Nucleoside H-Phosphonates. 12. Synthesis of Nucleoside 3'-(Hydrogen-phosphonothioate) Monoesters via Phosphinate Intermediates

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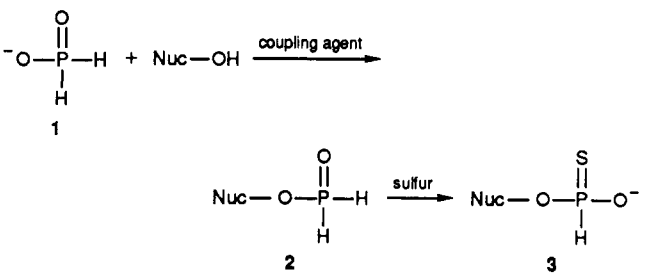
Reactions of phosphinic acid with suitably protected nucleosides in the presence of condensing agents have been studied using ^{31}P NMR spectroscopy. It was found that rapid disproportionation of phosphinic acid occurring during course of the reactions can be avoided if the proper ratio of the reactants is chosen, and the phosphinate esters can be produced quantitatively. The utility of phosphinate esters as synthetic intermediates was demonstrated by designing a convenient method for the preparation of nucleoside H-phosphonothioates. It consists of the in situ formation of nucleoside phosphinates from phosphinic acid and appropriate nucleosides in the presence of a condensing agent, followed by their oxidation with elemental sulfur. Ribo- and deoxyribonucleoside 3'-H-phosphonothioates have been synthesized in ~80-90% yield using this method.

Various aspects of the H-phosphonate chemistry, directed toward the preparation of biologically relevant compounds via H-phosphonate intermediates, have been investigated in this laboratory during the past few years.[1] As a continuation of these studies, we have become involved in synthesis of the thio analogues of H-phosphonates, namely the nucleoside H-phosphonothioate esters.[2]

This class of compounds seems to be most interesting, both from theoretical and synthetic points of view. It may be a valuable tool in the elucidation of some reaction mechanisms as well as in investigations of important processes in the H-phosphonate chemistry, e.g. the tautomeric equilibrium or the phosphorus-bounded hydrogen exchange. On the other hand, these compounds may also be rather versatile synthetic intermediates on the way to various phosphorus-containing natural product analogues. Another aspect of the H-phosphonothioates is a chirality of the phosphorus center in monoesters. This feature may be exploited in stereospecific synthesis of chiral phosphorothioate and phosphate esters.

The major obstacle in pursuing this line of investigations was the lack of a suitable method for the preparation of H-phosphonothioate monoesters. To our knowledge, in literature there is only one preparative procedure reported by Michalski et al.[3] for the preparation of H-phosphonothioates (ethyl H-phosphonothioate). Unfortunately, this method, which consists of treatment of diethyl chlorophosphite with hydrogen sulfide, followed by aqueous sodium hydroxide hydrolysis, is not suitable for the preparation of nucleoside H-phosphonothioates.

Thus, we decided to explore the possibility of synthesizing nucleoside H-phosphonothioate monoesters via the reaction of suitably protected nucleosides with phosphinic acid in the presence of a condensing agent, followed by oxidation with elemental sulfur, as shown below:



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In this paper some ^{31}P NMR studies concerning various aspects of the above reaction sequence are described. These enabled us to design a convenient method for the preparation of nucleoside 3'-*H*-phosphonothioate monoesters.

