Synthesis of a 4'-Selenated 2-Deoxyadenosine Derivative: A Novel Precursor suitable for the Preparation of Modified Oligonucleotides

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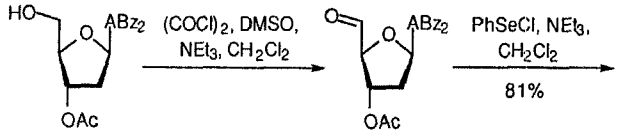
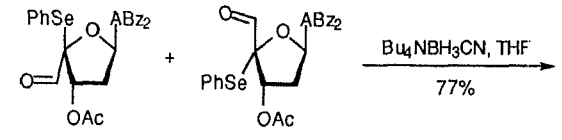
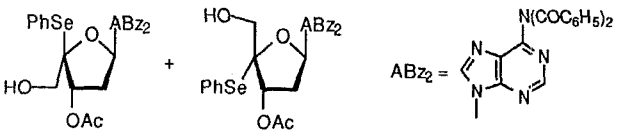
Abstract: Swern oxidation, subsequent selenation and reduction gave the selenated deoxyadenosine derivatives **4a** and **4b**. Isomer **4b** was converted into the phosphoramidite **7**, a building block for modified oligonucleotides **8**.

During the course of our studies on the radical induced DNA cleavage[1] we have looked for a nucleotide that can be used (a) for the generation of 4'-nucleotide radicals and (b) as a building block for oligonucleotide synthesis. It has turned out that selenide **7** fulfils both conditions.[2]

The synthesis of **7** starts from ribosyl derivative **1**.[3] Swern oxidation[4] led to aldehyde **2**, subsequent selenation with phenylselenyl chloride that was activated by triethylamine gave selenides **3a** and **3b** in 3.8:1 ratio. The corresponding thymidine derivative yielded exclusively the *lyxo* isomer.[5] Obviously, the benzoylated adenine shields the ß-position of the deoxyribose to a larger extend than thymine. The reduction of **3a** and **3b** turned out to be difficult because of the competing reduction of the phenylselenyl group.[6] But with tetrabutylammonium cyanoborohydride the reduction occurred in 77% yield. Products **4a** and **4b** were separated by flash chromatography. The *ribo* configuraton of **4b** was assigned by NOE experiments.

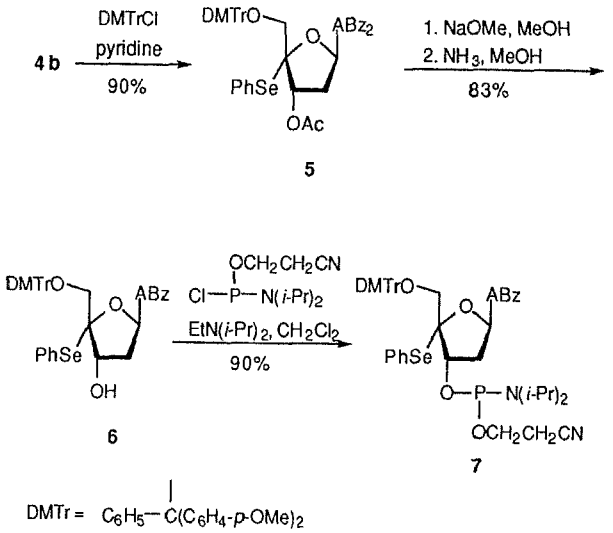


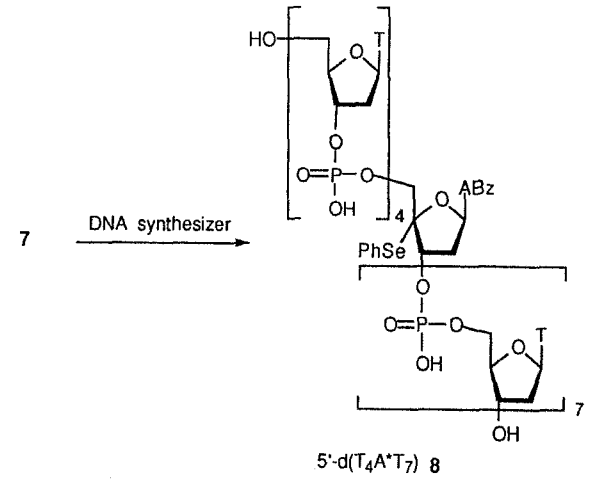




Isomer **4b** was tritylated[7] (**4b**→**5**), the acetate and one of the benzoyl groups removed (**5**→**6**) and the resulting sec. alcohol phosphitylated[8] (**6**→**7**).

