STUDIES ON OXIDATIVE TRANSFORMATIONS OF DINUCLEOSIDE H-PHOSPHONOSELENOATES

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Dedicated to Professor Antonín Holý on the occasion of his 70th birthday.

The utility of a new type of synthetic intermediates, H-phosphonoselenoate diesters, in the preparation of potentially biologically important nucleotide analogues containing the P–Se bond, was explored by converting dinucleoside H-phosphonoselenoates **1** into various phosphorus(V) derivatives under oxidative conditions.

Keywords: H-Phosphonoselenoates; H-Phosphonates; Oxidations; Phosphoroselenothioates; Phosphorodiselenoates; Phosphorofluoridoselenoates; Oligonucleotides; Dinucleotides.

Since most synthetically useful methods for the preparation of selenophosphates rely on oxidative conversion of P(III) to P(V) compounds using electrophilic selenium[1–5], we searched for an alternative methodology utilizing as a starting material selenophosphorus compounds at a lower oxidation state. This would provide an alternative way for preparing selenophosphate derivatives and permit synthesis of novel selenophosphate analogues, not accessible by traditional methods.

For this purpose we recently embarked on exploration of H-phosphonoselenoates as a new type of synthetic intermediates and developed efficient protocols for the preparation of H-phosphonoselenoate mono- and diesters[6–8] (see also the preceding paper in this issue[9]). We hoped that a distinctive feature of H-phosphonoselenoates, i.e. the presence of selenium bound to a phosphorus(III) atom, should enable further oxidative transformations at the phosphorus center in these compounds that could be exploited in the synthesis of new phosphate analogues.

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In this paper oxidative transformations of dinucleoside H-phosphonoselenoate **1** to produce various nucleotide analogues containing the P–Se bond, are discussed.

RESULTS AND DISCUSSION

Since H-phosphonoselenoate diesters were intended to be synthetic intermediates rather than target compounds, their oxidative transformations to provide access to various selenium-containing phosphate analogues were of crucial practical importance.

Oxidation to Phosphoroselenoates

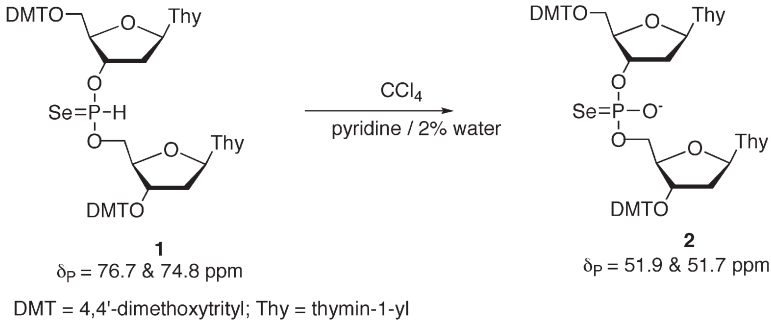
Oxidation involving iodine in the presence of water, which results in replacement of the P–H bond with a P–O bond, is a standard procedure in H-phosphonate chemistry[10] to convert P(III) into P(V) compounds. An analogous oxidation of H-phosphonoselenoate diesters should yield the corresponding phosphoroselenoate derivatives; however, the problem is that phosphoroselenoate diesters are known to undergo deselenization in the presence of iodine and water, giving rise to phosphate diesters[5].

Indeed, it was found that under standard oxidation conditions used for H-phosphonate diesters (2 equivalents of iodine in pyridine containing 2% water)[10], H-phosphonoselenoates **1** underwent rapid (<1 min) and quantitative conversion to the corresponding dinucleoside phosphate with complete selenium removal. Using an equimolar amount of iodine, the expected phosphoroselenoate **2** (δ_P 51.9 and 51.7 ppm, $^1J_{PSe}$ = 824 and 823 Hz) was formed as a major product (^{31}P NMR spectroscopy), but still deselenization to the corresponding phosphate diester occurred to ca. 20%. Similar results were obtained when iodine was replaced by *N*-iodosuccinimide or when oxidation was carried out in acetonitrile in the presence of limited amounts of a base and water.

By performing the reaction with iodine under anhydrous conditions, we hoped to generate the intermediate iodophosphoroselenote (analogously to iodophosphorothioate[11]) that was expected to be less prone to deselenization. Unfortunately, this reaction produced a complex mixture of products as indicated by ^{31}P NMR spectra.