Results and Discussion

Reaction of Phosphinic Acid with Nucleosides. According to the above reaction scheme, the crucial step in synthesis of nucleoside H-phosphonothioates is the formation of phosphinate intermediate **2**. Unfortunately, phosphinic ester are rare intermediates in organic synthesis, mainly because of their instability and lack of a general method for their preparation. Standard esterification methods, e.g. reaction of alcohols with anhydrides or halides of the corresponding acids, are not applicable, since the appropriate anhydride or halides are not known. Thus, only simple alkyl phosphinates, which can be prepared by treatment of phosphinic acid with, e.g., diazoalkanes,[4] orthocarbonyl compounds,[5] triethyloxonium tetrafluoroborate,[6] or by using aliphatic alcohols in the presence of salts at elevated temperature,[7] have been described in literature. Recently, Sekine et al.[8] on the occasion of nucleoside H-phosphonates synthesis mentioned that a reaction of phosphinic acid with nucleosides in the presence of a condensing agent, followed by oxidation with iodine, afforded a complex mixture of products. Since the reaction of phosphinic acid with hydroxylic components in the presence of a condensing agent can be considered as a convenient and general method for the preparation of phosphinic acid esters, we decided to have a closer look at this reaction.

When pivaloyl chloride (PV-Cl, 3 equiv) was added to a reaction mixture containing 5'-*O*-(dimethoxytrityl)thymidine (dmt-T, 1 equiv) and triethylammonium phos-

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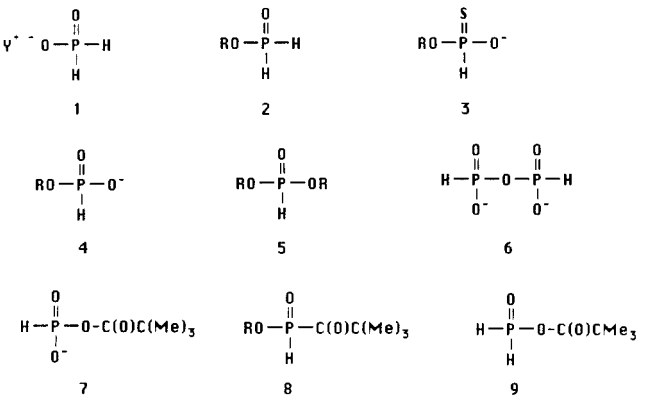
phinate (**1a**, 3 equiv), a yellowish color appeared immediately, followed by the formation of a yellow-brown precipitate. After 5 min, TLC analysis (silica gel) of the supernatant showed the presence of only one UV absorbing product (R_f = 0.40, system A) in addition to a small amount of the starting nucleoside. Chromatographic mobility indicated a neutral compound, and a smooth oxidation with iodine into a polar product suggested the presence of the P–H bond. ^{31}P NMR analysis revealed, however, that the coupling product (δ =7.42 ppm) contained only one P–H bond ($^1J_{PH}$ = 714.0 Hz, d, and $^3J_{PH}$ = 8.6 Hz, t), instead of the expected two for the intermediate **2a**. The chemical shift value, the splitting pattern of signals, and comparison with a reference compound allowed us to identify the coupling product as a symmetrical diester, bis(5′-*O*-(dimethoxytrityl)thymidin-3′-yl) H-phosphonate **5a**.



1a, Y=TEAH+
1b, Y=PyH+
1c, Y=H
2a,4a,5a, R=5′-O-dimethoxytritylthymidin-3′-yl
2b,4b,5b, 8, R=ethyl
3a, R=5′-O-dimethoxytritylthymidin-3′-yl
3b, R=5′-O-dimethoxytrityl-N-benzoyldeoxycytidin-3′-yl
3c, R=5′-O-dimethoxytrityl-N-benzoyldeoxyadenosin-3′-yl
3d, R=5′-O-dimethoxytrityl-N-isobutyryldeoxyguanosin-3′-yl
3e, R=5′-O-dimethoxytrityl-2′-O-t-butyldimethylsilyluridin-3′-yl
3f, R=ethyl

