Nucleic acid related compounds. 77. 2′,3′-Didehydro-2′,3′-dideoxy-2′(and 3′)-methylnucleosides via [3,3]-sigmatropic rearrangements of 2′(and 3′)-methylene-3′(and 2′)-*O*-thiocarbonyl derivatives and radical reduction of a 2′-chloro-3′-methylene analogue[1]

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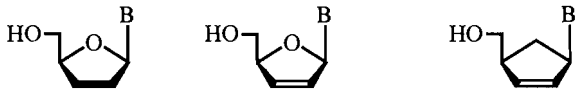
Treatment of 5′-*O*-(*tert*-butyldiphenylsilyl)-2′(and 3′)-deoxy-2′(and 3′)-methyleneuridine (and adenosine) derivatives with phenyl chlorothionocarbonate gave the 3′(and 2′)-*O*-phenoxythiocarbonyl intermediates, which underwent spontaneous [3,3]-sigmatropic rearrangement to give the 2′,3′-didehydro-2′,3′-dideoxy-2′(and 3′)-(phenoxycarbonylthio)methyl analogues. These allylic thioesters were subjected to tributylstannane-mediated hydrodesulfurization and deprotection to give 2′,3′-didehydro-2′,3′-dideoxy-2′(and 3′)-methyluridine (and adenosine). Tributylstannane-mediated hydrodehalogenation of a 2′-chloro-2′,3′-dideoxy-3′-methyleneuridine derivative afforded the 2′,3′-didehydro-2′,3′-dideoxy-3′-methyl product of allylic transposition exclusively.

VINCENTE SAMANO et MORRIS J. ROBINS. Can. J. Chem. **71**, 186 (1993).

Le traitement des dérivés 5′-*O*-(*tert*-butyldiphénylsilyl)-2′(et 3′)-désoxy-2′(et 3′)-méthylèneuridine (et adénosine) avec du chlorothionocarbonate de phényle conduit à des intermédiaires 3′(et 2′)-*O*-phénoxythiocarbonyles qui subissent une transposition sigmatropique-[3,3] spontanée fournissant les analogues 2′,3′-didéhydro-2′,3′-didésoxy-2′(et 3′)-(phénoxycarbonylthio)méthyles. On a soumis ces thioesthers allyliques à une hydrodésulfurisation catalysée par le tributylstannane et à une déprotection conduisant à la 2′,3′-didéhydro-2′,3′-didésoxy-2′ (et 3′)-méthyluridine (et adénosine). L'hydrodéshalogénation, catalysée par le tributylstannane, d'un dérive 2′-chloro-2′,3′-didésoxy-3′-méthylèneuridine conduit uniquement au produit 2′,3′-didéhydro-2′,3′-didésoxy-3′-méthyle provenant de la transposition allylique.
[Traduit par la rédaction]

Introduction

A number of 2′,3′-dideoxynucleoside (**A**) and 2′,3′-unsaturated (2′,3′-didehydro) analogue triphosphates cause selective inhibition of the HIV reverse transcriptase in vitro (1). Potent anti-HIV activity has been reported for the 2′,3′-didehydro-2′,3′-dideoxy analogues of cytidine (2) (**B**), thymidine (3, and references therein) (**C**), and carbocyclic



A **B** B = cytosin-1-yl **C** B = thymin-1-yl **D** B = guanin-9-yl

guanosine (4) (**D**). We have reported 2′(and 3′)-deoxy-2′(and 3′)-methylene (**8** and **1**, respectively) pyrimidine (5*a*) and purine (5*b*) nucleosides and their mechanism-based inhibition of ribonucleotide reductase (6) and *S*-adenosyl-L-homocysteine hydrolase (7). We now describe conversions of **1** and **8** into 2′,3′-didehydro-2′,3′-dideoxy-3′(and 2′)-methyl nucleosides (**7** and **14**) via [3,3]-sigmatropic rearrangements of the 2′(and 3′)-*O*-phenoxythiocarbonyl intermediates **3** and **10**, respectively. The endocyclic alkenes **7** and **14** also are produced exclusively by radical dehalogenation of the allylic chloro derivatives **4** and **12**, respectively. During our investigation, Ueda and co-workers (8) reported obtaining the 2′,3′-didehydro-2′,3′-dideoxy-2′(and 3′)-methyl-5-methyluridines via a similar rearrangement of 2′(and 3′)-deoxy-3′(and 2′)-*O*-(imidazol-1-yl)thiocarbonyl-2′(and 3′)-methylene derivatives. Czernecki *et al.* (9) also prepared 2′,3′-didehydro-2′,3′-dideoxy-3′-methyl-5-methyluridine starting from 1,2-*O*-isopropylidene-α-D-xylofuranose via sugar transformations, coupling, and an analogous rearrangement.