Due to the high reactivity of the P–H bond in H-phosphonoselenoates **1** on one hand, and high propensity of selenium in phosphoroselenoate diesters **2** toward oxidation, on the other, we thought that tetrachloromethane[12] in the presence of a weak base should secure rapid oxidation of **1**

without affecting the selenium in product **2**. It was rewarding to find out that, indeed, treatment of H-phosphonoselenoate **1** in pyridine containing 2% water with 10 equivalents of CCl_4 effected rapid (<5 min) and clean oxidation to dinucleoside phosphoroselenoate **2** (Scheme 1). Under the anhydrous reaction conditions, the intermediacy of the corresponding phosphoroselenochloridates (δ_P 62.7 and 64.2 ppm) in this reaction could be established by ^{31}P NMR spectroscopy.



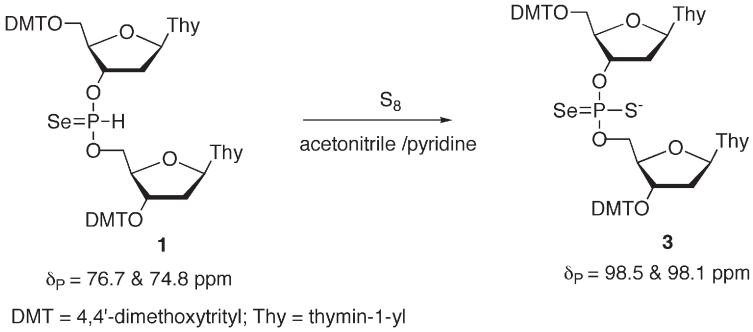
SCHEME 1

Having in mind the possibility of a pyridine-mediated ligand-exchange process in H-phosphonoselenoate diesters (analogously to H-phosphonothioate diesters[13]), we investigated also other reaction conditions for the oxidation of **1**, namely, by using CCl_4 (10 equivalents) in acetonitrile containing limited amount of pyridine (20 equivalents) and water (50 equivalents). Using this protocol, the oxidation of H-phosphonoselenoate **1** was complete within 10 min without detectable (^{31}P NMR spectroscopy) side products formation (deselenization or ligands exchange). In a separate experiment we also found that the produced phosphoroselenoate diester **2** was resistant to oxidation with CCl_4 even upon prolonged reaction time (few hours).

Sulfurization to Phosphoroselenothioates

Synthesis of phosphoroselenothioate diesters by oxidation of precursor H-phosphonoselenoate **1** with sulfur, was investigated. Sulfurization of H-phosphonate[14–16] or H-phosphonothioate[17,18] diesters with elemental sulfur in pyridine is a common procedure for converting P(III) compounds to various phosphorothioate derivatives. This reaction, when carried out with H-phosphonoselenoates **1** in acetonitrile containing pyridine (20 equivalents) in the presence of sulfur (3 equivalents) was, as expected, unevent-

ful and afforded the corresponding dinucleoside phosphoroselenothioates **3** (δ_P 98.1 and 98.5, $^1J_{PSe}$ = 759 and 761 Hz) quantitatively within 10 min (Scheme 2).



DMT = 4,4'-dimethoxytrityl; Thy = thymin-1-yl

SCHEME 2

Sulfurization of H-phosphonoselenoates **1** on a preparative scale was carried out with elemental sulfur (3 equivalents) in acetonitrile containing pyridine (20 equivalents) and the corresponding dinucleoside phosphoroselenothioates **3** were obtained after chromatography on silica gel in 95% yield. The reaction was also carried out on separate diastereomers of **1**. ^{31}P NMR spectroscopy revealed that sulfurization of these H-phosphonoselenoate diesters was completely stereospecific producing from a faster moving diastereomer of **1** (δ_P 74.8 ppm), a diastereomer of **3** with chemical shift δ_P 98.1 ppm, and from a slower moving diastereomer of **1** (δ_P 76.7 ppm), a diastereomer of **3** resonating at δ_P 98.5 ppm. Similarly to other sulfurization reaction of P(III) compounds[19–21], formation of phosphoroselenothioates **3** occurred most likely with retention of configuration at the phosphorus centre.