Such a course of the coupling reaction can be explained by initial formation of the phosphinate intermediate **2a**, which undergoes rather fast oxidation to the nucleoside H-phosphonate **4a**, and this in turn, in the presence of a condensing agent and a nucleoside, gives the H-phosphonate diester **5a**. The proposed reaction pathway was substantiated by ^{31}P NMR analysis of the reaction carried out in the presence of 1 equiv of a coupling agent (PV-Cl). In such a reaction mixture, signals corresponding to **1a**, the nucleoside phosphinate **2a**, and the H-phosphonate monoester **4a** were indeed observed. Upon addition of another equivalent of PV-Cl, signals from the latter compound were replaced by a new one, corresponding to the H-phosphonate diester **5a**, while resonances from **1a** disappeared. Since **1a** (or more likely, a reactive intermediate derived from it) is assumed to act as a oxidizing agent, the yellow-brown precipitate most likely should be the reduction product of phosphinic acid (see also later in the text). A similar course of the reaction was observed when other condensing agents, e.g. diphenyl phosphorochloridate (DPCP), 5,5-dimethyl-2-oxo-2-chloro-1,3,2-dioxaphosphorinane (NPCP), were used instead of PV-Cl.

Reaction of Phosphinic Acid with Condensing Agents. Phosphinic acid is known to undergo oxidation to phosphonic and phosphoric acid and also to disproportionate to phosphine and phosphonic acid.[9] Its salts, however, are rather stable, and we did not observe oxidation of pyridinium or triethylammonium phosphinates upon storage at room temperature for several weeks.[10] On the other hand, addition of iodine in aqueous pyridine to these salts resulted in their quantitative conversion into the corresponding salts of phosphonic acid (~15 min, ^{31}P NMR, δ = 2.28 ppm, $^1J_{PH}$ = 625.0 Hz). Sulfur also readily oxidizes the phosphinate salts to H-phosphonothioates, as judged from the ^{31}P NMR spectra (1 h, over 90% conversion; δ = 51.89 ppm, $^1J_{PH}$ = 585.9 Hz).

Since condensing agents facilitate phosphinate esters synthesis, one may infer initial formation of some kind of activated species derived from phosphinic acid. Unfortunately, our attempts to observe such species under various experimental conditions using ^{31}P NMR spectroscopy failed. Addition of a condensing agent (PV-Cl, DPCP, NPCP) into a solution of **1**, irrespective of the solvent used (pyridine, THF, acetonitrile, chloroform) and presence or absence of a base, caused formation of a yellow-brown precipitate. It occurred almost immediately when pyridine and PV-Cl or DPCP were used, or during ~20 min in acetonitrile with NPCP. Stepwise addition of PV-Cl (1 + 1 + 1 equiv) into a pyridine solution of **1a** was followed by ^{31}P NMR spectroscopy. A gradual disappearance of signals from the phosphinate **1a** (δ = 2.85 ppm) was observed, and it was accompanied by appearance of new resonances corresponding to the H-pyrophosphonate **6** (δ = −6.55 ppm). These latter signals were replaced completely by resonances from the mixed anhydride **7** (δ = −3.26 ppm), when the last portion of PV-Cl was added. The yellow-brown precipitate formed during the reaction was not soluble in any of organic solvents tried or their mixtures (at least to such an extent as would allowed recording of ^{31}P NMR spectra), and its physical properties (see Experimental) seem to indicate elemental phosphorus. Assuming that it is the final product of the reaction, a chemical equation for the disproportionation of phosphinic acid induced by condensing agents may be tentatively summarized as follows:

$$6H_3PO_2 \xrightarrow{\text{coupling agent}} 2H_3PO_3 + P_4 + 6H_2O$$

The amount of isolated precipitate formed in the above reaction was in agreement with the stoichiometry of the equation.

The mechanism of phosphinic acid disproportionation can be a complex one, and ^{31}P NMR spectroscopy provides little insight into it. One may speculate, however, that a multistep activation of phosphinic acid with a condensing agent results in the formation of various reactive species having nucleophilic and electrophilic phosphorus centers. These might react with each other, leading finally to the disproportionation of phosphinic acid. Since water is removed by the condensing agent, the equilibrium should be shifted to the right.