Results and discussion

Protection of the 3′-deoxy-3′-methylene nucleosides **1***a* (5*a*) and **1***b* (5*b*) (Scheme 1) with *tert*-butyldiphenylsilyl (TBDPS) chloride/pyridine (10) gave the 5′-*O*-TBDPS derivatives **2***a* (94%) and **2***b* (95%). Treatment of **2**(*a* and *b*) with phenyl chlorothionocarbonate/DMAP/MeCN (11) at ambient temperature resulted in spontaneous conversion into their 2′,3′-didehydro-2′,3′-dideoxy-3′-(phenoxycarbonylthio)methyl analogues **5***a* (80%) and **5***b* (93%). The ^{1}H NMR spectrum of **5***a* (Table 1) had an olefinic proton peak at δ 6.99 for H2′ and an AB system at δ 3.59, 3.89 (J = 15.6 Hz) for the CH_2S group. Similar ^{1}H NMR data were observed for **5***b*. Precedent for the spontaneous [3,3]-sigmatropic rearrangement of the allylic 2′-*O*-phenoxythiocarbonyl intermediates **3***a,b* (observed at lower temperatures by ^{1}H NMR) was noted with allyl *S*-methyl xanthate in 1909 (12), and the mechanism and synthetic applications have been studied (13, and references therein). Tributyltin hydride-mediated hydrodesulfurization (Bu_3SnH/AIBN/toluene/Δ) of **5***a* and **5***b* gave **6***a* (85%) and **6***b* (90%) exclusively, and deprotection with tetrabutylammonium fluoride in tetrahydrofuran (TBAF/THF) and purification gave crystalline 1-(2,3-dideoxy-3-methyl-β-D-*glycero*-pent-2-enofuranosyl)uracil (2′,3′-didehydro-2′,3′-dideoxy-3′-methyluridine) (**7***a*, 60%) and **7***b* (60%), respectively.

Since these exomethylene allylic thioesters, **5**, with an endocyclic double bond gave only the exomethyl endocyclic alkenes, the 2′-chloro-2′-deoxy derivative **4***a* was prepared to evaluate whether initial generation of a radical

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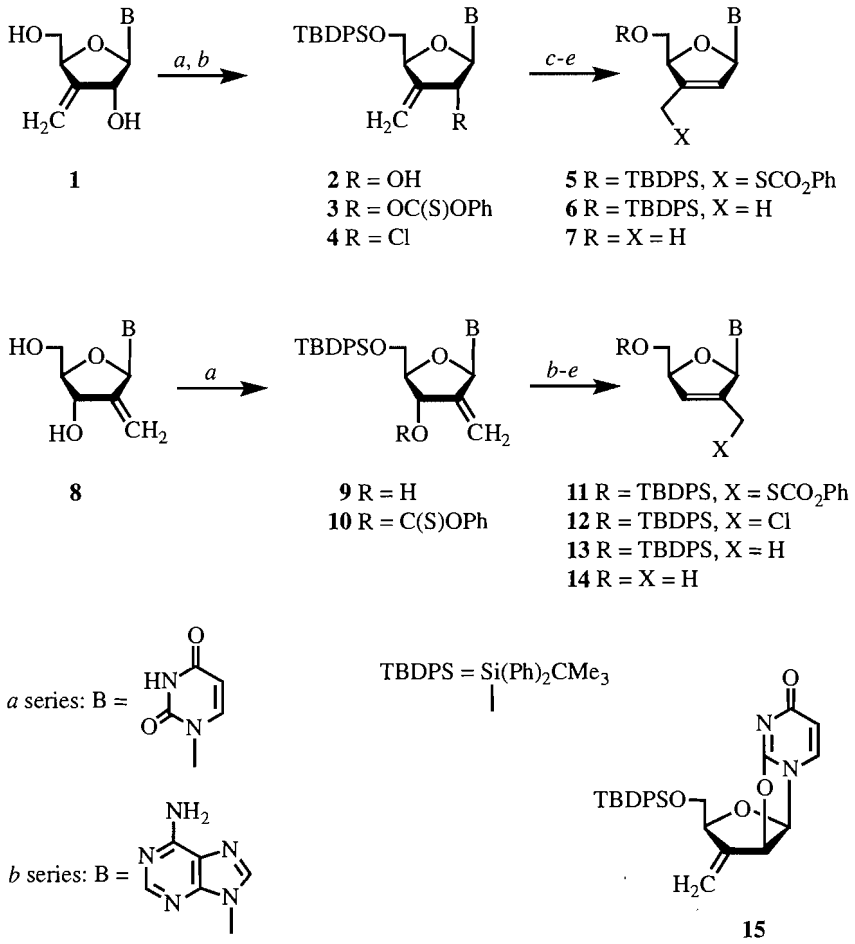