Phosphoramidite **7** is a suitable building block for modified oligonucleotides.[2] Thus, using the DNA synthesizer[9] oligomers like the dodecamer **8** could be synthesized in high yield. The molecular mass of **8** was determined by MALDI-TOF MS.[10]





All temperatures quoted are uncorrected. All reagents are commercially available and used as received. The solvents were purified and dried according to standard procedures. The reactions were carried out in carefully dried apparatus and under argon atmosphere. Thin layer chromatography was performed on Merck precoated silica gel sheets F_{254} and flash chromatography on Merck silica gel 60 (40-63 µ). HPLC was performed on a Kontron Instruments system, using a Merck Lichrospher 10, 5 µ, RP-18 colum. NMR spectra were recorded on a Varian Gemini 300 (300 MHz). Chemical shifts are reported in ppm relative to internal TMS for ^1H (δ = 0.00 ppm), $CDCl_3$ for ^{13}C (δ = 77.0 ppm) and $OP(OPh)_3$ for ^{31}P (δ = -18.0 ppm). NOE experiments were done on a Varian VXR 400. FAB-MS were measured on a VC 70-250 (FAB: NAB and NAB+KCl). MALDI-TOF MS was performed with a Vestec, Benchtop II instrument. The spectrum was obtained using 2,4,6-trihydroxyacetophenone as a matrix at 337 nm laser wavelength and 15 kV acceleration voltage. The elemental analyses were performed by the Mikroanalytisches Labor at the University of Basel.

9-(3-*O*-Acetyl-2-deoxy-β-D-*erythro*-pento-5-aldo-1,4-furanosyl)-6,6-*N*,*N*-dibenzoyladenine (2):

To a solution of oxalyl chloride (0.77 mL, 8.98 mmol) in CH_2Cl_2 (10 mL), a solution of DMSO (0.85 mL, 11.9 mmol) in CH_2Cl_2 (5 mL) was added dropwise at -78°C. The mixture was stirred for 10 min at -78°C. Next, a cooled solution (-78°C) of the alcohol **1** (3.00 g, 5.98 mmol) in CH_2Cl_2 (40 mL) was added dropwise. After stirring for further 30 min at -78°C, Et_3N (2.50 mL, 17.9 mmol) was slowly added. The resulting solution of aldehyde **2** was directly selenated.

9-(3-*O*-Acetyl-2-deoxy-4-phenylseleno-α-L-*threo*-pento-5-aldo-1,4-furanosyl)-6,6-*N*,*N*-dibenzoyladenine (3a), 9-(3-*O*-Acetyl-2-deoxy-4-phenylseleno-β-D-*erythro*-pento-5-aldo-1,4-furanosyl)-6,6-*N*,*N*-dibenzoyladenine (3b):

Phenylselenyl chloride (1.72 g, 8.98 mmol) was dissolved in CH_2Cl_2 (20 mL) at RT and cooled to -78°C. This led to an orange suspension. Treatment with Et_3N (2.5 mL, 17.9 mmol) at -78°C gave a pale yellow solution. Now the solution of the above synthesized aldehyde **2** was added. After 30 min the mixture was warmed up to 0°C, stirred for another 2 h and diluted with ether (50 mL). Flash chromatography of the reaction mixture with Et_2O/CH_2Cl_2 = 3:2 gave a mixture of the diastereomers **3a** and **3b** in a 3.8:1 ratio, as light yellow foam in 81% yield (3.20g). This mixture gave the following spectroscopic data:

