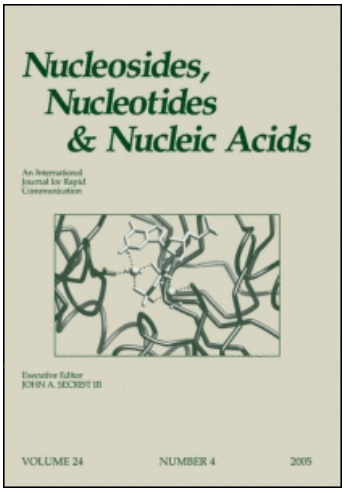

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Nucleosides. LVI[1] Synthesis and Chemical Modifications of 3'-Deoxy-Pyrimidine Nucleosides

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To cite this Article Rhie, Soo-Young and Pfleiderer, Wolfgang(1994) 'Nucleosides. LVI[1] Synthesis and Chemical Modifications of 3'-Deoxy-Pyrimidine Nucleosides', Nucleosides, Nucleotides and Nucleic Acids, 13: 6, 1425 — 1452
To link to this Article: DOI: 10.1080/15257779408012162
URL: http://dx.doi.org/10.1080/15257779408012162

NUCLEOSIDES & NUCLEOTIDES, 13(6&7), 1425-1452 (1994)

NUCLEOSIDES. LVI[1] SYNTHESIS AND CHEMICAL MODIFICATIONS OF 3'-DEOXY-PYRIMIDINE NUCLEOSIDES

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Abstract. 3′-Deoxyuridine(**1**) and 3′-deoxycytidine(**2**) were prepared with improved yields by two different methods applying either the Barton procedure to appropriate 2′,5′-di-*O*-protected pyrimidine nucleosides or by choosing the direct glycosylation of the pyrimidine bases with 1,2-di-*O*-acetyl-5-*O*-toluoyl-3-deoxy-D-*erythro*-pentofuranose via the silylation approach. Suitable protecting groups for the sugar moiety have been found in the trityl, *tert*-butyldimethylsilyl and the thexyl groups which are inert in the radical deoxygenation process. The newly synthesised compounds were characterised by elemental analyses and UV and ^{1}H-NMR spectra.

Introduction.- An exciting new chapter in oligonucleotide chemistry began with the discovery of so far unnatural 2′,5′-connected oligoadenylate 5′-*O*-triphosphates, [2,3] which were isolated from interferon treated cells and showing interesting antiviral properties. Some of the synthetically modified 2′,5′-oligoadenylate analogs also exhibit interesting antitumor and antiviral activities.[4] The identification of cordycepin, a naturally occuring nucleoside antibiotic, as 3′-deoxyadenosine [5] and reports

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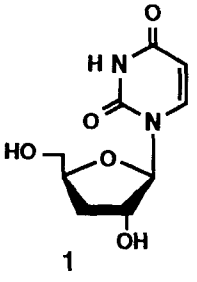
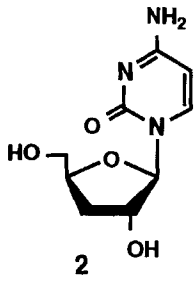
On the occassion of the 70th birthday of Prof.Dr.*Morio Ikehara* and in admiration of his important contributions to nucleic acid chemistry



1

3'-Deoxyuridine



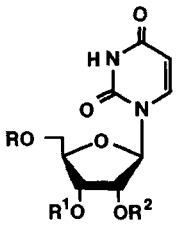
2

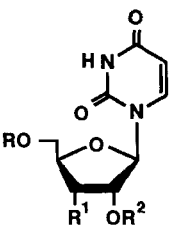
3'-Deoxycytidine

on its antitumoral properties [6,7] have stimulated considerable interest in the chemistry and biology of 3′-deoxynucleosides in general. We are interested in the properties of new types of 2′,5′- linked DNA oligomers and will report here upon the syntheses of various 3′-deoxypyrimidine nucleosides as potential starting materials. The 3′-deoxypyrimidine nucleosides were prepared either through ribosylation [8-11] of the corresponding pyrimidine bases by 3-deoxyribofuranose derivatives or by the Barton reduction of suitably 2′,5′-protected ribonucleosides.[12-15] For the synthesis of 3′-deoxycytidine, the first method was applied in a modified version, whereas the second approach worked well for the preparation of 3′-deoxyuridine. Moreover 2′,5′-diacetylated or 2′,5′-disilylated 3′-deoxyuridine could be converted into the appropriate 3′-deoxycytidine via the O^4- triazolyl derivative,[16] derived with o-chlorophenylphosphorodichloridate and 1,2,4-triazole in pyridine and followed by treatment with ammonia.