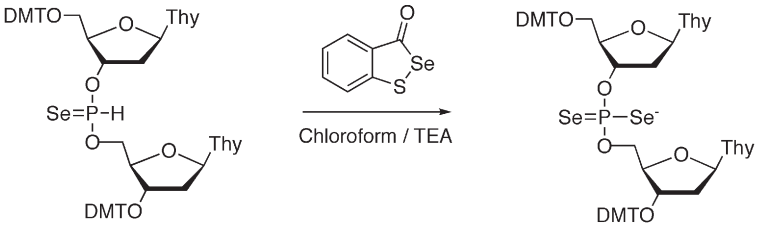
Selenization to Phosphorodiselenoates

There are two available approaches to the synthesis of dialkyl phosphorodiselenoates. One of them involves treatment of the appropriate alcohol with phosphorus pentaselenide[22] to produce symmetrical diselenoate diesters, and the other one is based on reaction of *N*-phenylphosphoroamidoselenoates with sodium hydride and carbon diselenide[23].

Neither of these procedures has been applied to the synthesis of nucleoside phosphorodiselenoate diesters, probably because of harsh reaction conditions or difficulties in obtaining appropriate starting materials. This might explain why the synthesis of nucleoside phosphorodiselenoate has not been yet described in the literature.

We found that by using 3*H*-1,2-benzothiaselenol-3-one (BTSe)[5], a selenium transferring reagent soluble in organic solvents, it was possible to cleanly convert H-phosphonoselenoate **1** into the corresponding diselenophosphate **4** (δP 85.5 ppm) that could be isolated in 85% yield (Scheme 3).

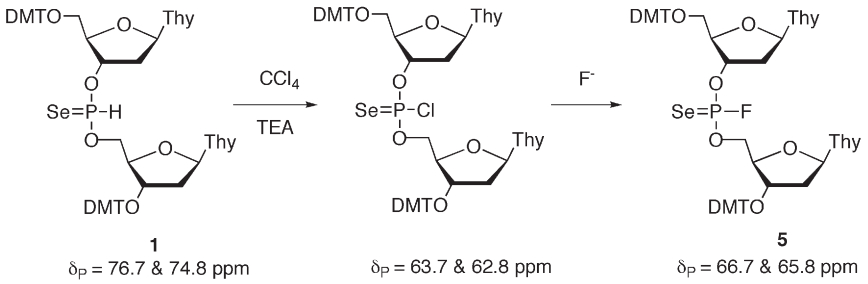
Generation of H-phosphonoselenoate diester **1** in situ, followed by the addition of BTSe (1.5. equivalents) allowed preparation of diselenoate **4** without prior isolation of the H-phosphonoselenoate diesters. Using elemental selenium instead of BTSe for the selenization step, gave inferior results.



SCHEME 3

Conversion to Phosphorofluoridoselenoates

When dinucleoside H-phosphonoselenoate **1** in chloroform was treated with tetrachloromethane (10 equivalents) and triethylamine (TEA, 4 equivalents) a complete conversion to the corresponding chlorophosphoroselenoate (δ_P 63.7 and 62.8 ppm; see Scheme 4) occurred within 5 min. The subsequent addition of triethylamine trishydrofluoride (TAF)[24] furnished



SCHEME 4

clean and instantaneous formation of dinucleoside phosphorofluoridoselenoate **5** (δP 66.7 and 65.8 ppm, $^1J_{PF}$ = 1147 and 1159 Hz).

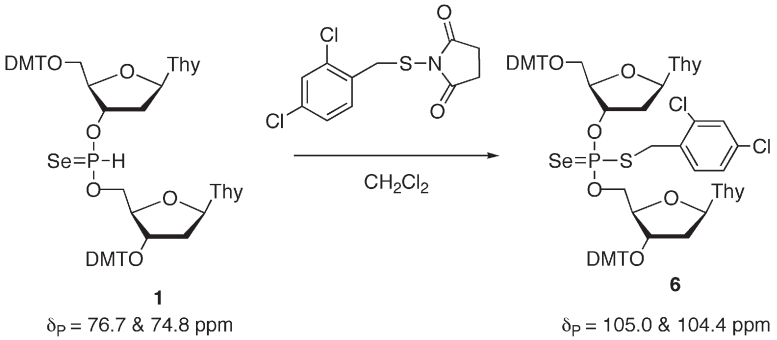
The above transformation was virtually quantitative and the produced phosphorofluoridoselenoate **5** was stable enough to be isolated in pure state by column chromatography on silica gel in 80% yield.