^{1}H NMR (300 MHz, $CDCl_3$) **3a**: δ = 2.09 (s, 3 H, $OCOCH_3$), 2.79-2.88 (ddd, 1 H, H-2'b, $J_{2'a,2'b}$ = 12.5, $J_{1',2'b}$ = 6.3, $J_{2'b,3'}$ = 4.9), 3.39-3.49 (ddd, 1 H, H-2'a, $J_{2'a,1'}$ = 8.5, $J_{2'a,3'}$ = 5.2), 5.92 (m, 1 H, H-3'), 6.87 (dd, 1 H, H-1'), 7.23-7.61 (m, 11 H, $H_{arom.}$), 7.85 (d, 4 H, $H_{arom.}$, *J* = 8.2), 8.55 (s, 1 H, H-2), 8.68 (s, 1 H, H-8), 9.25 (s, 1 H, CHO).

^{13}C NMR (75 MHz, $CDCl_3$, selection of characteristic resonances) **3a**: δ = 20.62 ($OCO\underline{C}H_3$), 37.75 (C-2'), 76.76 (C-3'), 85.35 (C-1'), 95.90 (C-4'), 169.3 ($O\underline{C}OCH_3$), 172.2 (NCOPh), 185.6 (CHO).

^{1}H NMR (300 MHz, $CDCl_3$) **3b**: δ = 2.24 (s, 3-H, $OCOCH_3$), 2.79-2.88 (m, 1 H, H-2'b, this signal is covered under H-2'b from **3a**), 3.01-3.08 (ddd, 1 H, H-2'a, $J_{2'a,2'b}$ = 12.8, $J_{2'a,1'}$ = 6.9, $J_{2'a,3'}$ = 7.4), 6.11 (dd, 1 H, H-3', $J_{3',2'b}$ = 5.2), 6.71 (t, 1 H, H-1', $J_{3',2'b}$ = 6.3), 7.23-7.61 (m, 11 H, $H_{arom.}$), 7.80 (d, 4 H, $H_{arom.}$, *J* = 7.5), 8.23 (s, 1 H, H-8), 8.60 (s, 1 H, H-2), 9.29 (s, 1 H, CHO).

^{13}C NMR (75 MHz, $CDCl_3$, selection of characteristic resonances) **3b**: δ = 20.62 ($OCO\underline{C}H_3$), 36.75 (C-2'), 72.94 (C-3'), 84.05 (C-1'), 97.89 (C-4'), 169.4 ($OCOCH_3$), 172.2 (NCOPh), 187.9 (CHO).

MS (FAB): *m/z* = 695 $(M+K)^+$, 656 $(M+H)^+$.

$C_{32}H_{25}N_5O_6Se$ (654.50) calc.: C 58.73, H 3.85, N 10.70, found: C 58.67, H 4.07, N 10.29.

9-(3-*O*-Acetyl-2-deoxy-4-phenylseleno-α-L-*threo*-pento-1,4-furanosyl)-6,6-*N*,*N*-dibenzoyladenine (4a), 3'-*O*-Acetyl-2'-deoxy-6,6-*N*,*N*-dibenzoyl-4'-phenylseleno-adenosine (4b):

To a solution of Bu_4NBH_3CN (2.47 g, 8.73 mmol) in THF (50 mL) the mixture of selenoaldehydes **3a** + **3b** (2.20 g, 3.36 mmol) in THF (30 mL) was added slowly at -78°C. After stirring for 15 min at -78°C and 60 min at 0°C the reaction was quenched with tartaric acid (5% solution in water, 30 mL). The THF was removed *in vacuo* (20°C). The aqueous residue was extracted with CH_2Cl_2 (5 x 70 mL), washed with sat. $NaHCO_3$ (2 x 50 mL), brine (2 x 30 mL), dried with Na_2SO_4 and evaporated *in vacuo*. Flash chromatography of the yellow oil with Et_2O/CH_2Cl_2/MeOH = 100:70:2 gave the alcohol **4a** 1.26 g (57%) and **4b** 440 mg (20%).