Syntheses. Our first efforts have been concerned with comparative studies to find an effective synthesis for 3′-deoxyuridine (**1**) by achieving a selective 2′,5′ protection of uridine (**3**) and its 5′-*O*-trityl derivative (**4**) [17,18] with trityl chloride but all attempts resulted in the formation of mixtures of the 2′,5′ and 3′,5′ isomers, as well as the tritrityl derivative, from which the required 2′,5′-di-*O*-trityluridine (**5**) could be isolated as the main product by chromatographical means. In this tritylation procedure, apart from pyridine, 1,8 -diazabicyclo[5.4.0]undec-7-ene (DBU),1,5-diazabicyclo-[4.3.0]non-5-en (DBN), imidazole and N-methylimidazole were used as bases in acetonitrile as solvent. Pyridine and DBU gave better results and showed some selectivity towards the 2',5'-isomer whereas the use of imidazole, N-methylimidazole resulted in poor yields of the products but with a preference of the 3′,5′-isomer. On using DBU and DBN, no 2′,3′,5′-tri-*O*-trityluridine (**7**) could be detected.

Secondly, the selective introduction of the tert-butyldimethylsilyl (tbds) group[19-22] into the 2′-and 5′-position was tried with some success. Uridine (**3**) gave 50 % of the required isomer **21** when DBU in CH_3CN was used as a base at r.t. for 2 h.





	R	R^1	R^2
3	H	H	H
4	Tr	H	H
5	Tr	H	Tr
6	Tr	Tr	H
7	Tr	Tr	Tr
8	Tr	H	tds
9	Tr	tds	H
10	Tr	tds	tds
11	DMTr	H	H
12	DMTr	H	tds
13	DMTr	tds	H

	R	R^1	R^2
14	DMTr	tds	tds
15	Tr	H	tbdms
16	Tr	tbdms	H
17	Tr	tbdms	tbdms
18	tds	H	tds
19	tds	tds	H
20	tds	tds	tds
21	tbdms	H	tbdms
22	tbdms	tbdms	H
23	tbdms	tbdms	tbdms

	R	R^1	R^2
24	Tr	O-ptc	Tr
25	Tr	H	Tr
26	Tr	O-ptc	tds
27	Tr	H	tds
28	DMTr	O-ptc	tds
29	DMTr	H	tds
30	Tr	O-ptc	tbdms
31	Tr	H	tbdms
32	tds	O-ptc	tds
33	tds	H	tds
34	tbdms	O-ptc	tbdms
35	tbdms	H	tbdms
36	Tr	H	H
37	DMTr	H	H

5′-*O*-trityluridine yielded 48 % of the 2′-isomer **15** under analogous condition after 15 h stirring at r.t. On the other hand treatment of 5′-*O*-monomethoxytrityl uridine with tert-butyldimethylsilyl chloride in presence of $AgNO_3$ in THF [19] was claimed to give 68 % of 5′-O-monomethoxytrityl-2′-*O-tert*-butyldimethylsilyluridine. The same conditions for the silylation of uridine did not succeed due to solubility problems.

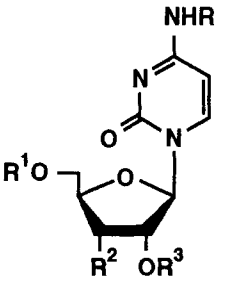
Thirdly, we tried to protect the 2′ and 5′-hydroxy functions of uridine as well as the 2′-hydroxyl group in 5′-tritylated uridine with thexyldimethylsilyl chloride (tds-Cl) which was prepared from dimethylchlorsilane and 2,3-dimethyl-2-butene and which is also a suitable protecting group for amino, amide, mercapto and carboxy functions [23]. In comparison to *tert*-butyl-dimethylsilyl chloride, thexyldimethylsilyl chloride (tds-Cl) has the advantages of easy applicability, lower price and higher stability . It was again observed that the use of DBU in CH_3CN gave the best yields of the required 2′,5′ isomers **8**, **12**, **18** and moreover DBU is an interesting base which increases the solubility of uridine in CH_3CN and activates the silylating agents due to its mesomeric amidine type structure more effectively in directing towards the more acidic 2′-hydroxy group.