The following conclusions can be drawn from the above considerations. Salts of phosphinic acid undergo rather fast disproportionation induced by various condensing agents, and the rate-limiting step in such a transformation seems to be the formation of the first reactive species, most likely, a corresponding mixed anhydride. In the absence of other nucleophiles in the reaction mixture, such an anhydride may undergo further activation, affording species which can act as oxidants. One may infer from

(9) Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon Press: Oxford, 1986; p 591.
(10) **1a** and **1b** contained ~2% of phosphonic acid salts, apparently due to contamination with phosphonic acid of the starting material used for their preparation.

Table I. ^{1}H NMR Chemical Shift Values (in ppm) of Some Diagnostic Signals of Nucleoside 3'-(Hydrogen-phosphonothioates)[a]

	P-H ($^1J_{PH}$, Hz)	1'-H ($^3J_{HH}$, Hz)	2'-H	3'-H	4'-H	5'-H	2-H	5-H or 5-Me	6-H	8-H
3a	8.06 (579), d	6.45, m	2.67	5.32	4.36	3.54, 3.39	–	1.39	7.61	–
	7.99 (583), d		2.39		4.26	3.42		1.37		
3b	7.90 (566), d	6.15 (5.8), t	2.64	5.13	4.31	3.38	–	*b*	8.17	–
	7.87 (570), d	6.14 (5.8), t	2.34		4.24					
3c	7.93 (569), d	6.47 (6.6), t	3.07	5.28	4.37	3.33	8.25	–	–	8.55
	7.90 (570), d	6.45 (6.6), t	2.66		4.31		8.24			
3d	8.06 (581), d	6.17, m	3.10	5.73	4.31	3.36	–	–	–	7.75
	7.94 (586), d		2.61		4.21					
3e	8.17 (587), d	6.05 (5.9), d	4.49	5.16	4.43	3.68, 3.38	–	5.21	8.07	–
	7.96 (579), d	5.90 (2.6), d	4.43	5.05	4.35	3.58, 3.51		5.15	7.85	

[a] Spectra were recorded in $CDCl_3$ except for **3c**, which was in CD_3CN. Multiplicity of signals due to the presence of P-diastereoisomers in **3a–e** (ratio ca. 1:1) caused overlapping of some resonances. No attempt was made to assign the signals to a particular diastereoisomer. [b] Signal buried in multiplets of the aromatic protons.

Table II. ^{31}P NMR Data for Some Phosphinate, H-Phosphonate, and H-Phosphonothioate Derivatives[a]

compd	chemical shift, ppm	$^1J_{PH}$, Hz	$^3J_{PH}$, Hz
1a	2.85	517.0, t	–
2a	14.22	571.9, t	9.8, d
2b	13.34	560.3, t	9.8, t
3a	53.56	568.8, d	11.0, d
	53.02	570.0, d	10.9, d
3b	54.06	568.9, d	10.9, d
	53.41	573.7, d	11.0, d
3c	53.54	570.1, d	10.3, d
	53.41	570.1, d	10.3, d
3d	53.55	567.0, d	10.3, d
	53.10	570.0, d	11.5, d
3e	55.83	578.6, d	13.4, d
	54.51	573.7, d	13.4, d
3f	56.71	578.6, d	9.8, t
4a	3.75	608.2, d	8.8, d
5a	7.42	714.0, d	8.6, t
6	–6.55	637.0[b]	2.6,[b] $^2J_{PP}$ = 19.4[b]
7	–3.26	651.8, d	–
8	18.90	577.8, d	9.8, t

[a] Spectra recorded in pyridine. 2% H_3PO_4 in D_2O as an external reference. [b] Calculated value for the spin system AA'XX'.

these that to avoid oxidation of phosphinate esters produced from phosphinic acid in the presence of a condensing agent a hypothetical mixed anhydride (e.g. the intermediate **9** in case of PV-Cl) should be trapped by a nucleophile, before the next activation step takes place.