(*a*) TBDPS-Cl/pyridine; (*b*) $SOCl_2$/pyridine; (*c*) PhOC(S)Cl/DMAP; (*d*) Bu_3SnH/AIBN/toluene/100°C; (*e*) Bu_4NF/THF

SCHEME 1

at C2′ would have any effect on product formation. Treatment of **2***a* with thionyl chloride/pyridine/dichloromethane afforded **4***a* (62%) and the cyclonucleoside **15** (14%). O^2,2′-Anhydronucleoside intermediates such as **15** have been identified in various preparations (14) of pyrimidine 2′-deoxy-2′-halonucleosides from 2′-hydroxy precursors. Treatment of **4***a* with Bu_3SnH/AIBN/toluene/Δ gave **6***a* (95%) as the only observed product. Thus, this radical species underwent highly preferential allylic hydrogen transfer at the exocyclic methylene carbon to give the *endo* unsaturated compound, in harmony with the greater thermodynamic stability of 1-methylcyclopentene relative to methylenecyclopentane (15).

The rearrangement/desulfurization/dehalogenation sequence worked equally well with 2′-deoxy-2′-methylene nucleosides. Silylation of **8***a* (5*a*) and **8***b* (5*b*) gave **9***a* (90%) and **9***b* (95%), respectively. Treatment of **9***a* and **9***b* with phenyl chlorothionocarbonate afforded the rearranged products **11***a* (85%) and 9-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-2-(phenoxycarbonylthio)methyl-β-D-*glycero*-pent-2-enofuranosyl]adenine (**11***b*, 87%). Treatment of **11***a* and **11***b* with Bu_3SnH/AIBN/toluene/Δ gave **13***a* (85%) and **13***b* (84%), which were deprotected to afford **14***a* (95%) and **14***b* (95%), respectively. Compound **14***a* was previously synthesized in low yield from a 2′,3′-didehydro-2′,3′-dideoxy-3′-phenylselenone nucleoside (16).

Treatment of **9***a* with $SOCl_2$/pyridine/CH_2Cl_2 afforded the allylic transposition product **12***a* (89%) in contrast to the results with **2***a* (*vide supra*). Formation of pyrimidine O^2,3′-anhydronucleosides is much less facile than cyclization at the 2′-position (17). Thus, the initially formed 3′-chlorosulfite presumably underwent S_N2' substitution by attack of chloride at the exocyclic 2′-methylene carbon to gave **12***a*. Treatment of **12***a* with Bu_3SnH/AIBN/toluene/Δ again gave the exomethyl endocyclic alkene **13***a* (88%) exclusively.

In summary, we have developed mild conversions of 2′(and 3′)-deoxy-2′(and 3′)-methylenenucleosides into their corresponding 2′,3′-didehydro-2′,3′-dideoxy-2′(and 3′)-methyl analogues via formation of phenyl thionocarbonate esters, spontaneous rearrangement of the latter to allylic thioesters at ambient temperature, and tributylstannane-mediated allylic hydrodesulfurization. We also have demonstrated that the radical-mediated hydrodehalogenations of 5′-*O*-TBDPS-2′-chloromethyl-2′,3′-didehydro-2′,3′-dideoxyuridine and 5′-*O*-TBDPS-2′-chloro-2′,3′-dideoxy-3′-methyleneuridine give the more thermodynamically stable 2′(and 3′)-methyl-2′,3′-didehydro-2′,3′-dideoxyuridine derivatives (exomethyl endocyclic alkenes).

TABLE 1. ^{1}H NMR spectral data[a]