Barton[24,25] showed for the first time the effectiveness of *O*-thiocarbonyl derivatives for the reduction of hydroxyl groups to CH function using tributyltin hydride

(Bu_3SnH) in a radical chain mechanism. Robins et al[26,27] applied this method to nucleoside chemistry very successfully and demonstrated its general applicability. Phenoxythiocarbonylation of **5,8,12,15,18,21** with phenoxythiocarbonylchloride (ptc-Cl) required 2.5-7.5 equivalents of 4-(dimethylamino)pyridine (DMAP) in CH_3CN for 24-48h at r.t. to give **24,26,28,30,32** and **34** in 52-81% yield.These derivatives were then reduced with tributyltin hydride in presence of azoisobutyronitrile (AIBN) as radical starter at 75°C in dry toluene to give the corresponding 3′-deoxyuridine deivatives **25,27,29,31,33** and **35**.

For the deblocking reactions, the trityl group was removed from **25** and **36** by $ZnBr_2$ in CH_2Cl_2 [28] within 5 min and proceeded in good yield to **1** without any side reactions. Desilylation of 5′-*O*-trityl-2′-*O*-*tert*-butyldimethylsilyl (**31**) and 5′-*O*-dimethoxytrityl-2′-*O*-thexyldimethylsilyluridine (**29**) with 1-3 equivalent of tetrabutylammonium fluoride (TBAF) in THF at 75 °C gave 5′-*O*-trityl- (**36**) and 5′-*O*-dimethoxytrityl-3'-deoxyuridine (**37**) in high yield whereas in the case of the 2′, 5′-di-*O*-silyl derivatives **33** and **35** only 60 % yield of isolated material was obtained. Problems arose during the work-up of 3′-deoxyuridine (**1**), which is highly soluble in H_2O and had to be separated from the reagent and purified by using ion exchange chromatography on Lewatit M 500 MB (OH^- form) eluting first the salts and impurities with H_2O and followed by 0.5 N HCOOH to give the desired product (**1**).

The synthesis of 3'-deoxycytidine (**2**) was achieved by four different methods starting either from cytidine or from uridine (**3**) and 3'-deoxyuridine (**1**), respectively, or applying a glycosylation reaction to N^4-acetylcytosine (**56**). In the first ap-

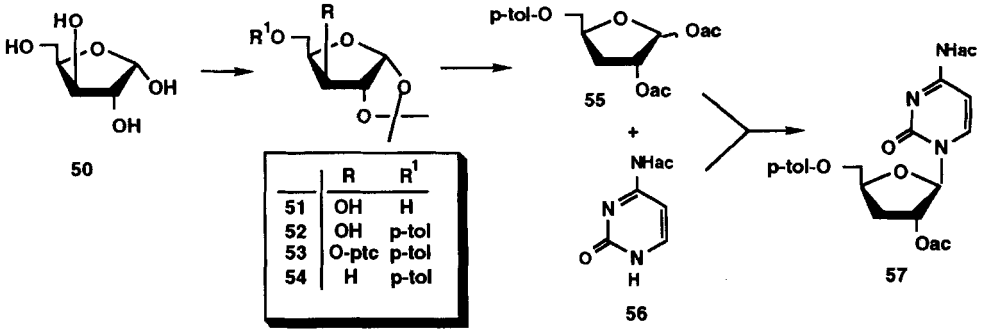


	R	R^1	R^2	R^3
38	ac	H	OH	H
39	bz	H	OH	H
40	npeoc	H	OH	H
41	ac	tds	OH	tds
42	ac	tds	Otds	H
43	ac	tds	Otds	tds

