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

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Received (in Cambridge, UK) 6th April 2000, Accepted 20th April 2000 Published on the Web 5th June 2000

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-mesyl⁸ or a 1-nitro group⁹ 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}l 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

$$\underset{B^3}{\overset{R^1}{\underset{B^2}{\longrightarrow}}} \underset{B^2}{\overset{R^1}{\underset{B^2}{\longrightarrow}}} \qquad \underset{B \xrightarrow{P(O)X_2}{\underset{B^3}{\longrightarrow}} + O \xrightarrow{R^1}_{\underset{B^2}{\xrightarrow{P(O)X_2}}}$$

N-(alk-1-enyl) nucleobase X = Ph or OEt 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 ¹³C NMR ¹⁵), and the minor *N*-7 isomer could be removed by column chromatography after *N*-6 protection with a dibutyl-formamidine 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

DOI: 10.1039/b002744h

J. Chem. Soc., Perkin Trans. 1, 2000, 2015–2021 2015

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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 CH₂). 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-1enyl) 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-envl) nucleobases could be isolated. According to ¹H 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).



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 benzovl 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



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



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 oxide¹⁹ 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 $\delta_{\rm H}$ and $\delta_{\rm C}$, 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 (CDCl₃): $\delta_{\rm P}$ 14.7. $\delta_{\rm H}$ 8.44 (2H, m, Ar), 8.15 (2H, m, Ar), 4.32 (2H, d, J 9.6, CH₂P), 4.17 (4H, dq, J 7.1 and 7.1, Et), 1.34 (6H, t, J 7.1, Et). $\delta_{\rm C}$ 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 C₁₁H₁₆NO₈PS: 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)diphenylphosphine 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-Et₃N-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-d₆): 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, CH₂P), 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). $\delta_{\rm C}$ 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 C₂₇H₃₃N₆OP: 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 CH₂Cl₂ (200 ml) and sat. aq. NH₄Cl (100 ml). The organic phase was extracted with water (100 ml), brine (50 ml), dried over Na₂SO₄, and the solvent removed *in vacuo* to give the crude product (4.06 g). Flash chromatography on silica, with CH₂Cl₂–MeOH 98:2 v/v followed by CH₂Cl₂–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): $\delta_{\rm P}$ 26.7. $\delta_{\rm H}$ 7.88–7.52 (16H, m, Ar + H6), 4.92 (2H, d, *J* 4.4, CH₂P), 1.82 (3H, s, CH₃). $\delta_{\rm C}$ 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 C₂₅H₂₁N₂O₄P: 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. NH₃ (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 \times 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. NH₄Cl (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, CH₂), 1.71 (3H, s, CH₃). The compound had too low a solubility for ¹³C NMR. FAB⁺ MS: 341.3 (M + H⁺ calc. 341.1) (Found: C, 63.4; H, 5.0; N, 8.4. Calc. for C₁₈H₁₇-N₂O₃P: 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 ³¹P 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-Et₃N 90:5:5 v/v/v, to give pure 14a (4.40 g, 55%) as a yellow oil. NMR (CDCl₃): 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, CH₂P), 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 K₂CO₃ (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 CH₂Cl₂ (200 ml) and sat. aq. NH₄Cl (100 ml). The organic phase was extracted with water (100 ml), brine (50 ml), dried over Na₂SO₄, and the solvent removed in vacuo to give the crude product (3.12 g) as an oil. Flash chromatography on silica, with CH₂Cl₂-MeOH 98:2 v/v as eluent, gave pure 14b (2.19 g, 66%) as a colourless oil. NMR (CDCl₃): $\delta_{\rm P}$ 19.3. $\delta_{\rm H}$ 7.87–7.39 (5H, m, phenyl), 7.18 (1H, q, J 1, thymine), 4.05-4.15 (6H, m, CH₂P 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 N2 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 Na₂SO₄ and evaporated in vacuo. The residue was purified by column chromatography on silica, eluted with heptane-EtOAc-Et₃N, 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 (CDCl₃): $\delta_{\rm H}$ 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 (CDCl₃): 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 C22H28N6: 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 N2. 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 $(3 \times 40 \text{ ml})$, the ethyl acetate solution dried (MgSO₄) 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 $(E:Z \mid 1:5 \text{ according to})$ ¹H NMR). The isomers were not separated. NMR (CDCl₃): *E* isomer: $\delta_{\rm H}$ 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: $\delta_{\rm H}$ 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 N₂. 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 $(3 \times 50 \text{ ml})$, the ethyl acetate solution dried (Na₂SO₄) and evaporated in vacuo, and the residue purified by column chromatography on silica, eluted with heptane-EtOAc-MeOH-Et₃N 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: $\delta_{\rm H}$ 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 C₁₃H₁₂N₂O₂: C, 68.4; H, 5.3; N, 12.3%).