^{1}H NMR (300 MHz, $CDCl_3$) **4a**: δ = 2.16 (s, 1 H, $OCOCH_3$), 2.79 (ddd, 1 H, H-2'b, $J_{2'b,1'}$ = 6.6, $J_{2'b,3'}$ = 7.1, $J_{2'a,2'b}$ = 14.0), 3.14 (ddd, 1 H, H-2'a, $J_{2'a,1'}$ = 8.2, $J_{2'a,3'}$ = 7.0), 3.98 (d, 1 H, H-5'b, $J_{5'a,5'b}$ = 12.3), 4.11 (s, 1 H, OH), 4.53 (d, 1 H, H-5'a), 4.63 (m, 1 H, H-3'), 6.86 (t, 1 H, H-1'), 7.20-7.52 (m, 11 H, $H_{arom.}$), 7.86 (d, 4 H, $H_{arom.}$, *J* = 8.4), 8.66 (s, 1 H, H-2), 8.74 (s, 1 H, H-8).

^{13}C NMR (75 MHz, $CDCl_3$) **4a**: δ = 21.04 ($OCO\underline{C}H_3$), 40.16 (C-2'), 62.73 (C-5'), 76.27 (C-3'), 84.52 (C-1'), 96.94 (C-4'), 125.4 (SePh), 127.4 (C-5), 128.7, 129.2, 129.3, 129.4, 132.9, 134.1, 136.8 ($C_{arom.}$), 143.7 (C-8), 151.9 (C-6), 152.5 (C-2), 153.1 (C-4), 169.4 ($O\underline{C}OCH_3$), 172.2 (NCOPh).

MS (FAB): *m/z* = 696 $(M+K)^+$, 658 $(M+H)^+$.

$C_{32}H_{27}N_5O_6Se$ (656.50) calc.: C 58.55, H 4.15, N 10.67, found: C 58.55, H 4.30, N 10.62.

^{1}H NMR (300 MHz, $CDCl_3$) **4b**: δ = 2.21 (s, 1 H, $OCOCH_3$), 2.66 (ddd, 1 H, H-2'b, $J_{2'b,1'}$ = 6.6, $J_{2'b,3'}$ = 4.3, $J_{2'a,2'b}$ = 14.0), 3.17 (ddd, 1 H, H-2'a, $J_{2'a,1'}$ = 7.6, $J_{2'a,3'}$ = 7.3), 3.73 (dd, 1 H, H-5'b, $J_{5'a,5'b}$ = 3.2, $J_{5'b,OH}$ = 10.4), 3.92 (dd, 1 H, OH), 4.17 (dd, 1 H, H-5'a, $J_{5'a,OH}$ = 12.3), 6.01 (dd, 1 H, H-3'), 6.53 (t, 1 H, H-1'), 7.2-7.6 (m, 9 H, $H_{arom.}$), 7.66 (d, 2 H, $H_{arom.}$, *J* = 6.8), 7.84 (d, 4 H, $H_{arom.}$, *J* = 8.1), 8.19 (s, 1 H, H-8), 8.61 (s, 1 H, H-2). NOE's (irradiated H → affected H; ++ = strong, + = medium, (+) = weak): H-2'b → H-1'(++); H-2'a → H-5'a (+) and H-3' (++); H-5'b → H-3' ((+)); 5'-OH → H-3'(+); H-5'a → H-3' (+) and H-2 (++); H-3' → H-5'a (+) and 5'-OH ((+)); H-1' → H_5C_6Se (++) and H-8 (++); H_5C_6Se → H-1' ((+)); H-8 → H-1' (++) and H-3' ((+)); H-2 → H-5'a (+).

^{13}C NMR (75 MHz, $CDCl_3$) **4b**: δ = 20.74 ($OCO\underline{C}H_3$), 38.29 (C-2'), 67.13 (C-5'), 74.48 (C-3'), 85.08 (C-1'), 96.82 (C-4'), 125.3 (SePh), 128.3 (C-5), 128.7, 129.0, 129.4, 133.1, 133.9, 137.4 ($C_{arom.}$), 143.6 (C-8), 152.0 (C-2, C-4), 152.2 (C-6), 152.5 (C-4), 169.6 ($O\underline{C}OCH_3$), 172.2 (NCOPh).