	R	R^1	R^2	R^3
44	ac	tbdms	OH	tbdms
45	ac	tds	O-ptc	tds
46	ac	tbdms	O-ptc	tbdms
47	ac	tds	H	tds
48	ac	tbdms	H	tbdms
49	ac	H	H	H

proach N^4-acetylcytidine (**38**)[29] was silylated with thexyldimethylsilyl chloride (tds-Cl) in presence of DBU in CH_3CN for 3 h and the required 2′, 5′-di-*O*-thexyldimethylsilyl derivative **41** was obtained in 52% yield after column chromatography. In this case the yield of **41** could be increased to 70% if DBU was replaced by imidazole. Subsequent reactions with phenoxythiocarbonyl chloride (ptc-Cl) in presence of 5 equivalents of 4-(dimethylamino)pyridine (DMAP) to **45**, Barton reduction to 2',5' di-O-thexyldimethylsilyl-3'-deoxycytidine (**47**) and cleavage of the silyl groups by fluoride ions resulted in N^4-acetyl-3'-deoxycytidine (**49**) in a reasonable overall yield. An analogous reaction sequence using the *tert*-butyldimethylsilyl (tbds) group for 2′,5′-OH protection according to **38**, **44**, **46**, **48** and **49** worked also well with similar yields. Applying N^4-benzoyl- (**39**)[29] and N^4-[2-(4-nitrophenyl)ethoxycarbonyl)cytidine (**40**),[37] respectively, on the same lines, silylation and thioacylation proceeded well in the usual manner but the reduction step to the corresponding 3′-deoxycytidine derivates failed.

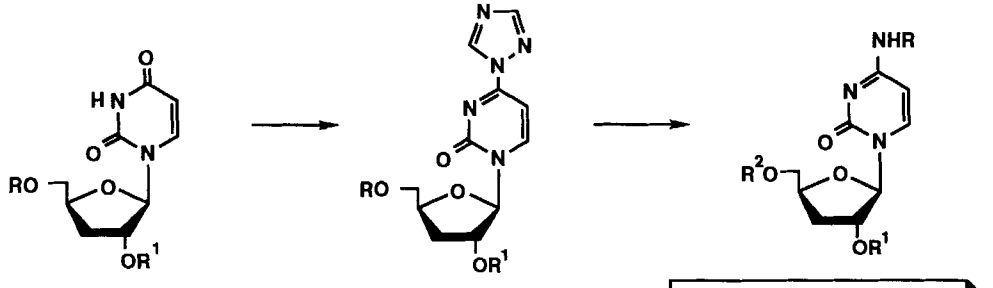
In a second approach 3′-deoxycytidine (**2**) was prepared via a glycosylation reaction treating N^4-acetylcytosine (**56**) with 1,2-di-*O*-acetyl-5-*O*-p-toluoyl-3′deoxy-D-*erythro*-pentofuranose (**55**) according to the silyl method. The sugar component was synthesized from D(+)-xylose (**50**)[38,39] introducing first the 1,2-isopropylidene residue (**51**)[30], followed by 5′-*O*-toluoylation to **52**, further thioacylation to **53** and subsequent reduction to **54** in a Barton-type radical chain reaction. After cleavage of the isopropylidene group with 75% HCOOH and subsequent acetylation **55** was obtained as an α,β-anomeric mixture. N^4-Acetylcytosine (**56**) was then treated with hexamethyldisilazane (HMDS) and the corresponding trimethylsilyl derivative glycosylated with the blocked sugar **55** under Vorbrüggen conditions using trimethylsilyl triflate as a Lewis catalyst to give **57** in 70% yield. The cleavage of the protecting groups in 0.05 N CH_3ONa afforded the crude product **2** which was purified on



	R	R¹
51	OH	H
52	OH	p-tol
53	O-ptc	p-tol
54	H	p-tol

Dowex 50 H^+-form with 0.1 N NH_4OH as eluant. The overall yield of this 7 step synthesis was 36%. Recently 3′-deoxy-5-methyluridine has been synthesized in a similar manner [31].