Compound	H1′[b] (J)	H2′[c] (J)	H3′ ($J_{3'-4'}$)	H4′	H5′[d] ($J_{5'-5''}$)	H5″[d] ($J_{5''-4'}$)	CH_AH_B[e] (J)	CH_AH_B[e] (J)	H5[b](2)[f]	H6[b](8)[f]	$NH(NH_2)$[g]	OH2′[b]/3′[b]/5′[h] ($J_{OH-2'/3'/5'5''}$)	Others
2*a*	5.84 (5.8)	4.64 (1.6)[i,j]		4.76[c]	4.01 (11.4)	3.77 (3.0)	5.17 (2.0)	5.47 (2.2)	5.48 (8.0)	7.76	9.20	3.75[g]	1.01 ($SiCMe_3$) 7.3–7.6 ($SiPh_2$)
2*b*	5.69 (6.4)	5.03 (2.1)[i,j]		4.86[c]	3.88 (11.0)	3.75 (3.5)	5.22 (2.8)	5.48 (2.4)	8.01	8.28	5.75	3.77[g]	0.92 ($SiCMe_3$) 7.2–7.6 ($SiPh_2$)
4*a*	6.14 (6.2)	4.66 (1.8)[j]		4.74[k] (2.2)	4.09 (11.6)	3.81 (2.6)	5.27 (1.8)	5.54 (2.0)	5.39 (8.4)	7.67	8.22		1.04 ($SiCMe_3$) 7.3–7.6 ($SiPh_2$)
5*a*	5.86[g]	6.99		4.87[c]	4.09 (12.0)	3.95 (2.4)	3.59[l] (15.6)	3.89[l]	4.99 (8.2)	7.68	8.40		1.1 ($SiCMe_3$) 7.1–7.6 ($SiPh_2$, OPh)
5*b*	6.06[g]	7.02		4.95[c]	3.91 (11.5)	3.82 (3.5)	3.68[l] (16.0)	3.94[l]	7.94	8.37	5.55		1.01 ($SiCMe_3$) 7.1–7.7 ($SiPh_2$, OPh)
6*a*	5.48[g]	6.92[c] (1.6)		4.63[c]	4.04 (12.0)	3.86 (2.2)			4.90 (8.2)	7.75	8.09		1.1 ($SiCMe_3$) 7.3–7.6 ($SiPh_2$) 1.91[g] (Me3′)
6*b*	5.70[c] (1.5)	6.99 (1.5)		4.74[g]	3.88 (11.6)	3.75 (3.5)			7.99	8.38	5.66		1.06 ($SiCMe_3$) 7.2–7.7 ($SiPh_2$) 1.92[g] (Me3′)
7*a*	5.53[g]	6.71[g]		4.55[g]	3.62[m] (2.7)				5.55 (8.3)	7.86	11.25	4.98 (4.9)	1.81[g] (Me3′)
7*b*	5.75[g]	6.84[g]		4.68[g]	3.62[m]				8.12	8.22	7.25	5.10 (4.8)	1.86[g] (Me3′)
9*a*	6.65[c]		4.83[n] (7.0)	3.78[o]	4.03 (12.0)	3.91 (2.6)	5.42 (1.6)	5.53 (2.0)	5.39 (8.2)	7.50	9.12	2.27 (7.0)	1.05 ($SiCMe_3$) 7.3–7.7 ($SiPh_2$)
9*b*	6.75[k] (1.6)		5.02 (1.5)[i,j]	3.92[c]	3.44[m]		5.39 (1.9)	5.59 (1.6)	7.90	8.34	5.75	3.35[g]	1.05 ($SiCMe_3$) 7.3–7.8 ($SiPh_2$)
11*a*	6.23[g]		7.04[d] (3.4)	4.88[c]	3.99 (12.0)	3.84 (2.8)	3.57[l] (15.4)	3.64[l]	5.20 (8.2)	7.75	9.90		1.09 ($SiCMe_3$) 7.1–7.7 ($SiPh_2$, OPh)
11*b*	6.32[g]		7.02[g]	5.00[g]	3.83[m] (4.5)		3.40[l] (15.5)	3.66[l]	7.99	8.32	6.17		1.05 ($SiCMe_3$) 7.1–7.7 ($SiPh_2$, OPh)
12*a*	6.21[c] (1.4)		7.00[d] (3.6)	4.87[c]	4.10 (12.0)	3.86 (2.8)	4.04[p]		5.20 (8.0)	7.75	8.78		1.03 ($SiCMe_3$) 7.3–7.7 ($SiPh_2$)
13*a*	5.83[k] (1.6)		6.82[g]	4.81[c]	3.93 (11.8)	3.80 (3.0)			5.16 (8.0)	7.60	8.25		1.04 ($SiCMe_3$) 7.3–7.7 ($SiPh_2$) 1.7[g] (Me2′)
13*b*	5.96[k] (1.6)		6.85[g]	4.93[c]	3.77[m] (4.8)				7.85	8.33	5.81		1.05 ($SiCMe_3$) 7.2–7.7 ($SiPh_2$) 1.66[g] (Me2′)
14*a*	6.02[k] (1.6)		6.66[g]	4.73[c]	3.56[m]				5.64 (8.0)	7.75	11.4	4.97 (4.7)	1.60[g] (Me2′)
14*b*	6.05[g]		6.74[g]	4.82[g]	3.57[m,d] (4.5)				8.12	8.21	7.30	5.06 (5.0)	1.60[g] (Me2′)
15	6.17 (2.5)	4.96[g]		4.72[g]	4.29 (12.1)	3.96 (2.5)	5.25[g]	5.54[g]	5.77 (6.9)	8.28			1.05 ($SiCMe_3$) 7.3–7.7 ($SiPh_2$)

[a]Chemical shifts (δ, Me_4Si internal); coupling constants (Hz, in parentheses); solvents: $CDCl_3$ for **2***a*–**6***b* and **9***a*–**13***b*, Me_2SO-d_6 for **7***a*,*b* and **14***a*,*b*.
[b]Doublet (unless noted otherwise).
[c]Multiplet.
[d]Doublet of doublets.
[e]($J_{\text{"apparent"}}$) from incompletely resolved peaks.
[f]Singlet.
[g]Broad singlet.
[h]Triplet (unless noted otherwise).
[i]After D_2O exchange.
[j]Doublet of "apparent" quartets ($J_{\text{"q"}}$).
[k]"Apparent" quartet.
[l]Broad doublet.
[m]H5′,5″ collapsed ($J_{5'-4'}$).
[n]Broad triplet.
[o]Doublet of triplets.
[p]$H_{A,B}$ collapsed.

