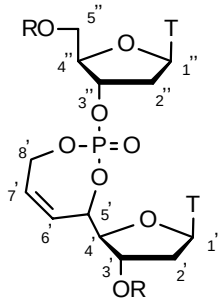
Experimental

All commercial reagents were used as supplied. All reactions were performed under an atmosphere of nitrogen. Column chromatography was carried out on glass columns using Silica gel 60 (0.040-0.063 mm). NMR spectra were obtained on a Varian Gemini 2000 spectrometer. ^{1}H NMR spectra were recorded at 300 MHz, ^{13}C NMR spectra were recorded at 62.5 MHz and ^{31}P NMR spectra were recorded at 121.5 MHz. Values for δ are in ppm relative to tetramethylsilane as internal standard or 85% H_3PO_4 as external standard. FAB mass spectra were recorded in positive ion mode on a Kratos MS50TC spectrometer. Accurate mass determinations were performed an Ionspec Ultima Fourier Transform mass spectrometer. Microanalyses were performed at The Microanalytical Laboratory, Department of Chemistry, University of Copenhagen.

Numbers of NMR-signals are following the conventional nucleoside numbering except for compounds **11** and **12** following this system:



Preparation of Diallyl 3'-O-(5'-O-*tert*-butyldimethylsilyl)thymidinyl phosphoric ester (4)
Compound **3** (92mg, 0,26mmol) was coevaporated twice with anhydrous CH_3CN and redissolved in anhydrous CH_3CN (3,0ml). Diisopropylamine (66µl, 0,50mmol) was added followed by di-O-allyl-N,N-diisopropylphosphoramidite (204µl, 0,77mmol) and a 0,45M solution of 1H-tetrazole in CH_3CN (1,05ml, 0,47mmol). The mixture was stirred at RT fof 16 h. The reaction was quenched with anhydrous MeOH (0,50ml) and concentrated *in vacuo*. The residue was coevaporated twice with anhydrous CH_2Cl_2 and redissolved in anhydrous CH_2Cl_2 (2,0ml). The reaction mixture was cooled to 0°C and a 3,0M solution of *tert*-butylhydrogenperoxide in toluene (400µl, 1,2mmol) was added. After stirring at 0°C for 2½h the reaction mixture was diluted with MeOH (1,0ml) and concentrated *in vacuo*. The product was purified by column chromatography (½-2% MeOH in CH_2Cl_2) and isolated as a clear oil.
Yield 107mg, 80%; R_f 0.55 (8% MeOH in CH_2Cl_2, one spot on TLC); Found C: 50.21 H: 7.20 N: 5.18 Calc. $C_{22}H_{37}N_2O_8PSi$, ½H_2O C: 50.27 H: 7.29 N: 5.33; ^{1}H NMR ($CDCl_3$) δ 0.12 (6H, s, $Si(CH_3)_2$), 0.92 (9H, s, $C(CH_3)_3$), 1.92 (3H, s, CH_3), 2.11 (1H, m, H-2'), 2.55 (1H, dd, *J* 5.1 and 13.8, H-2'), 3.81-3.94 (2H, m, 2 x H-5'), 4.28 (1H, m, H-4'), 4.52-4.62 (4H, m, 2 x $OCH_2CH=CH_2$), 4.99 (1H, m, H-3'), 5.25-5.44 (4H, m, 2 x $CH=CH_2$), 5.86-6.03 (2H, m, 2 x $CH=CH_2$), 6.37 (1H, dd, *J* 5.1 and 9.0, H-1'), 7.48 (1H, d, *J* 1.2, H-6), 8.65 (1H, br s, NH); ^{13}C NMR ($CDCl_3$) δ -5.45, 12.50, 18.30, 25.90, 39.35, 63.29, 68.50, 78.60, 84.57, 85.78, 111.16, 118.77, 132.07, 134.94, 150.16, 163.51; ^{31}P NMR ($CDCl_3$) δ -0.66; MS(FAB) *m/z*: 517 (MH^+, 51%); HiRes MALDI FT-MS *m/z* [MNa^+] (found/calc.) (539.1940/539.1935).