Horner reactions with ketones

N⁶-(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 N₂ 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 \times 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-Et₃N 58:38:4 v/v/v. Yield: 0.26 g (79%, oil), $R_{\rm f} = 0.11$ (heptane-EtOAc-Et₃N 58:38:4 v/v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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, CH₃), 1.73 (3H, d, J 1.1, CH₃), 1.68 (4H, m, Bu), 1.40 (4H, m, Bu), 0.96 (6H, t, J 7.3, Bu). $\delta_{\rm C}$ 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 C₁₈H₂₈N₆: 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), $R_{\rm f}$ = 0.26 (heptane–EtOAc–Et₃N 58:38:4 v/v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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). $\delta_{\rm C}$ 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 C₂₂H₃₆N₆: 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), $R_{\rm f} = 0.17$ (heptane–EtOAc–Et₃N 58:38:4 v/v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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). $\delta_{\rm C}$ 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 C₂₀H₃₀N₆: C, 67.8; H, 8.5; N, 23.7%).

N⁶-(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), $R_{\rm f} = 0.20$ (heptane–EtOAC–Et₃N 58:38:4 v/v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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). $\delta_{\rm C}$ 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 C₂₁H₃₂N₆: C, 68.4; H, 8.75; N, 22.8%).

N⁶-(Dibutylaminomethylene)-9-(2,3,3-trimethylbut-1-enyl)adenine (16ae). Prepared in the same way as 16aa from 2,2dimethylbutan-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-Et₃N 58:38:4 v/v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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, CH₃), 1.67 (4H, m, Bu), 1.39 (4H, m, Bu), 1.25 (9H, s, Bu^t), 0.96 (6H, m, Bu). $\delta_{\rm C}$ 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–Et₃N 58:38:4 v/v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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, CH₃), 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 C₂₁H₃₄N₆•0.1H₂O: C, 67.7; H, 9.3; N, 22.6%).

N⁶-(Dibutylaminomethylene)-9-(2-methyl-3-phenoxyprop-1enyl)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-Et₃N 58:38:4 v/v/v). The isomers were not separated. The E isomer: NMR (CDCl₃): $\delta_{\rm H}$ 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, OCH₂), 3.62 (2H, m, Bu), 3.29 (2H, m, Bu), 2.00 (3H, s, CH₃), 1.54 (4H, m, Bu), 1.28 (4H, m, Bu), 0.84 (6H, m, Bu). The Z isomer: NMR (CDCl₃): $\delta_{\rm H}$ 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, OCH₂), 3.62 (2H, m, Bu), 3.29 (2H, m, Bu), 1.82 (3H, s, CH₃), 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 C₂₄H₃₂-N₆O: 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 N₂. 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 (MgSO₄) 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, $R_{\rm f}$ = 0.44 (hexane–ethyl acetate 2:3 v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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 C₁₆H₁₆N₂O₃: 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, $R_{\rm f}$ = 0.57 (hexane–ethyl acetate 2:3 v/v). NMR (DMSO- d_6): $\delta_{\rm H}$ 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 C₁₂H₁₄N₂O₂: 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, $R_{\rm f}$ = 0.64 (hexane-ethyl acetate 2:3 v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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-CH₂), 2.05 (2H, t, J 7.7, *Z* C=C-CH₂), 1.98 (3H, d, J 1.2, T-Me), 1.49 (4H, m, 2 × C-CH₂-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 C₂₀H₂₄N₂O₃: 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, $R_{\rm f}$ = 0.21 (hexane–ethyl acetate 2 : 3 v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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 C₉H₁₂N₂O₂: 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, $R_{\rm f}$ = 0.38 (hexane–ethyl acetate 2:3 v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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-CH₂), 1.93 (2H, t, J 7.7, *Z* C=C-CH₂), 1.86 (3H, d, J 1.2, T-Me), 1.41 (4H, m, 2 × C-CH₂-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 C₁₃H₂₀N₂O₂: 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, $R_{\rm f}$ = 0.32 (ethyl acetate–hexane 3:2 v/v). NMR (CDCl₃): $\delta_{\rm H}$ 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=CCH₂), 2.11 (2H, t, *J* 5.5, *Z* C=CCH₂), 1.92 (3H, d, *J* 1.2, T-Me), 1.60 (6H, m, CH₂CH₂CH₂). FAB⁺ MS: 221.0 (M + H⁺ calc. 220.1) (Found: C, 64.9; H, 7.35; N, 12.7. Calc. for C₁₂H₁₆N₂O₂: C, 65.4; H, 7.3; N, 12.7%).

HWE reactions

N⁶-(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 Na₂SO₄ and evaporated *in vacuo*. The residue was purified by column chromatography on silica, eluted with heptane–EtOAc–Et₃N, 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 ¹H 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 N₂ 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 \times 40 ml). The combined organic phases were washed with brine, dried (MgSO₄) 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 Zisomers (E:Z1:3 according to ¹H 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-4one, 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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