TABLE 2. ^{13}C NMR spectral data[a]

Compound	C2	C4	C5	C6	C8	CH_2/CH_3	C1′	C2′	C3′	C4′	C5′
2*a*	152.18	164.27	103.14	140.74		110.64	89.80	77.25	146.04	82.04	66.51
2*b*	153.10	149.50	120.05	156.07	139.17	109.59	91.55	77.50	146.39	83.29	67.01
4*a*	150.68	163.07	103.68	139.72		112.99	89.16	60.63	144.00	81.73	65.99
5*a*	151.19	163.74	102.96	141.30		27.56	88.80	124.73	144.18	87.09	64.02
5*b*	153.87	151.64	120.00	155.90	139.25	27.83	87.66	123.34	144.90	87.37	65.14
6*a*	151.19	163.53	102.67	141.71		13.13	89.09	121.33	144.66	88.94	64.19
6*b*	153.74	150.52	120.00	155.94	139.50	13.04	89.35	120.21	145.20	87.75	65.01
7*a*	151.24	163.70	101.46	141.78		12.28	88.71	120.31	144.49	88.26	60.85
7*b*	152.74	149.31	120.03	156.27	139.00	12.63	89.40	120.26	143.55	87.31	61.62
9*a*	151.38	163.97	103.38	141.23		114.31	85.01	149.05	70.76	84.52	62.81
9*b*	153.77	150.32	120.00	156.00	139.00	114.08	84.85	148.73	71.98	83.33	63.48
11*a*	151.12	163.14	103.47	141.00		26.99	90.00	135.77	132.07	86.81	65.34
11*b*	153.87	150.64	120.25	156.28	139.54	27.07	89.06	134.95	132.05	87.26	66.01
12*a*	151.04	163.17	103.41	141.02		37.34	89.70	136.45	133.18	86.70	65.30
13*a*	151.67	164.02	103.47	140.97		12.05	91.57	135.87	128.34	86.76	65.72
13*b*	153.84	150.79	120.18	156.03	139.44	12.00	90.50	134.99	128.59	87.19	66.48
14*a*	151.37	163.41	102.44	140.94		11.51	90.73	133.94	129.08	86.93	62.66
14*b*	153.04	149.73	119.07	156.43	139.50	11.41	89.97	133.92	128.13	87.53	63.06
15	112.80	167.57	105.72	144.17		114.45	91.93	62.35	142.26	82.19	67.77

[a]δ (Me_4Si internal) in $CDCl_3$ except **7***a,b* and **14***a,b* in Me_2SO-d_6.

Experimental section

General procedures

Uncorrected melting points were obtained with a capillary melting tube apparatus. Ultraviolet (UV) spectra of MeOH solutions were determined with a Hewlett–Packard 8451A spectrophotometer. ^1H (200 MHz) (Table 1) and ^{13}C (50 MHz) (Table 2) NMR spectra were obtained with a Varian Gemini-200 spectrometer. Low-resolution electron-impact mass spectra (MS) were determined with a Finnigan MAT 8430 spectrometer at 20 eV. Flash evaporations (<35°C bath temperatures) were effected with a rotary evaporator with water aspirator or mechanical oil pump vacuum. Flash chromatography was performed with E. Merck Kieselgel 60, 230–400 mesh. Unless specified otherwise, the solvent for chromatography was hexanes/EtOAc (7:3, v/v). Reagent grade solvents and reagents were distilled prior to use. Pyridine was dried by refluxing with and distillation from CaH_2. MeCN and toluene were distilled from P_4O_{10}. Elemental analyses were determined by M-H-W Laboratories, Phoenix, Ariz.