Preparation of 2-(2(*R*)-(*tert*-butyldimethylsilyl)oxymethyl-5(*R*)-(thymin-1-yl)tetrahydrofuran-3(*S*)-oxyl)-2-oxo-4,7-dihydro-1,3-dioxa-2-phosphepine (5)

A) Compound **4** (32mg, 0,062mmol) was coevaporated with anhydrous CH_2Cl_2 and redissolved in anhydrous CH_2Cl_2 (3,0ml). Catalyst **1** (5,1mg, 0,0062mmol) was added and the reaction mixture was stirred at 40ºC for 20h. The solution was concentrated *in vacuo*, and the product was purified by column chromatography (½-3% MeOH in CH_2Cl_2) and isolated as an off-white solid. Yield 15,8mg, 52%.

B) Same procedure as A using **4** (28mg, 0,054mmol) and catalyst **2** (4,6mg, 0,0054mmol), reaction time 45min. Yield 25.6mg, 97%.

R_f 0.47 (8% MeOH in CH_2Cl_2, one spot on TLC); ^{1}H NMR ($CDCl_3$) δ 0.13 (6H, s, $Si(CH_3)_2$), 0.92 (9H, s, $C(CH_3)_3$), 1.92 (3H, s, CH_3), 2.14 (1H, m, H-2'), 2.57 (1H, dd, *J* 5.2 and 13.9, H-2'), 3.90 (2H, m, 2 x H-5'), 4.31 (1H, m, H-4'), 4.59-4.83 (4H, m, 2 x O*C*H_2CH=CH), 5.13 (1H, m, H-3'), 5.78 (2H, m, C*H*=C*H*), 6.40 (1H, dd, *J* 5.2 and 8.9, H-1'), 7.50 (1H, s, H-6), 9.00 (1H, s, NH); ^{13}C NMR ($CDCl_3$) δ -5.50, -5.45, 12.47, 18.26, 25.89, 39.31, 63.29, 64.38, 79.37, 84.52, 85.79, 111.23, 126.75, 134.88, 150.33, 163.61; ^{31}P NMR ($CDCl_3$) δ 3.85; MS(FAB) *m/z*: 489 (MH^+, 22%); HiRes MALDI FT-MS *m/z* [MNa^+] (found/calc.) (511.1633/511.1636).

Preparation of 2-(2(*R*)-hydroxymethyl-5(*R*)-(thymin-1-yl)tetrahydrofuran-3(*S*)-oxyl)-2-oxo-4,7-dihydro-1,3-dioxa-2-phosphepine (6)

Compound **5** (14,8mg, 0,0303mmol) was dissolved in 90% TFA (1,0ml) and the solution was stirred at RT for 15min. The reaction mixture was concentrated *in vacuo* and coevaporated with anhydrous EtOH. The product was purified by column chromatography and isolated as a white solid. Yield 10.5mg, 93%; R_f 0.40 (10% MeOH in CH_2Cl_2, one spot on TLC); ^{1}H NMR (CD_3OD) δ 1.91 (3H, s, CH_3), 2.42 (1H, m, H-2'), 2.56 (1H, ddd, *J* 14.2, 5.8 and 2.0, H-2'), 3.77-3.88 (2H, m, 2 x H-5'), 4.24 (1H, m, H-4'), 4.70-4.84 (4H, m, 2 x O*C*H_2CH=CH), 5.17 (1H, m, H-3'), 5.83-5.90 (2H, m, C*H*=C*H*), 6.34 (1H, dd, *J* 5.8 and 8.4, H-1'), 7.83 (1H, d, *J* 1.0, H-6); ^{31}P NMR (CD_3OD) δ 3.95; MS(FAB) *m/z*: 375 (MH^+, 87%).

Preparation of 3'-O-(*tert*-butyldimethylsilyl)-5'-C-vinylthymidin (8).

Compound **7** (2,50g, 7,01mmol) was dissolved in anhydrous CH_2Cl_2 (25ml) and the Dess-Martin periodinane (3,47g, 8,18mmol) was added. The reaction mixture was stirred at RT for 3h. The mixture was added CH_2Cl_2 (50ml) and filtered through a layer of celite. The filtrate was washed with a 10% aqueous solution of $Na_2S_2O_3$ (2 x 75ml), H_2O (75ml), a saturated aqueous solution of $NaHCO_3$ (2 x 75ml) and brine (75ml). The organic phase was dried with Na_2SO_4 and concentrated *in vacuo*. The product was purified by column chromatography (30-70% EtOAc in hexanes) and the aldehyde intermediate isolated as an off-white solid (yield 1,99g, ~80%) which was used without further purification. The crude aldehyde (318mg, 0,897mmol) was dissolved in anhydrous THF (10ml) and a 1,0M solution of vinylmagnesium bromide in THF (2,25ml, 2,25mmol) was added dropwise during 10min. The reaction mixture was stirred at RT for 20h. The reaction was quenched with H_2O (30ml) and neutralised to pH~6 with 4M acetic acid. The mixture was extracted with CH_2Cl_2 (100ml), and the organic phase was washed with a saturated aqueous solution of $NaHCO_3$ (40ml), dried with Na_2SO_4, and concentrated *in vacuo*. The product was purified with column chromatography (30-50% EtOAc in hexanes) and isolated as a clear oil and as a ~1:1 mixture of epimers.

