_{13}H_{20}N_2O_2$: C, 66.1; H, 8.5; N, 11.85%)

1-(Cyclohexylidenemethyl)thymine (16cc). Prepared in the same way as **16ba** from **13c**, 2 mmol of NaH, and cyclohexanone, reaction time 3 days. Yield: 0.150 g (68%), mp 159–160 °C, R_f = 0.32 (ethyl acetate–hexane 3 : 2 v/v). NMR ($CDCl_3$): δ_H 8.91 (1H, s, NH), 6.88 (1H, q, *J* 1.2, H-6), 6.12 (1H, s, NCH=C), 2.21 (2H, t, *J* 5.5, *E* C=CCH_2), 2.11 (2H, t, *J* 5.5, *Z* C=CCH_2), 1.92 (3H, d, *J* 1.2, T-Me), 1.60 (6H, m, $CH_2CH_2CH_2$). FAB^+ MS: 221.0 ($M + H^+$ calc. 220.1) (Found: C, 64.9; H, 7.35; N, 12.7. Calc. for $C_{12}H_{16}N_2O_2$: C, 65.4; H, 7.3; N, 12.7%).

HWE reactions

***N*^{6}-(Dibutylaminomethylene)-9-(2-phenylethenyl)adenine (15a).** Compound **14a** (0.42 g, 1 mmol) was evaporated *in vacuo* from pyridine (10 ml), dissolved under N_2 in dry DMF (10 ml), benzaldehyde (0.20 ml, 2 mmol) was added, and the mixture was cooled to 0 °C. Sodium hydride (55% suspension in mineral oil, 0.045 g, 1 mmol) was added in one portion and the mixture stirred for 2 hours at 0 °C. Water (10 ml) was added, and the solution extracted with diethyl ether (7 × 10 ml). The combined organic layers were dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by column chromatography on silica, eluted with heptane–EtOAc–Et_3N, 58 : 38 : 4 v/v/v, to give **15a** (0.15 g, 39%) as an oily mixture of *E* and *Z* isomers (*E* : *Z* 1 : 3 according to ^{1}H NMR). The isomers were not separated. The product had identical data to the same compound prepared by the Horner reaction.

3-Benzoyl-1-(2-phenylethenyl)thymine (15b). Compound **14b** (0.38 g, 1 mmol) was evaporated from dry pyridine (10 ml), dissolved in dry DMF (10 ml), and NaH (55% suspension in mineral oil, 0.090 g, 2 mmol) was added under N_2 at rt. After 5 min benzaldehyde (0.15 ml, 1.5 mmol) was added, and the mixture stirred for 1 h at rt. Diethyl ether (60 ml) followed by water (60 ml) were added. The phases were separated, and the water phase extracted with diethyl ether (2 × 40 ml). The combined organic phases were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*, and the residue purified by column chromatography on silica, eluted with hexane–ethyl acetate 3 : 2 v/v, to give **15b** (0.18 g, 55%) as a semisolid mixture of *E* and *Z* isomers (*E* : *Z* 1 : 3 according to ^{1}H NMR). R_f = 0.52 for the *E* isomer and R_f = 0.47 for the *Z* isomer (ethyl acetate–hexane, 3 : 2 v/v). The isomers were not separated. The product had identical data to the same compound prepared by the Horner reaction.

***N*^{6}-(Dibutylaminomethylene)-9-(2-methylprop-1-enyl)adenine (16aa).** Prepared in the same way as **15a** from **14a** and acetone, yield 0.060 g (18%). The product had identical data to the same compound prepared by the Horner reaction.

***N*^{6}-(Dibutylaminomethylene)-9-(2-propylpent-1-enyl)adenine (16ab).** Prepared in the same way as **15a** from **14a** and heptan-4-one, yield 0.008 g (2%). The product had identical data to the same compound prepared by the Horner reaction.

3-Benzoyl-1-(2-methylprop-1-enyl)thymine (16ba). Prepared in the same way as **15b** from **14b** and acetone, yield 0.020 g (7%). The product had identical data to the same compound prepared by the Horner reaction.

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