Another interesting possibility for the preparation of **2** is the transformation of 3′-deoxyuridine (**1**) into the cytidine analog applying the elegant triazolide method. Based upon findings of Reese et al.[32] and Sung[16,33] the amide function in uridines and thymidines can be modified at O^4 by sulfonation or phosphorylation and subsequent reaction with triazoles or imidazoles[41] to reactive intermediates which are prone to a series of nucleophilic displacements.[34] Starting from 2′,5′-di-*O*-acetyl-3'-deoxyuridine (**58**) reaction with o-chlorophenylphosphorodichloridate in presence of 1,2,4-triazole led to the O^4-triazolide derivative **59** which was subjected to ammonolysis forming 3′-deoxycytidine (**2**) in 75% yield, which totals for 3 steps to 47%. Analogously 2′,5′-di-*O*-*tert*-butyldimethylsilyl-3′-deoxyuridine (**35**) was converted into the corresponding 3′-deoxycytidine derivative **63** in 54% yield.



	R	R^1
58	ac	ac
35	tbdms	tbdms
29	DMTr	tds

	R	R^1
59	ac	ac
60	tbdms	tbdms
61	DMTr	tds

	R	R^1	R^2
2	H	H	H
62	H	ac	ac
63	H	tbdms	tbdms
64	H	tds	DMTr
65	H	H	DMTr
66	npeoc	tds	DMTr
67	npeoc	H	DMTr
68	npeoc	H	H
69	bz	H	H
70	bz	H	DMTr

A fourth synthetic approach was derived from uridine (**3**) which was transferred subsequently into 5′-*O*-dimethoxytrityl-uridine taking into account the advantage of high solubility of this intermediate in organic aprotic solvents for the anticipated addi-

tional interconversions. Reaction with thexyldimethylsilyl chloride in a $AgNO_3$ catalysed silylation gave with high regioselectivity 5′-*O*-dimethoxytrityl-2′-*O*-thexyldimethylsilyl-uridine (**12**) in 85% yield. Acylation of the 3′-OH group by phenoxythiocarbonyl chloride / DMAP in CH_3CN afforded **28** in 76% yield and the subsequent reduction by tri-butyltinhydride under Barton conditions led to 88% of 5′-*O*-dimethoxytrityl-2′-*O*-thexyldimethylsilyl-3′-deoxyuridine (**29**).

This intermediate was then converted into the corresponding cytidine derivative **64** applying the triazolide method for the exchange of the amide against the amidine function. Desilylation of **64** by fluoride ions resulted in **65** which was further protected at the amino group by the 2-(4-nitrophenyl)ethoxycarbonyl residue introduced selectively by 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride [35-37] in 89% yield to give the important building block **67** for 2′-*O*-phosphitylation and further chain elongation in oligonucleotide synthesis. The analogous acylations of **64** to **66** and of 3'-deoxycytidine (**2**) to **68** proceeded also very well but the cleavage of the silyl group in **66** by tetrabutylammonium fluoride removed simultaneously the newly introduced npeoc group due to the fact that the fluoride ion functions in aprotic solvents as a strong base giving rise to β-elimation reactions. Finally benzoylation of 3'-deoxycytidine (**2**) led to **69** which gave on dimethoxytritylation N^4-benzoyl-5'-*O*-dimethoxytrityl-3'-deoxycytidine (**70**) in good yield.

Physical Data.-All newly synthesised compounds were characterised in the usual manner, by elemental analysis, UV and ^{1}H-NMR spectra. Conversion of 3′-deoxyuridine derivative into the corresponding 3′-deoxycytidine derivatives is accompanied by a small bathochromic shift of the long wave absorption maxima. The 4-(triazol-1-yl) derivatives **59**, **60** and **61**, respectively, absorb in the range of 310 -314 nm indicating a substantial electronic interaction between the two heterocyclic rings. Introduction of the npeoc group at the N^4 amino position of 3′-deoxycytidine is reflected in an increase of the extinction of the long wavelength band by ca 10000.

The ^{1}H-NMR spectra can be analysed exactly according to the structural features. The introduction of a phenoxythiocarbonyl group at the 3′-position causes the chemical shifts of H-C(2′), H-C(3′), and H-C(4′) to lower field of about 0.5-0.8 ppm. Both the diastereotopic 3′-protons of the 3′-deoxyuridine and 3′-deoxycytidine derivatives are deshielded regarding the other sugar protons as expected, since this carbon atom is not attached to an electronegative oxygen. Their chemical shifts appear between 1.6-2.2 ppm as multiplets due to two vicinal and one geminal couplings and are in general separated up to 0.5 ppm.