Formation of Phosphinate Esters. To verify the above line of reasoning, an experiment was carried out using 1 equiv of phosphinate **1a**, 5 equiv of ethanol, and 2 equiv of PV-Cl in pyridine. Under these experimental conditions (excess of a hydroxylic component over phosphinate **1**), the yellow-brown precipitate was not formed, and the ^{31}P NMR spectrum showed a quantitative formation of ethyl phosphinate **2b**. When ethanol was replaced in the above reaction by a nucleoside (dmt-T), a quantitative formation of the nucleoside phosphinate **2a** was observed, as judged from the ^{31}P NMR spectrum (see Table II). During optimization of the ratio of reactants, it was found that it is possible to lower the excess of a hydroxylic component in this reaction to 1.5–2 equiv, and the amount of a condensing agent to 1.5 equiv. Reactions in which equimolar amounts of phosphinate **1** and a hydroxylic component were used always afforded some symmetrical H-phosphonate diesters of type **5**.

Having optimized conditions for the in situ formation of phosphinate esters, their basic chemical properties have been investigated. These compounds were found to hydrolyze rapidly upon addition of water and also during TLC analysis (presence of only a nucleoside was detected). In agreement with previous reports on transesterification of alkyl phosphinates,[11] we found that the nucleoside phosphinate **2a** was converted into ethyl phosphinate **2b** by treatment with an excess of ethanol. Also ethyl phosphinate can be rapidly transesterified with nucleosides (1 equiv), affording the corresponding nucleoside phosphinates **2** (~30–40%, ^{31}P NMR). In contradistinction to phosphinic acid salts, its esters do not undergo disproportionation in the presence of condensing agents. However, PV-Cl (5 equiv) seems to react with ethyl phosphinate upon standing, producing what we believe is ethyl acylphosphinate **8**.[12] Formation of this kind of possible side products was never observed under regular coupling conditions.

Synthesis of Nucleoside H-Phosphonothioates. To investigate the feasibility of synthesizing the H-phosphonothioates **3** via the phosphinates **2** as intermediates, 1.5 equiv of PV-Cl was added to a pyridine solution containing **1a** (1 equiv) and dmt-T (2 equiv). The ^{31}P NMR spectrum showed that the reaction went to completion during ~2 min, producing the nucleoside phosphinate **2a** as single phosphorus-containing species. After addition of 2 equiv of sulfur, the reaction mixture was stirred for 15 min and then another spectrum was recorded. No signal from the starting material **2a** was detected, and two singlets at ~54 ppm indicated the presence of two diastereoisomers of the H-phosphonothioate **3a**. Ethanol reacted similarly under these reaction conditions, affording **3f**. The H-phosphonothioates **3** were resistant toward further oxidation, even after a prolonged (overnight) treatment with sulfur.

The above experimental conditions have been used for preparative syntheses of various nucleoside H-phosphonothioates **3**. After reverse-phase column chromatography, compounds **3a–e** were isolated in ~80–90% yield and were characterized by elemental analysis and spectral methods. They are stable solids which can be handled similarly to the corresponding nucleoside H-phosphonates. Recently we demonstrated that compounds of type **3** can be used for the preparation of phosphorodithioate diesters and other phosphate analogues.[2]

In conclusion, it was found that phosphinate esters are formed practically quantitatively under mild conditions when triethylammonium or pyridinium phosphinate is activated by condensing agents in the presence of an excess (1.5–2 equiv) of a hydroxylic component. These can be converted into compounds having phosphorus in a higher oxidation state. A synthetic utility of the in situ produced

(11) Gallagher, M. J.; Honegger, H. *J. Chem. Soc., Chem. Commun.* **1978**, *54–55*.