Yield 142mg, 41%; R_f 0.45 (75% EtOAc in hexanes, one spot on TLC); ^{1}H NMR ($CDCl_3$) δ 0.04-0.10 (12H, m, $Si(CH_3)_2$), 0.86-0.92 (18H, m, $C(CH_3)_3$), 1.91 (6H, s, CH_3), 2.12 (1H, m, H-2'),

2.19 (1H, m, H-2'), 2.90 (1H, br s, OH), 3.12 (1H, br s, OH), 3.89 (1H, m, H-5') 3.95 (1H, m, H-5'), 4.27 (1H, br s, H-4'), 4.43-4.55 (3H, m, H-4' and H-3'), 5.23-5.51 (4H, m, CH=CH_2), 5.97 (2H, m, CH=CH_2), 6.15 (2H, m, H-1'), 7.46 (1H, br s, H-6), 7.49 (1H, br s, H-6), 9.05 (2H, br s, NH); ^{13}C NMR ($CDCl_3$) δ -4.81, -4.74, -4.65, -4.54, 12.47, 17.79, 17.91, 25.67, 25.70, 40.10, 40.51, 70.80, 72.51, 72.59, 72.64, 87.22, 87.36, 89.52, 90.17, 110.87, 110.92, 116.69, 116.73, 136.37, 137.21, 137.40, 137.54, 150.32, 150.43, 163.85; MS(FAB) *m/z*: 383 (MH^+, 32%).

Preparation of Allyl 3'-O-(5'-O-*tert*-butyldimethylsilyl)thymidinyl 5'-O-(3'-O-*tert*-butyldimethylsilyl)-5'-vinyl)thymidinyl phosphoric ester (10)

A mixture of compound **8** (235mg, 0,614mmol) and compound **9** (835mg unpurified material ~1,0mmol) was coevaporated twice with anhydrous CH_3CN and redissolved in anhydrous CH_3CN (40ml). A 0,45M solution of 1H-tetrazole in CH_3CN (4,10ml, 1,85mmol) was added. The reaction mixture was stirred at RT for 1h and the reaction was quenched with anhydrous MeOH (1,0ml). The residue was concentrated *in vacuo*, coevaporated twice with CH_2Cl_2, and redissolved in anhydrous CH_2Cl_2 (25ml). The solution was cooled to 0°C and a 3,0M solution of *tert*-butylhydrogenperoxide i toluene (1,25ml, 3,75mmol) was added. The reaction mixture was stirred at 0°C for 2½h, diluted with MeOH (2,0ml) and concentrated *in vacuo*. The product was purified twice by column chromatography (0-6% MeOH i CH_2Cl_2 and afterwards 10% EtOAc in hexanes) and isolated as a white solid and as an equimolar mixture of 4 diastereomers.

Yield 449mg, 87%; R_f 0.30 (5% MeOH in $CHCl_3$, one spot on TLC); ^{1}H NMR ($CDCl_3$) δ 0.07-0.14 (12H, m, 2 x Si(CH_3)$_2$), 0.87-0.94 (18H, m, 2 x C(CH_3)$_3$), 1.90-1.97 (6H, m, 2 x thymine CH_3), 1.97-2.32 (3H, m, H-2'), 2.46-2.70 (1H, m, H-2'), 3.77-3.99 (3H, m, 2 x H-5' and H-4'), 4.22 (1H, m, H-4'), 4.36-4.63 (3H, m, H-3' and OCH_2CH=CH_2) 4.80-5.04 (2H, m, H-3' and H-5'), 5.23-5.57 (4H, m, 2 x CH=CH_2), 5.83-6.04 (2H, m, 2 x CH=CH_2), 6.24-6.40 (2H, m, H-1'), 7.41-7.59 (2H, m, 2 x thymine H-6), 8.44-8.67 (2H, m, NH); ^{31}P NMR ($CDCl_3$) δ -1.97, -1.46, -1.25, -0.85; MS(FAB) *m/z*: 841 (MH^+, 1%); HiRes MALDI FT-MS *m/z* [MNa^+] (found/calc.) (863.3462/863.3454).