Experimental Part

General. TLC: Precoated silica-gel sheets *F1500 LS 254* from *Schleicher & Schüll* and *60 F 254* from *Merck*. Cellulose sheets *F 1440 LS 254* from Schleicher & Schüll. Prep.TLC: silica gel 60 PF_{254} (*Merck*). Prep.column chromatography (CC): silica gel (*Merck* 60, 0.063-0.2 mesh); FC = flash chromatography. Prep. ion exchange chromatography: *Lewatit M 500 MB*, OH^- form from Bayer AG Leverkusen. M.P: *Büchi* apparatus, model Dr.Tottoli; no corrections. UV/VIS : *Uvikon* 820, Kontron, and *Perkin Elmer, Lambda* 5; in nm (log ε). ^{1}H- NMR : *Bruker AC 250*; δ in ppm rel to TMS, $CDCl_3$ and DMSO-D_6, respectively, as internal standard.

3′-Deoxyuridine (1). a) A solution of **24** (1.42 g, 1.6 mmole) in dry toluene (50 ml) was treated with AIBN (0.05 g, 0.3 mmole) and Bu_3SnH (0.65 ml, 2.4 mmole) at 75° with stirring for 20 h under nitrogen atmosphere. Again AIBN (0.03g, 0.18 mmole) and Bu_3SnH (0.4 ml ,1.4 mmole) were added and the temperature. raised to 90 °C and kept here for 72 h. After cooling was evaporated and the residue was taken up in $CHCl_3$ (50 ml) and washed with phosphate buffer (pH 7, 50 ml).The organic phase was dried over Na_2SO_4 and again evaporated to dryness. The crude product was purified by CC (silica gel, 20 x 2 cm) and the pure product **25** eluted with toluene / EtOAc (10:1). For detritylation the solid **25** was taken up in CH_2Cl_2 and treated with anhydrous $ZnBr_2$ (2.66 g, 11.8 mmole) in MeOH (3 ml). After 0.5 h, H_2O (5 ml) was added and stirred for 10 min. The solvent was removed in *vacuo* and the residue was taken up in EtOAc (50 ml) and shaken with H_2O (50 ml). The aqueous phase was evaporated and in order to remove the Zn salt contamination, the residue was applied onto an ion exchange column (Lewatit M 500 MB, OH^- form, 100 ml wet volume, 45 x 2 cm) and washed first with H_2O to remove side products, and the pure **1** was eluted later with 0,5N HCOOH (250 ml), and crystallised from MeOH (3 ml). Yield: 0.15 g (43 %) Mp 177-179 °C Lit.[40] mp 178-179°C. UV (H_2O): 262 (3.98), 205 (3.93). ^{1}H-NMR (D_2O): 7.90 (d, H-C (6)); 5.79 (m, H-C(1′)); 5.83 (m, H-C(5)); 4.50 (m, H-C(2′), H-C(4′)); 2.02 (m, H-C(3′)); 3.90, 3.60 (2q, H-C(5′)). Calc for $C_9H_{12}N_2O_5$ (228.2): C, 47.37; H, 5.30; N, 12.28. Found: C, 46.97; H 5.36, N, 12.08. Rf on cellulose in H_2O = 0.84, on SiO_2 in $CHCl_3$ / MeOH (4:1) = 0.33. b). A solution of **36** (0.3 g,0.64 mmole) in CH_2Cl_2 (2 ml) was treated with $ZnBr_2$ (0.72 g,3.2 mmole) in MeOH (1 ml) for 20 min. The reaction was stopped by addition of H_2O (5 ml) and stirring for 10 min. The reaction mixture was diluted with CH_2Cl_2 (15 ml), washed with H_2O (20 ml), evapo-

rated and the crude **1** purified with ion exchange chromatography as described in the preceeding procedure to give colorless crystals. Yield: 0.112g, (81 %.), mp 178°C. c). A solution of **32** (4.59 g, 6.9 mmole) or **34** (4.29 g, 6.9 mmole) in dry toluene (100 ml) was treated with AIBN (0.082 g, 0.5 mmole) and Bu_3SnH (2.76 ml, 10.4 mmole) under nitrogen atmosphere for 6 h at 75 °C. For desilylation TBAF (5.45 g, 17.3 mmole) in THF (50 ml) was added and after stirring for 1 h, the solvent removed and the residue treated with Et_2O and H_2O (50 ml). The aqueous phase was evaporated and the crude product purified by ion exchange column as described under a) to give colorless crystals. Yield: 1.2 g (58 %), mp 178°C.