Thiobenzylation of H-Phosphonoselenoates

The conversion of H-phosphonate or H-phosphonothioate diesters to the corresponding S-benzyl triesters can be accomplished via sulfurization, followed by S-benzylation, or oxidation followed by S-benzylation, respectively. This synthetic approach is, however, not an option in the case of H-phosphonoselenoate diesters, since the phosphoroselenothioate intermediate was expected to be preferentially alkylated on the selenium atom[25].

We found, however, that *N*-(2,4-dichlorobenzyl)thiosuccinimide[26], a reagent developed by van Boom et al., can effect synthesis of the thioseleno phosphotriester **6** in one step using the corresponding H-phosphonoselenoate diester as a starting material.

To this end, dinucleoside H-phosphonoselenoate **1** (generated in situ from the corresponding nucleoside H-phosphonoselenoate monoesters and a suitably protected nucleoside) in methylene chloride was treated with *N*-(2,4-dichlorobenzyl)thiosuccinimide (2 equivalents). The reaction was clean and produced within 25 min **6** (δ_P 105.0 and 104.4 ppm) as the sole nucleotidic product (Scheme 5).



SCHEME 5

In acetonitrile–pyridine (4:1, v/v) the oxidative thiobenzylation of **1** with *N*-(2,4-dichlorobenzyl)thiosuccinimide was even faster (5 min), and, after work-up, the triester **6** was isolated in 85% yield. Compound **6** has been previously prepared by Michalski et al. employing a protocol that involved an intermediate dinucleoside S-dichlorobenzyl phosphite, followed by its oxidation with elemental selenium[27].

In conclusion, by preparing new kinds of nucleotide analogues we demonstrated the usefulness of H-phosphonoselenoate diesters in the synthesis of nucleotide analogues bearing the P–Se bond. The added value of the described procedures is that they can be performed with similar efficiency both on isolated and on in situ produced dinucleoside H-phosphonoselenoates. Easy access to H-phosphonoselenoates should expand and complement synthetic methods of the preparation of biologically important phosphate analogues based on the H-phosphonate and H-phosphonothioate methodology developed in this Laboratory[28–30].

EXPERIMENTAL

Materials and Methods

Pyridine, 2,6-lutidine, acetonitrile, and triethylamine (TEA) were refluxed with CaH_2 and then distilled and stored over 4Å molecular sieves or CaH_2 (TEA). Dinucleoside H-phosphonoselenoate diester **1** was prepared via condensation of 5′-*O*-(4,4′-dimethytrityl)thymidine 3′-H-phosphonoselenoate monoester[6–8] with 3′-*O*-(4,4′-dimethytrityl)thymidine as described in the preceding paper in this issue. TLC analyses were carried out on Merck plates precoated with silica gel 60 F_{254} using the following eluents: toluene–methanol (9:1, v/v; system A); chloroform–methanol (9:1, v/v; system B). ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were measured in $CDCl_3$; chemical shifts (δ scale) are given in ppm, coupling constants (*J*) in Hz. ^{31}P NMR experiments were carried out in 10-mm tubes using phosphorus compound **1** (0.05 mmol) in a solvent (2 ml). H_3PO_4 (2%) in D_2O was used as external standard (coaxial inner tube). The values of the chemical shifts for the intermediates produced in situ in some experiments varied (±1 ppm) depending on the reaction conditions.

Triethylammonium 5′-*O*-(4,4′-Dimethoxytrityl)thymidin-3′-yl 3′-*O*-(4,4-Dimethoxytrityl)thymidin-5′-yl Phosphoroselenoate (**2**)