*1-(5-O-TBDPS-3-deoxy-3-methylene-β-D-*erythro-*pentofuranosyl)uracil* **2**a

Procedure A (10)

TBDPS-Cl (0.40 mL, 0.42 g, 1.56 mmol) was added to a solution of **1***a* (5*a*) (0.25 g, 1.04 mmol) in pyridine (5 mL) and the mixture was stirred at ambient temperature for 18 h. Solvent was evaporated and the residue partitioned between EtOAc (50 mL) and ice-cold 0.01 N HCl/H_2O (30 mL). The aqueous phase was extracted (EtOAc) and the combined organic phase was washed (saturated $NaHCO_3/H_2O$ and brine), dried (Na_2SO_4), and evaporated. The colorless foam (0.55 g) was used without further purification. For characterization, this material was chromatographed (hexane/EtOAc, 1:2) to give **2***a* (0.47 g, 94%) as a colorless solid foam: UV_{max}: 260 nm; MS *m/z*: 420 (10, M − CMe_3 − H), 309 (90, M − CMe_3 − BH), 281 (14, M − CMe_3 − BCHO), 199 (100, Ph_2SiOH).

*9-(5-O-TBDPS-3-deoxy-3-methylene-β-D-*erythro-*pentofuranosyl)adenine* **2**b

Procedure A was applied to **1***b* (5*b*) (0.56 g, 2.13 mmol) to give **2***b* (1.0 g, 95%) as a colorless solid foam: UV_{max}: 260 nm; MS *m/z*: 502 (4, MH^+), 444 (100, M − CMe_3), 309 (18, M − CMe_3 − BH), 199 (75, Ph_2SiOH).

*1-(5-O-TBDPS-2-chloro-2,3-dideoxy-3-methylene-β-D-*erythro-*pentofuranosyl)uracil* **4**a

Procedure B

$SOCl_2$ (37 μL, 60 mg, 0.5 mmol) in CH_2Cl_2 (0.5 mL) was added to **2***a* (50 mg, 0.10 mmol) and pyridine (41 μL, 40 mg, 0.5 mmol) in CH_2Cl_2 (1.5 mL) at 0°C. The mixture was stirred at ambient temperature for 48 h, diluted (CH_2Cl_2, 10 mL), and poured into saturated $NaHCO_3/H_2O$ (5 mL, 0°C). The aqueous phase was extracted (CH_2Cl_2) and the combined organic phase was dried (Na_2SO_4) and evaporated. The residue was chromatographed (hexane/EtOAc, 3:1) to give cyclonucleoside **15** (6.5 mg, 14%) and **4***a* (32 mg, 62%) as a colorless solid foam. **15**: UV_{max}: 306 nm; MS *m/z*: 403 (80, M − CMe_3), 327 (6, M − CMe_3 − Ph), 293 (40, M − CMe_3 − B), 199 (100, Ph_2SiOH). **4***a*: UV_{max}: 259 nm (ε 9000); MS *m/z*: 439 (3, M[^{35}Cl] − CMe_3), 441 (1, M[^{37}Cl] − CMe_3), 403 (40, M − CMe_3 − HCl), 293 (10, M − CMe_3 − Cl − B), 87 (100, M − BCHO − $Ph_2Si(CMe_3)OCH_2$). Anal. calcd. for $C_{26}H_{29}ClN_2O_4Si$: C 62.83, H 5.88, N 5.64; found: C 63.00, H 5.98, N 5.62.

*1-[5-O-TBDPS-2,3-dideoxy-3-(phenoxycarbonylthio)methyl-β-D-*glycero-*pent-2-enofuranosyl]uracil* **5**a

Procedure C (11)

DMAP (0.32 g, 2.7 mmol) was added to a solution of crude **2***a* (0.55 g) in MeCN (25 mL). Phenyl chlorothionocarbonate (0.18 mL, 0.22 g, 1.35 mmol) was added and the mixture was stirred at ambient temperature under N_2 for 18 h. Volatiles were evaporated and the residue was partitioned between EtOAc (50 mL) and brine/H_2O (1:1, 30 mL). The aqueous phase was extracted (EtOAc) and the combined organic phase was washed (saturated $NaHCO_3/H_2O$ and brine), dried (Na_2SO4), and evaporated. Chromatography (hexane/EtOAc, 1:1) gave **5***a* (0.51 g, 80% from **1***a*) as a colorless solid foam: UV_{max}: 260 nm (ε 9700); MS *m/z*: 557 (1, M − CMe_3), 445 (100, M − CMe_3 − BH), 291 (98, M − CMe_3 − BH_2 − PhOCOS). Anal. calcd. for $C_{33}H_{34}N_2O_6SSi$: C 64.47, H 5.57, N 4.56, S 5.22; found: C 64.45, H 5.64, N 4.54, S 5.30.

*9-[5-O-TBDPS-2,3-dideoxy-3-(phenoxycarbonylthio)methyl-β-D-*glycero-*pent-2-enofuranosyl]adenine* **5**b

Procedure C was applied to **2***b* (0.60 g, 1.2 mmol) to give **5***b* (0.70 g, 93%) as slightly colored needles (EtOAc/hexanes): mp 111–112°C; UV_{max}: 260 nm (ε 16 700); MS *m/z*: 580 (10, M −

CMe_3), 445 (100, M − CMe_3 − BH). Anal. calcd. for $C_{34}H_{35}N_5O_4SSi$: C 64.03, H 5.53, N 10.98; found: C 63.66, H 5.60, N 10.99.