(12) The compound was formed only when pivaloyl chloride was used as a condensing agent. The presence of one P–H bond, apparent from the ^{31}P NMR spectrum, together with the value of chemical shift and the splitting pattern of resonances, are consistent with a tentatively assigned structure **8** for the reaction product.

phosphinate esters was demonstrated by designing an efficient method for the preparation of the deoxyribo- and ribonucleoside 3′-H-phosphonothioates **3**. The main features of the method are: (i) one-pot synthesis involving two experimentally simple steps, namely, condensation and oxidation with sulfur, (ii) mild reaction conditions, (iii) reasonable high yield of the H-phosphonothioates after reversed-phase silica gel chromatography, (iv) an excess of hydroxylic component can be easily recovered during chromatography, if it is desired, (v) the reagents are stable and commercially available, (vi) the possibility of synthesizing various phosphonate analogues via changing reaction conditions for the second step.

Experimental Section

Materials and Methods. ^1H and ^{31}P NMR spectra were recorded on a JEOL GSX-270 FT spectrometer. ^1H NMR spectra were referenced to the internal TMS signal, and for ^{31}P NMR spectra 2% H_3PO_4 in D_2O was used as an external standard (coaxial inner tube). TLC was carried out on Merck silica gel 60 F_{254} or Kieselgel 60 F_{254} silanized precoated plates using chloroform/methanol, 9:1 (v/v) (system A), or acetone/water, 6:4 (v/v) (system B), respectively. Pyridine was refluxed with CaH_2 overnight and then distilled and stored over molecular sieves (4 Å) or CaH_2. Pivaloyl chloride (Aldrich) and 50% aqueous phosphinic acid (BDH) were commercial grade. Suitably protected deoxyribonucleosides,[13] 5′-*O*-(dimethoxytrityl)-2′-*O*-(*tert*-butyldimethylsilyl)uridine,[14] and 5,5-dimethyl-2-oxo-2-chloro-1,3,2-dioxaphosphorinane[15] were prepared by standard methods. Anhydrous triethylammonium phosphinate **1a** and pyridinium phosphinate **1b** were prepared by neutralization of 50% aqueous phosphinic acid with triethylamine and pyridine, respectively, followed by repeated evaporation of added pyridine.

The ^{31}P NMR experiments were carried out in 10-mm tubes using 0.05 mmol of phosphorus-containing compounds in 2 mL of pyridine. Spectra were recorded at 25 °C. The reference compounds **5a**, **6**, and **7** used for the identification of some reaction products were prepared as follows: **5a**, by adding 2 equiv of pivaloyl chloride to the equimolar amounts of **4a** and 5′-*O*-(dimethoxytrityl)thymidine in pyridine; **6** and **7**, by the reaction of phosphonic acid in pyridine with 0.5 and 1 equiv of pivaloyl chloride, respectively.

Reaction of Triethylammonium Phosphinate with Pivaloyl Chloride. To a solution of triethylammonium phosphinate **1a** (0.1 mmol) in acetonitrile (1.5 mL) was added pivaloyl chloride (0.3 mmol). Immediately a yellow color appeared, followed by formation of a yellow-brown precipitate. After 20 min the precipitate was separated by centrifugation, washed consecutively (3 × 1.5 mL) with water, ethanol, and ethyl ether, and dried under vacuum. An amorphous, yellow-brown substance (20 mg) was obtained. The substance did not show any noticeable solubility in chloroform, acetonitrile, dioxane, DMSO, or carbon disulfide. Upon heating, the substance melted, producing yellowish vapors which ignited and condensed on the walls of test tube, showing green chemiluminescence. Elemental analysis gave exceedingly variable results for phosphorus content (from ~70% to 90%) and a low value for carbon (~6%). Since the isolated precipitate has to be considered as a crude material, the low content of carbon in the analyzed sample most likely is due to the presence of organic contaminations.