MS (FAB): *m/z* = 696 $(M+K)^+$, 658 $(M+H)^+$.

$C_{32}H_{27}N_5O_6Se$ (656.50) calc.: C 58.55, H 4.15, N 10.67, found: C 58.56, H 4.24, N 10.57

3'-*O*-Acetyl-2'-deoxy-6,6-*N*,*N*-dibenzoyl-5'-*O*-(4,4'-dimethoxytriphenylmethyl)-4'-phenylseleno-adenosine (5):

A solution of **4b** (400 mg, 0.609 mmol) and 4,4'-dimethoxytriphenylmethyl chloride (DMTrCl) (248 mg, 0.731 mmol) in pyridine (5 mL) was stirred for 6 h at 25°C. After the reaction was completed, CH_3OH (10 mL) was added. Then, the solvent was removed *in vacuo* (38°C, 20 mbar). The residue was flash chromatographed with Et_2O/CH_2Cl_2/pentane /Et_3N = 1:1:0.5:0.01 and gave 530 mg (90%) of product **5** as a colorless foam:

^{1}H NMR (300MHz, $CDCl_3$): δ = 2.14 (s, 3H, $OCOCH_3$), 2.76 (ddd, 1 H, H-2'b, $J_{1',2'b}$ = 7.2 = $J_{2'b,3'}$, $J_{2'a,2'b}$ = 13.9), 3.05 (ddd, 1 H, H-2'a, $J_{1',2'a}$ = 5.2, $J_{2'a,3'}$ = 7.2), 3.42 (d, 1 H, H-5'b, $J_{5'a,5'b}$ = 10.7), 3.52 (d, 1 H, H-5'a), 3.73 (s, 6 H, OCH_3), 5.97 (t, 1 H, H-3'), 6.61 (dd, 1 H, H-1'), 6.71 (dd, 4 H, $H_{arom.}$, *J* = 8.8, *J* = 3.3), 7.5-7.1 (m, 20 H, $H_{arom.}$), 7.84 (d, 4 H, $H_{arom.}$, *J* = 7.3), 8.18 (s, 1 H, H-8), 8.61 (s, 1 H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.74 ($OCO\underline{C}H_3$), 37.61 (C-2'), 55.16 (OCH_3), 65.46 (C-5'), 74.19 (C-3'), 82.70 (C-1'), 86.71 ($\underline{C}(Ph)(PhOMe)_2$), 95.51 (C-4'), 113.1 ($C_{arom.}$), 125.7 (SePh), 126.8 (C-5), 128.2-144.3 ($C_{arom.}$), 143.2 (C-8), 152.5 (C-6), 152.4 (C-2), 151.9 (C-4), 158.5 ($\underline{C}OCH_3$), 169.5 ($O\underline{C}OCH_3$), 172.2 (NCOPh).

MS (FAB): *m/z* = 998 $(M+K)^+$, 960 $(M)^+$, 802 $(M\text{-}SePh)^+$.

6-*N*-Benzoyl-2'-deoxy-5'-*O*-(4,4'-dimethoxytriphenylmethyl)-4'-phenylseleno-adenosine (6):

Alcohol **5** (530 mg, 0.542 mmol) was dissolved in MeOH/CH_2Cl_2 = 8:2 (10 mL) and cooled to 0°C. $NaOCH_3$ (10 mg) was added and stirred for 10 min at 0°C. Next, 50% NH_3 in MeOH (10 mL) was added and stirred for 2 h at 0°C. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with tartaric acid (5% solution in water, 2 x 30 mL), brine (2 x 30 mL), dried over Na_2SO_4 and evaporated *in*