*1-(5-O-TBDPS-2,3-dideoxy-3-methyl-β-D-*glycero*-pent-2-enofuranosyl)uracil* **6**a

Procedure D

AIBN (0.042 g, 0.25 mmol) and Bu_3SnH (0.56 mL, 0.61 g, 2.1 mmol) were added to a solution of **5***a* (0.43 g, 0.70 mmol) in toluene (20 mL). The solution was deoxygenated (N_2) for 20 min and then heated at 100°C under N_2 for 10 h. Volatiles were evaporated and the residue was chromatographed (hexane/EtOAc, gradient 4:1 → 1:1) to give **6***a* (0.27 g, 85%) as a colorless foam: UV_{max}: 260 nm; MS *m/z*: 293 (100, M − CMe_3 − BH), 199 (90, Ph_2SiOH), 187 (60, M − CMe_3 − BCH_2O − Ph). Analogous treatment of **4***a* (17 mg, 0.034 mmol) gave **6***a* (15 mg, 95%) with identical spectral data.

*9-(5-O-TBDPS-2,3-dideoxy-3-methyl-β-D-*glycero*-pent-2-enofuranosyl)adenine* **6**b

Procedure D was applied to **5***b* (0.44 g, 0.69 mmol) to give **6***b* (0.29 g, 90%) as colorless needles (EtOAc/hexane): mp 121–122°C; UV_{max}: 260 nm; MS *m/z*: 428 (95, M − CMe_3), 293 (100, M − CMe_3 − BH), 187 (90, M − CMe_3 − BCH_2O − Ph).

*1-(2,3-Dideoxy-3-methyl-β-D-*glycero*-pent-2-enofuranosyl)uracil (2',3'-didehydro-2',3-dideoxy-3'-methyluridine)* **7**a

Procedure E

Bu_4NF/THF (1 M; 0.54 mL, 0.54 mmol) was added to a solution of **6***a* (0.25 g, 0.54 mmol) in THF (15 mL) at 0°C. After 1 h at 0°C, the solution was evaporated (<25°C) and the residue was chromatographed (Dowex 50 (Na^+) resin/H_2O; elution with H_2O) to give a colorless residue containing uracil (TLC). Chromatography ($CHCl_3$/EtOH, 47:3) and crystallization (acetone/Et_2O) afforded **7***a* (0.072 g, 60%) as a colorless powder: mp 123–124°C; UV_{max}: 260 nm (ε 9600); MS *m/z*: 112 (100, M − BH). Anal. calcd. for $C_{10}H_{12}N_2O_4$: C 53.57, H 5.39, N 12.49; found: C 53.47, H 5.29, N 12.57.

*9-(2,3-Dideoxy-3-methyl-β-D-*glycero*-pent-2-enofuranosyl)-adenine (2',3'-didehydro-2',3'-dideoxy-3'-methyl-adenosine)* **7**b

Procedure E was applied to **6***b* (0.25 g, 0.51 mmol) with evaporation (<25°C) and direct chromatography ($CHCl_3$/EtOH, 93:7) to give **7***b* (0.075 g, 60%) as a colorless solid: mp 110–112°C; UV_{max}: 260 nm (ε 14 000); MS *m/z*: 248 (30, MH^+), 231 (100, MH − OH). Anal. calcd. for $C_{11}H_{13}N_5O_2 \cdot 0.25$ EtOH: C 53.38, H 5.65, N 27.06; found: C 53.35, H 5.36, N 26.82.

*1-(5-O-TBDPS-2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)uracil* **9**a

Procedure A was applied to **8***a* (5*a*) (0.70 g, 2.91 mmol) to give **9***a* (1.25 g, 90%) as colorless prisms (EtOAc/hexane): mp 146–147°C; UV_{max}: 260 nm; MS *m/z*: 421 (96, M − CMe_3), 309 (20, M − CMe_3 − BH), 293 (100, M − CMe_3 − B − OH).

*9-(5-O-TBDPS-2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)adenine* **9**b

Procedure A was applied to **8***b* (5*b*) (0.37 g, 1.4 mmol) to give **9***b* (0.66 g, 95%) as a colorless solid foam: UV_{max}: 260 nm; MS *m/z*: 444 (100, M − CMe_3), 309 (8, M − CMe_3 − BH).