Preparation of 2-(2(*R*)-(*tert*-butyldimethylsilyl)oxymethyl-5(*R*)-(thymin-1-yl)tetrahydrofuran-3(*S*)-oxyl)-4-(3(*S*)-(*tert*-butyldimethylsilyl)oxy-5(*R*)-(thymin-1-yl)tetrahydrofuran-2(*S*)-oxyl)-2-oxo-4,7-dihydro-1,3-dioxa-2-phosphepine (11)

A) Compound **10** (50mg, 0,059mmol) was coevaporated with anhydrous CH_2Cl_2 and redissolved in anhydrous CH_2Cl_2 (3,0ml). Catalyst **1** (5,0mg, 0,0061mmol) was added and the reaction mixture was stirred at 40ºC for 48h. The solution was concentrated *in vacuo* and the product was purified by column chromatography (45-80% EtOAc in hexanes) and isolated as a clear off-white oil and as an equimolar mixture of 4 diastereomers. Yield 39 mg as a mixture of product and starting material, ~65% pure **11** estimated *via* ^{31}P NMR.

B) Same procedure as A using compound **10** (38mg, 0,045mmol), anhydrous CH_2Cl_2 (2,2ml) and catalyst **2** (1,9mg, 0,0023mmol), reaction time 2h. Yield 33,4mg, 91%.

R_f 0.33 and 0.44 (25% hexanes in EtOAc, two spots on TLC); ^{1}H NMR ($CDCl_3$) δ 0.07-0.15 (12H, m, 2 x Si(CH_3)$_2$), 0.87-0.93 (18H, m, 2 x C(CH_3)$_3$), 1.88-1.98 (6H, m, 2 x thymine CH_3), 2.10-2.67 (4H, m, H-2' and H-2''), 3.82-3.96 (2H, m, 2 x H-5''), 3.97-4.08 (1H, m, H-4'), 4.23-4.33 (1H, m, H-4''), 4.42-5.32 (5H, m, H-3', H-3'', H-5' and 2 x H-8') 5.73-5.96 (2H, m, H-6' and H-7'), 6.23-6.44 (2H, m, H-1' and H-1''), 7.45-7.53 (2H, m, 2 x thymine H-6), 8.52-9.03 (2H, m, NH); ^{31}P NMR ($CDCl_3$) δ 1.80, 2.00, 2.42, 2.71; HiRes MALDI FT-MS *m/z* [MNa^+] (found/calc.) (835.3141/835.3141).

Preparation of 2-(2(*R*)-hydroxymethyl-5(*R*)-(thymin-1-yl)tetrahydrofuran-3(*S*)-oxyl)-4-(3(*S*)-hydroxy-5(*R*)-(thymin-1-yl)tetrahydrofuran-2(*S*)-oxyl)-2-oxo-4,7-dihydro-1,3-dioxa-2-phosphepine (12)

Compound **11** (8,8mg, 0,011mmol) was dissolved in 90% TFA (0,75ml) and the reaction mixture was stirred at RT for 1h. The solution was concentrated *in vacuo* and the residue was coevaporated with anhydrous EtOH. The product was purified by preparative TLC (10%MeOH in CH_2Cl_2), and isolated as a white solid and as an equimolar mixture of 4 diastereomers.

Yield 6.0mg, 95%; R_f 0.44 (15% MeOH in CH_2Cl_2), one spot on TLC); ^{1}H NMR (CD_3OD) δ 1.79-1.96 (6H, m, 2 x thymine CH_3), 2.10-2.60 (4H, m, 2 x H-2' and 2 x H-2''), 3.69-5.40 (9H, m, H-3', H-3'', H-4', H-4'', H-5', 2 x H-5''and 2 x H-8'), 5.80-6.05 (2H, m, H-6' and H-7'), 6.19-6.41 (2H, m, H-1' and H-1''), 7.45-7.83 (2H, m, 2 x thymine H-6); ^{31}P NMR (CD_3OD) δ 1.91, 1.91, 2.41, 2.80; MS(FAB) *m/z*: 585 (MH^+, 6%).