vacuo. Flash chromatography (CH_2Cl_2/MeOH/NEt_3 = 20:1:0.1) of the residue yielded 360 mg (83%) product **6**.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.7-2.9 (m, 2 H, H-2'), 3.09 (d, 1 H, 3'-OH, $J_{3',OH}$ = 3.4), 3.44 (d, 1 H, H-5'b, $J_{5'a,5'b}$ = 9.9), 3.55 (d, 1 H, H-5'a), 3.77 (s, 6 H, OCH_3), 5.04 (ddd, 1 H, H-3', $J_{3',2'a} = J_{3',2'b}$ = 8.3), 6.36 (dd, 1 H, H-1', $J_{1',2'a}$ = 3.8, $J_{1',2'b}$ = 7.7), 6.78 (d, 4 H, $H_{arom.}$, J = 8.8), 7.1-7.7 (m, 17 H, $H_{arom.}$), 7.97 (s, 1 H, H-2), 8.01 (d, 2 H, $H_{arom.}$, J = 7.4), 8.70 (s, 1 H, H-8), 9.04 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.61 (C-2'), 55.23 (OCH_3), 66.26 (C-5'), 74.72 (C-3'), 83.21 (C-1'), 86.97 (C(Ph)(PhOMe)$_2$), 100.0 (C-4'), 113.2 ($C_{arom.}$), 123.4 (SePh) 126.1 (C-5), 127.1-137.4 ($C_{arom.}$), 141.7 (C-8), 144.1 (C-4), 149.5 (C-6), 152.7 (C-2), 158.7 (C-OCH_3), 164.5 (NCOPh).

MS (FAB): *m/z* = 852 $(M+K)^+$, 814 $(M+H)^+$, 656 $(M-SePh)^+$.

6-*N*-Benzoyl-3'-*O*-(2-cyanoethyl *N*,*N*-diisopropyl-phosphoramidite)-2'-deoxy-5'-*O*-(4,4'-dimethoxytriphenylmethyl)-4'-phenylseleno-adenosine (7):

Alcohol **6** (244 mg, 0.30 mmol), *N*,*N*-diisopropylethylamine (278 µL, 1.62 mmol) and 2-cyanoethyl *N*,*N*-diisopropyl-chlorophosphoramidite (154 µL, 0.69 mmol) were dissolved in CH_2Cl_2 (3 mL) and stirred for 1 h at 25°C. Then, the solvent was removed under reduced pressure at 15°C and the residue was flash chromatographed with ethyl acetate/hexane/NEt_3 = 6:4:0.5. The separation gave 274 mg (90%) of two diastereomers of **7**; R_f (diastereomer a) = 0.5 (ethyl acetate/hexane/NEt_3 = 6:4:0.5); R_f (diastereomer b) = 0.6 (ethyl acetate/hexane/NEt_3 = 6:4:0.5).

^1H NMR (300 MHz, $CDCl_3$) (diastereomer a): δ = 1.20 (d, 12 H, N(CH(CH_3)$_2$)$_2$, $J_{N(CH(CH_3)_2)_2}$ = 6.7), 2.65 (t, 2 H, CH_2CN, $J_{CH_2CH_2CN}$ = 6.2), 2.9-3.1 (m, 2 H, H-2'), 3.4-3.9 (m, 12 H, OCH_3, H-5', N(CH(CH$_3$)$_2$)$_2$, CH_2O), 5.23-5.35 (m, 1 H, H-3'), 6.65 (dd, 1 H, H-1', $J_{1',2'a}$ = 5.0, $J_{1',2'b}$ = 7.4), 6.72 (t, 4 H, $H_{arom.}$), J = 8.0, 7.0-7.7 (m, 17 H, $H_{arom.}$), 8.00 (d, 2 H, $H_{arom.}$, J = 7.6), 8.23 (s, 1 H, H-2), 8.80 (s, 1 H, H-8), 9.05 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$) (diastereomer a): δ = 20.23-20.51 (N(CH(CH_3)$_2$)$_2$, 24.54-24.88 (CH_2CN), 38.49 (N(CH(CH$_3$)$_2$)$_2$), 43.42 (C-2', $J_{C-2',P}$ = 12.6), 55.15 (OCH_3), 58.99 (CH_2O, $J_{CH_2O,P}$ = 17.5), 64.75 (C-5'), 72.46 (C-3', $J_{C-3',P}$ = 18.4), 82.85 (C-1'), 86.52 (C(Ph)(PhOMe)$_2$), 98.24 (C-4', $J_{C-4',P}$ = 10.1), 113.0 ($C_{arom.}$), 117.5 (CN), 123.3 (SePh), 126.4-151.2 ($C_{arom.}$), 152.7 (C-2), 165.0 (NCOPh).