5′-*O*-(4,4′-Dimethoxytrityl)thymidin-3′-yl 3′-*O*-(4,4′-dimethoxytrityl)thymidin-5′-yl H-phosphonoselenoate (**1**; 0.1 mmol) was treated with CCl_4 (1 mmol) in MeCN containing pyridine (2 mmol) and water (50 mmol) for 10 min. TEA (0.5 mmol) was added, the reaction mixture was concentrated and separated on a silica gel column using CH_2Cl_2 containing a gradient of methanol (0–5%) and triethylamine (0.1%). Phosphoroselenoate **2** was isolated as a white solid in 95% yield (purity > 98% by ^{1}H NMR). ^{31}P NMR: 49.51 and 49.26 ($^1J_{PSe}$ = 818 and 820). ^{1}H NMR: 7.72 (s, 1 H); 7.67 (s, 1 H); 7.59 (s, 1 H); 7.53 (s, 1 H); 7.27 (m, 40 H); 6.80 (m, 16 H); 6.47 (m, 1 H); 6.36 (m, 1 H); 6.17 (dd, ^3J = 8.79 and 5.86, 2 H); 5.36 (m, 2 H); 4.30 (m, 2 H); 3.95 (m, 4 H); 3.77 (s, 6 H); 3.76 (s, 6 H); 3.74 (s, 6 H); 3.71 (s, 6 H);

3.65 (m, 2 H); 3.32 (m, 4 H); 3.12 (q, ^3J = 7.22, 12 H); 2.63 (m, 2 H); 2.23 (m, 2 H); 1.87 (m, 4 H); 1.83 (s, 6 H); 1.29 (m, 24 H). ^{13}C NMR: 164.34, 164.09, 158.92, 150.86, 150.70, 145.35, 145.28, 144.63, 137.38, 136.56, 136.50, 135.77, 135.49, 130.47, 130.44, 130.38, 128.51, 128.19, 127.29, 114.29, 113.54, 111.52, 111.39, 111.14, 87.47, 87.42, 87.36, 86.87, 74.63, 62.72, 55.48, 45.00, 39.02, 34.03, 32.13, 29.89, 29.71, 29.56, 29.36, 29.16, 22.89, 14.33, 12.66, 11.79, 8.81

Triethylammonium 5′-*O*-(4,4′-Dimethoxytrityl)thymidin-3′-yl 3′-*O*-(4,4′-Dimethoxytrityl)thymidin-5′-yl Phosphoroselenothioate (**3**)

5′-*O*-(4,4′-Dimethoxytrityl)thymidin-3′-yl 3′-*O*-(4,4′-dimethoxytrityl)thymidin-5′-yl H-phosphonoselenoate (**1**; 0.1 mmol) was treated with sulfur (0.3 mmol) in MeCN containing pyridine (2 mmol) for 10 min. The reaction mixture was treated with TEA (0.5 mmol), concentrated and purified on a silica gel column using CH_2Cl_2 containing a gradient of methanol (0–5%) and triethylamine (0.1%). The product was isolated as a white solid in 95% yields (purity > 98% by ^{1}H NMR).

Diastereoisomer obtained from faster moving H-phosphonoselenoate diester (R_P)-**1**: ^{31}P NMR: 98.11 ($^1J_{PSe}$ = 759). ^{1}H NMR: 7.80, 7.56, 7.29 (m, 20 H); 6.81 (m, 8 H); 6.54 (t, J = 7.42, 1 H); 6.35 (dd, J = 8.2 and 5.7, 1 H); 5.45 (m, 1 H); 4.42 (m, 1 H); 4.22 (m, 1 H); 3.76 (s, 6 H); 3.74 (s, 3 H); 3.73 (s, 3 H); 3.65 (m, 1 H); 3.39 (m, 2 H); 3.12 (q, J = 7.22, 6 H); 2.54 (m, 1 H); 2.28 (m, 1 H); 1.98 (m, 4 H); 1.35 (s, 3 H); 1.29 (t, J = 7.22, 9 H); 1.25 (s, 3 H). ^{13}C NMR: 164.38, 164.20, 158.90, 158.86, 150.95, 150.58, 145.33, 144.67, 139.49, 136.94, 136.59, 136.52, 136.00, 135.80, 135.57, 130.51, 130.46, 130.42, 128.59, 128.44, 128.22, 127.23, 114.29, 113.61, 113.49, 111.61, 111.35, 87.46, 87.20, 85.16, 84.93, 77.50, 75.69, 69.38, 66.48, 63.80, 55.48, 46.35, 39.45, 34.03, 32.13, 29.87, 29.71, 29.56, 29.36, 29.16, 22.89, 22.89, 12.69, 11.79, 8.90.