3'-Deoxycytidine (2). a). A suspension of compound **57** (3g, 7 mmole) in 0.05 N NaOEt solution (200 ml) was stirred at r.t. for 24 h.The reaction mixture was evaporated to dryness, the residue dissolved in H_2O (50 ml) and then washed with $CHCl_3$ (4x 50 ml). The crude product was applied onto an ion-exchange chromatography column (Dowex 50 H^+-form, 100 ml wet volume). The side products were removed with H_2O and **2** was eluted with 0.1N NH_4OH. After removal of the solvent compound **2** (1.5 g) was crystallised from n-PrOH / Et_2O (200 ml) to give colorless crystals. Yield: 1.14g (72 %), mp 223- 225°C. UV (MeOH): 271 (3.85).[11] ^{1}H-NMR (DMSO-D_6): 7.92 (d, H-C(6);7.10 (d, NH_2); 5.70 (d, H-C-5); 5.65 (s, H-C(1')); 4.25 (q, H-C(2')); 4.08 (s, H-C(4')); 3.73, 3.50, (2m, H-C-(5')); 1.80, 1.65 (s, m, H-C(3')). Calc for $C_9H_{13}N_3O_4$ (227.2): C, 47.57; H, 5.72; N, 18.49. Found: C, 47.41; H, 5.72; N, 18.21. Rf on cellulose in H_2O = 0.75. b). A mixture of **62** (1.0 g,3.21 mmole)and 0.05N NaOEt (100 ml) was stirred at r.t. for 24 h. The solvent was removed in *vacuo* , the residue taken up in H_2O (50 ml) and washed with CH_2Cl_2 (3 X 30 ml). The aqueous phase was applied onto a Dowex 50 column (H^+ form, 7 x 2.5 cm, 50 ml wet volume) and eluted with ammonia (0.1 N). The product fractions were collected and after evaporation the yellowish foam reprecipitated from n-PrOH (15 ml) by addition of ether (100 ml).The colorless solid was dried in high vacuum and recrystallised from EtOH to give colorless crystals. Yield: 0.6 g (82 %), mp 225°C. The material is identical in Rf, UV, and ^{1}H NMR with the sample of procedure a).

2',5'-Di-*O*-trityluridine (5).[14,17] a) A mixture of uridine (**3**) (5 g, 20.5 mmole), trityl chloride (17 g, 61.5 mmole) and DBU (9.8 ml, 65 mmole) in

CH_3CN (80 ml) was stirred at r.t. for 30 min and heated at 90 °C for 6 h. After cooling, the solvent was evaporated in *vacuo* and diluted with $CHCl_3$ (100 ml), washed with phosphate buffer (2 x 100 ml). The organic phase was dried over Na_2SO_4 and evaporated to dryness.The foam was purified by CC (silica-gel, 22 x 5.5 cm), TrOH was eluted first with toluene / EtOAc (6:1, 300 ml), second 2′,3′,5′ tritrityl derivative (**7**) with toluene / EtOAc (6:1, 150 ml) , then 4.42 g (31 %) of the required 2′,5′-di-*O*-trityl derivative **5** with toluene / EtOAc (4:1, 450 ml), followed by 3.30 g (22 %) of 3′,5′-di-*O*-trityl derivative **6** with toluene / EtOAc (3:1, 550 ml) and finally 2.0 g (20 %) of 5′-*O*-trityl uridine **4** . All these compounds are identical in mp, Rf values, UV and ^1H NMR data with the authentic materials.[17] b) A mixture of 5′-*O*-trityluridine (**4**) (0.5 g, 1.15 mmole) and DBU (0.68 ml, 4.6 mmole) in CH_3CN (10 ml) was treated with trityl chloride (0.64 g, 2.3 mmole). The reaction mixture became clear, and after 15 min a precipitate was formed. After stirring for 18 h at r.t. and 4 h at 90 °C, the precipitate was filtered off, the filtrate evaporated and the residue purified by silica-gel column chromatography in analogous manner as described under a) to give 0.35 g (42 %) of 2′,5′ (**5**) and 0.28 g (34 %) of 3′,5′-di-*O*-trityl derivatives (**6**).