^1H NMR (300 MHz, $CDCl_3$) (diastereomer b): δ = 1.23 (d, 12 H, N(CH(CH_3)$_2$)$_2$, $J_{N(CH(CH_3)_2)_2}$ = 6.9), 2.51 (t, 2 H, CH_2CN, $J_{CH_2CH_2CN}$ = 6.4), 2.9-3.0 (m, 2 H, H-2'), 3.4-3.9 (m, 12 H, OCH_3, H-5', N(CH(CH$_3$)$_2$)$_2$, CH_2O), 5.37-5.50 (m, 1 H, H-3'), 6.60 (dd, 1 H, H-1', $J_{1',2'a}$ = 4.6, $J_{1',2'b}$ = 6.9), 6.72 (t, 4 H, $H_{arom.}$, J = 8.6), 7.1-7.7 (m, 17 H, $H_{arom.}$), 8.01 (d, 2 H, $H_{arom.}$, J = 7.1), 8.23 (s, 1 H, H-2), 8.81 (s, 1 H, H-8), 8.94 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$) (diastereomer b): δ = 20.23-20.51 (N(CH(CH_3)$_2$)$_2$, 24.54-24.88 (CH_2CN), 39.10 (N(CH(CH$_3$)$_2$)$_2$), 43.50 (C-2', $J_{C-2',P}$ = 12.5), 55.15 (OCH_3), 58.00 (CH_2O, $J_{CH_2O,P}$ = 20.6), 64.89 (C-5'), 74.02 (C-3', $J_{C-3',P}$ = 14.9), 82.00 (C-1'), 86.52 (C(Ph)(PhOMe)$_2$), 98.01 (C-4', $J_{C-4',P}$ = 8.1), 113.0 ($C_{arom.}$), 117.5 (CN), 123.3 (SePh), 126.4-151.2 ($C_{arom.}$), 152.7 (C-2), 165.0 (NCOPh).

^{31}P NMR (121 MHz, $CDCl_3$): δ = 149.7.

MS (FAB): *m/z* = 1052 $(M+K)^+$, 1014 $(M+H)^+$, 856 $(M-PhSe)^+$.

$C_{53}H_{56}N_7O_7PSe$ (1013.0) calc.: C 62.84, H 5.57, N 9.68, found: C 62.21, H 5.85, N 9.25.

5'-d($T_4A^*T_7$) (8):

The synthesis of the oligonucleotide **8** was carried out on an ABI 392 DNA/RNA synthesizer in a 0.2 µmol scale (20 mol equiv. amidite per cycle, 500 Å CPG support). A standard procedure for β-cyanoethylphosphoramidites was used, except the coupling time of **7** was extended to 30 min. The coupling efficiency of the modified building block **7** was similar to those of the commercial available amidites (98%, assigned by conductivity measurements of the trityl salt released on each cycle). After the incorporation of **7**, the coupling efficiency decreased to 92-95%. Concentrated NH_3 was used to remove the oligonucleotide from the solid support and to hydrolyze the benzamide function (55°C, 8 h). The crude oligonucleotide was detritylated and desalted on a oligonucleotide purification cartrige (OPC, MWG-Biotech). Preparative HPLC (RP-18, linear gradient of 5-40% acetonitrile (20 min) in 0.1% triethylammonium acetate of pH = 7.0) lead after lyophilysation to 128 nmol (64%) of the oligonucleotide **8**.

MALDI-TOF MS: m/z = 3751.2 (cal. 3752.48) $(M-H)^+$, 1875,6 (calc. 1875.24) $(M-2H)^{2+}$.

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