Diastereoisomer obtained from slower moving H-phosphonoselenoate diester (S_P)-**1**: ^{31}P NMR: 98.48 ($^1J_{PSe}$ = 761). ^{1}H NMR: 7.80, 7.57, 7.30 (m, 20 H); 6.82 (m, 8 H); 6.53 (t, J = 6.93, 1 H); 6.16 (m, 1 H); 5.45 (m, 1 H); 4.36 (m, 1 H); 3.96 (m, 1 H); 3.77 (s, 6 H); 3.74 (s, 3 H); 3.73 (s, 3 H); 3.65 (m, 1 H); 3.32 (m, 2 H); 3.09 (q, J = 7.22, 6 H); 2.58 (m, 1 H); 2.30 (m, 1 H); 1.94 (m, 2 H); 1.70 (m, 2 H); 1.28 (m, 15 H). ^{13}C NMR: 164.24, 164.07, 158.94, 158.86, 150.89, 145.34, 144.67, 137.38, 136.55, 136.49, 135.81, 135.58, 130.48, 130.32, 128.60, 128.51, 128.44, 128.21, 127.32, 114.29, 113.62, 113.55, 113.53, 111.20, 111.16, 87.44, 87.21, 86.85, 85.14, 84.96, 75.68, 74.57, 63.82, 62.76, 55.48, 46.22, 39.45, 38.96, 34.03, 32.14, 29.89, 29.72, 29.57, 29.37, 29.17, 22.92, 12.67, 11.79, 8.97.

Triethylammonium 5′-*O*-(4,4′-Dimethoxytrityl)thymidine-3′-yl 3′-*O*-(4,4′-Dimethoxytrityl)thymidine-5′-yl Phosphorodiselenoate (**4**)

This compound was obtained by selenization of H-phosphonoselenoate **1** (0.1 mmol; produced in situ in acetonitrile–pyridine (4:1, v/v) as described above) with 3*H*-1,2-benzothiaselenol-3-one[5] (1.5 equiv.) in the presence of triethylamine (3 equiv.) for 5 min, followed by chromatography on silica gel using gradient of methanol (0–3%) in dichloromethane containing triethylamine (0.1%). Yield 76%, white foam (triethylammonium salt, purity > 98% by ^{1}H NMR). FAB HRMS $[M]^+$, found 1323.2131; $C_{62}H_{62}N_4Na_2O_{14}PSe_2$ requires 1323.2126. ^{31}P NMR: 85.50 (multiplet, $^1J_{PSe}$ = 751). ^{1}H NMR (selected signals): 6.50 (m, 1 H, H_b1'); 6.30 (m, 1 H, H_a1'); 5.52 (dd, 1 H, H_a3'); 4.39 (d, 1 H, H_b3'); 4.21 (s, 1 H, H_a4'); 3.78–3.65 (14 H,

4 × O-CH_3 and H_b5′); 3.44 and 3.26 (2 m, 2 H, H_a5′); 2.54 and 2.25 (2 m, 2 H, H_a2′); 1.93 (m, 2 H, H_b2′); 1.92 and 1.28 (2 s, 6 H, 2 × C5-CH_3). ^{13}C NMR (selected signals): 84.91 (2 C, C_b1′ and C_a4′), 84.84 (C_b4′), 84.64 (C_a1′), 77.48 (C_a3′), 75.53 (C_b3′), 66.54 (d, C_b5′), 63.59 (C_a5′), 12.52 and 11.50 (2 × C5-CH_3).

5′-*O*-(4,4′-Dimethoxytrityl)thymidine-3′-yl 3′-*O*-(4,4′-Dimethoxytrityl)thymidine-5′-yl Phosphorofluoridoselenoate (**5**)