General Procedure for the Synthesis of H-Phosphonothioates 3. A suitably protected nucleoside (3 mmol) and triethylammonium phosphinate (**1a**, 2 mmol) were rendered anhydrous by evaporation of added pyridine and then dissolved in the same solvent (10 mL). The solution was cooled on an ice bath, and pivaloyl chloride (3 mmol) was added with stirring. After 15 min the ice bath was removed and sulfur (3 mmol) was added. Stirring was continued for ca. 1 h (TLC analysis), and then the reaction was quenched with 2 M triethylammonium bicarbonate (TEAB) buffer (1 mL) and concentrated till dryness. The residue was partitioned between dichloromethane (50 mL) and 0.5 M TEAB (20 mL), the organic layer was evaporated, and the residue was purified on a reversed-phase silica gel column (Merck Kieselgel 60 silanized, 70–230 mesh), using a stepwise gradient of acetone in water. The desired compounds were eluted at the concentration of acetone of ~25%. Fractions containing the desired products were concentrated, extracted with dichloromethane, and, after evaporation of the solvent, triturated with ethyl ether/hexane (2:1, v/v), affording **3a–d** as white powder. For compound **3e**, because of its high lipophilicity, chromatography on a regular silica gel column (chloroform/methanol system) was found to be a more convenient way of purification.

5′-*O*-(4,4′-Dimethoxytrityl)thymidin-3′-yl hydrogenphosphonothioate, triethylammonium salt (3a): yield 1.31 g, 90%; R_f = 0.15 (system A), 0.71 (system B). For the ^1H and ^{31}P NMR date, see Tables I and II, respectively. Anal. Calcd for $C_{37}H_{48}N_3O_8PS$: C, 61.2; H, 6.7; N, 5.8; O, 17.6; P, 4.3; S, 4.4. Found: C, 60.9; H, 6.7; N, 5.8; O, 17.8; P, 4.3; S, 4.2.

5′-*O*-(4,4′-Dimethoxytrityl)-*N*⁴-benzoyldeoxyribocytidin-3′-yl hydrogen-phosphonothioate, triethylammonium salt (3b): yield 1.32 g, 81%; R_f = 0.12 (system A), 0.69 (system B). For the ^1H and ^{31}P NMR date, see Tables I and II, respectively. Anal. Calcd for $C_{43}H_{51}N_4O_8PS$: C, 63.4; H, 6.3; P, 3.8; S, 3.9. Found: C, 62.8; H, 6.4; P, 3.6; S, 3.7.

5′-*O*-(4,4′-Dimethoxytrityl)-*N*⁶-benzoyldeoxyriboadenosin-3′-yl hydrogen-phosphonothioate, triethylammonium salt (3c): yield 1.42 g, 85%; R_f = 0.21 (system A), 0.71 (system B). For the ^1H and ^{31}P NMR date, see Tables I and II, respectively. Anal. Calcd for $C_{44}H_{51}N_6O_7PS$: C, 63.0; H, 6.1; P, 3.7; S, 3.8. Found: C, 62.6; H, 6.3; P, 3.4; S, 3.6.

5′-*O*-(4,4′-Dimethoxytrityl)-*N*²-isobutyryldeoxyriboguanosin-3′-yl hydrogen-phosphonothioate, triethylammonium salt (3d): yield 1.30 g, 79%; R_f = 0.12 (system A), 0.73 (system B). For the ^1H and ^{31}P NMR date, see Tables I and II, respectively. Anal. Calcd for $C_{41}H_{53}N_6O_8PS$: C, 60.0; H, 6.5; P, 3.8; S, 3.9. Found: C, 59.2; H, 6.6; P, 3.6; S, 3.6.

5′-*O*-(4,4′-Dimethoxytrityl)-2′-*O*-(*tert*-butyldimethylsilyl)uridin-3′-yl hydrogen-phosphonothioate, triethylammonium salt (3e): yield 1.53 g, 91%; R_f = 0.27 (system A), 0.66 (system B). For the ^1H and ^{31}P NMR date, see Tables I and II, respectively. Anal. Calcd for $C_{42}H_{60}N_3O_9PSSi$: C, 59.9; H, 7.2; N, 5.0; P, 3.7; S, 3.8. Found: C, 59.8; H, 7.2; N, 5.0; P, 3.6; S, 3.7.

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