*1-[5-O-TBDPS-2,3-dideoxy-2-(phenoxycarbonylthio)methyl-β-D-*glycero*-pent-2-enofuranosyl]uracil* ***11***a

Procedure C was applied to **9***a* (0.40 g, 0.84 mmol) to give **11***a* (0.43 g, 85%) as a solid foam: UV_{max}: 260 nm (ε 9000); MS *m/z*: 556 (40, M − CMe_3 − H), 445 (100, M − CMe_3 − BH), 351 (30, M − CMe_3 − BH_2 − PhO), 293 (22, M − CMe_3 − B − PhOCOS). Anal. calcd. for $C_{33}H_{34}N_2O_6SSi$: C 64.47, H 5.57, N 4.56, S 5.22; found: C 64.59, H 5.41, N 4.56, S 5.15.

*9-[5-O-TBDPS-2,3-dideoxy-2-(phenoxycarbonylthio)methyl-β-D-*glycero*-pent-2-enofuranosyl]adenine* ***11***b

Procedure C was applied to **9***b* (0.40 g, 0.80 mmol) to give **11***b* (0.34 g, 87%) as a colorless solid foam: UV_{max}: 260 nm (ε 18 000); MS *m/z*: 325 (20, M − CMe_3 − B − PhOCO), 293 (22, M − CMe_3 − B − PhOCOS), 199 (100, Ph_2SiOH). Anal. calcd. for $C_{34}H_{35}N_5O_4SSi$: C 64.03, H 5.53, N 10.98; found: C 64.20, H 5.31, N 10.80.

*1-(5-O-TBDPS-2-chloromethyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)uracil* ***12***a

Procedure B was applied to **9***a* (50 mg, 0.10 mmol) to give **12***a* (46 mg, 89%) as a colorless solid foam: UV_{max}: 260 nm (ε 9400); MS *m/z*: 403 (12, M − CMe_3 − HCl), 327 (6, M − CMe_3 − BH), 293 (18, M − CMe_3 − BH − Cl), 199 (100, Ph_2SiOH). Anal. calcd. for $C_{26}H_{29}ClN_2O_4Si$: C 62.83, H 5.88, N 5.64; found: C 62.81, H 5.82, N 5.56.

*1-(5-O-TBDPS-2,3-dideoxy-2-methyl-β-D-*glycero*-pent-2-enofuranosyl)uracil* ***13***a

Procedure D was applied to **11***a* (0.30 g, 0.48 mmol) to give **13***a* (0.19 g, 85%) as colorless needles (Et_2O/hexane): mp 146–147°C; UV_{max}: 260 nm; MS *m/z*: 405 (5, M − CMe_3), 293 (100, M − CMe_3 − BH), 187 (60, M − CMe_3 − BCH_2O − Ph). Analogous treatment of **12***a* (36 mg, 0.076 mmol) by procedure D gave **13***a* (29 mg, 88%) with identical spectral data.

*9-(5-O-TBDPS-2,3-dideoxy-2-methyl-β-D-*glycero*-pent-2-enofuranosyl)adenine* ***13***b

Procedure D was applied to **11***b* (0.35 g, 0.54 mmol) to give **13***b* (0.22 g, 84%) as a colorless solid (EtOAc/hexane): mp 166–167°C; UV_{max}: 260 nm; MS *m/z*: 428 (8, M − CMe_3), 293 (20, M − CMe_3 − BH), 95 (100, M − BH − $Ph_2Si(CMe_3)O$).

*1-(2,3-Dideoxy-2-methyl-β-D-*glycero*-pent-2-enofuranosyl)uracil (2',3'-didehydro-2',3'-dideoxy-2'-methyluridine)* ***14***a *(16)*

Procedure E was applied to **13***a* (0.20 g, 0.43 mmol) to afford **14***a* (0.092 g, 95%) as a solid foam: UV_{max}: 259 nm (ε 9200); MS *m/z*: 224 (2, M^+), 193 (30, M − CH_2O), 113 (100, M − B). Anal. calcd. for $C_{10}H_{12}N_2O_4$: C 53.57, H 5.39, N 12.49; found: C 53.73, H 5.49, N 12.29.

*9-(2,3-Dideoxy-2-methyl-β-D-*glycero*-pent-2-enofuranosyl)-adenine (2',3'-didehydro-2',3'-dideoxy-2'-methyl-adenosine)* ***14***b

Procedure E was applied to **13***b* (0.185 g, 0.38 mmol) with evaporation (<25°C) followed directly by chromatography ($CHCl_3$/EtOH, 47:3) to give **14***b* (0.085 g, 91%) as a colorless powder: mp 177–178°C; UV_{max}: 259 nm, (ε 14 000); MS *m/z*: 247 (6, M^+), 217 (10, M − CH_2O), 135 (100, BH), 112 (20, M − BH). Anal. calcd. for $C_{11}H_{13}N_5O_2$: C 53.43, H 5.30, N 28.32; found: C 53.27, H 5.47, N 28.10.

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