This compound was obtained by treatment of H-phosphonoselenoate **1** (0.1 mmol) and triethylamine trihydrofluoride (1 equiv.) in chloroform (2 ml) with CCl_4 (10 equiv.) and triethylamine (4 equiv.) for 5 min. Chromatography on silica gel using toluene–ethyl acetate furnished **5** as ca. 1:1 mixture of diastereomers. Yield 80%, white powder after lyophilization (purity > 98% by ^{1}H NMR). FAB HRMS $[M]^+$, found 1239.3051; $C_{62}H_{62}FN_4NaO_{14}PSe$ requires 1239.3047. ^{31}P NMR (mixture of diastereomers): 68.00 (multiplet, $^1J_{PSe}$ = 1059, $^1J_{PF}$ = 1148) and 67.00 (multiplet, $^1J_{PSe}$ = 1064, $^1J_{PF}$ = 1160). ^{19}F NMR (mixture of diastereomers): –31.0 ($^2J_{FSe}$ = 146, $^1J_{FP}$ = 1150) and –31.5 ($^2J_{FSe}$ = 147, $^1J_{FP}$ = 1162). ^{1}H NMR (mixture of diastereomers, selected signals): 6.36 (m, 2 H, H_a1′ and H_b1′); 5.44 (m, 1 H, H_a3′); 4.28 (m, 1 H, H_b3′); 4.21 and 4.11 (2 m, 1 H, H_a4′); 4.06, 3.93 and 3.65 (3 m, 2 H, H_b5′); 3.95 (m, 1 H, H_b4′); 3.44 and 3.42 (2 m, 2 H, H_a5′); 2.44, 2.08 and 1.75 (3 m, 4 H, H_a2′ and H_b2′); 1.86, 1.84, 1.47 and 1.45 (4 s, 6 H, 2 × C5-CH_3). ^{13}C NMR (mixture of diastereomers, selected signals): 85.71 and 85.49 (C1′), 84.67 (d, *J* = 5, C_a4′), 84.49 (C1′ and C_a4′), 83.77 (m, C_b4′), 82.31 and 82.12 (C_a3′), 74.07 (C_b3′), 69.64 (m, C_b5′), 63.41 and 63.34 (C_a5′), 39.32 (C2′), 38.92 (m, C2′), 12.66, 12.59, 11.94 and 11.88 (2 × C5-CH_3).

S-(2,4-Dichlorobenzyl)-5′-*O*-(4,4′-dimethoxytrityl)thymidine-3′-yl 3′-*O*-(4,4′-Dimethoxytrityl)thymidine-5′-yl Phosphoroselenothioate (**6**)

This compound was obtained by treatment of H-phosphonoselenoate **1** (0.1 mmol; produced in situ in acetonitrile–pyridine (4:1, v/v) as described above) with *N*-(2,4-dichlorobenzyl)thiosuccinimide[26] (1.5 equiv.) for 5 min, followed by chromatography on silica gel using toluene–ethyl acetate. Yield 85%, white foam (ca. 1:1 mixture of diastereomers, purity > 98% by ^{1}H NMR). FAB HRMS $[M]^+$, found 1411.2543; $C_{69}H_{67}Cl_2N_4O_{14}PSSeNa$ requires 1411.2552. ^{31}P NMR (mixture of diastereomers): 100.5 (multiplet, $^1J_{PSe}$ = 924) and 98.50 (multiplet, $^1J_{PSe}$ = 921). ^{1}H NMR (mixture of diastereomers, selected signals): 6.30–6.40 (m, 2 H, H_a1′ and H_b1′); 5.36–5.47 (m, 1 H, H_a3′); 4,27 and 4.23 (2 m, 1 H, H_b3′); 4.11 and 4.02 (2 d, $^3J_{PH}$ = 15, 2 H, S-CH_2); 4.09 (m, 1 H, H_a4′); 3.89 and 3.92 (2 m, 1 H, H_b4′); 3.8–3.6 (m, 2 H, H_b5′); 3.35 (m, 2 H, H_a5′); 2.33, 1.97 and 1.63 (3 m, 2 H, H_a1′ and H_b1′); 1.85, 1.47 and 1.44 (3 s, 6 H, 2 × C5-CH_3). ^{13}C NMR (mixture of diastereomers, selected signals): 85.58 and 85.36 (C1′), 84.95 (d, *J* = 4.6, C_a4′), 84.47 and 84.43 (C1′), 84.03 (d, *J* = 5.5, C_a4′), 83.86 and 83.80 (2 d, *J* = 9.5, C_b4′), 80.49 and 80.31 (2 d, *J* = 5.4, C_a3′), 74.50 and 74.26 (C_b3′), 68.25 and 67.91 (2 d, *J* = 7, C_b5′), 63.34 and 63.13 (C_a5′), 39.24–38.86 (m, C_a2′ and C_b2′), 37.26 and 36.61 (2 d, *J* = 2.5 and 4, S-C), 12.68, 12.63, 11.88 and 11.81 (2 × C5-CH_3).

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