2′-*O*-Thexyldimethylsilyl-5′-*O*-trityluridine (8). A suspension of 5′-*O*-trityluridine (**4**) (5 g,10.3 mmole) in dry CH_3CN (100 ml) was treated with DBU (4.5 ml, 30 mmole) to give a clear solution. Tds-Cl (2.6 ml, 13.4 mmole) was then added whereby a precipitate was formed. The reaction mixture was stirred at r.t. for 15 h then diluted with $CHCl_3$ (200 ml) and washed with phosphate buffer (150 ml). The organic phase was dried over Na_2SO_4 and evaporated to dryness.The residue (8 g) was dissolved in toluene / EtOAc (10:1, 10 ml) and applied onto a silica gel column (100 g, 25 x 3.5 cm). Elution with toluene / EtOAc (10:1, 100 ml) gave 0.3 g (3 %) of 2′,3′-di-*O*-tds-5′-*O*-trityl uridine (**10**), then with toluene / EtOAc (5:1, 550 ml) 2.7 g (43%) of the required 2′-*O*-tds-5′-*O*-trityluridine (**8**) and finally 1.8 g (29 %) of the 3′-isomer **9** with EtOAc (300 ml). **8**: Mp 93-96°C. UV (MeOH): 262 (4.03), 202 (4.76). ^1H-NMR ($CDCl_3$): 8.50 (b,NH); 7.93 (d, H-C(6)); 7.10 (m, trityl); 5.96 (d, H-C(1′)); 5.26 (d, H-C(5)); 4.38 (m, C-(2′)); 4.36 (m, C-(3′)); 4.10 (s, H-C(5′)); 1.65 (q, H-C(tds)); 0.90 (m, CH_3-C(tds)); 0.28 (2s, CH_3-Si(tds)). Calc.for $C_{36}H_{44}N_2O_6Si$ (628.8) : C, 68.76; H, 7.05; N, 4.45. Found C, 68.78; H, 6.98; N, 4.50. Rf on SiO_2 in $CHCl_3$ / EtOAc (7:1) = 0.55. **9**: Mp 83-86°C. UV (MeOH): 262 (3.96), 202 (4.70). Rf on SiO_2 in $CHCl_3$ / EtOAc (7:1)= 0.33.

5′-*O*-Dimethoxytrityl-2′-*O*-thexyldimethylsilyluridine (12).

a) A mixture of 5′-*O*-DMTr-uridine (**11**)[22] (7.2 g,13.2 mmole) and imidazole (2.52 g 37 mmole) was coevaporated with dry pyridine (2 x 40 ml) and then dissolved in pyridine (100 ml) and treated with tds-Cl (3.62 ml, 18.4 mmole) and stirred at r.t. for 20 h. The reaction mixture was treated with MeOH (20 ml) and after stirring for 30 min evaporated to half of its volume, diluted with CH_2Cl_2 (50 ml) and then washed with 5 % $NaHCO_3$ solution. The organic phase was separated, dried over Na_2SO_4, evaporated to dryness and the pyridine removed by coevaporation with toluene.(2 x 30 ml). The crude product was dissolved in CH_2Cl_2 and applied onto a silica-gel column (20 x 5 cm) and to give on elution with CH_2Cl_2 / EtOAc (6:1, 350 ml) 6.8 g (75 %) of the 2′-isomer **12** and with CH_2Cl_2 / EtOAc (4:1, 500 ml) 1.48 g (16 %) of the 3′-isomer **13**. b) A solution of 5′-*O*-DMTr-uridine (**11**)[22] (11.5 g, 21.04 mmole) in dry THF (100 ml) was treated with silver nitrate (4.29 g, 25.25 mmole) and stirred at r.t. for 16 h. The mixture was then diluted with pyridine (8.2 ml, 0.1 mol), stirred for 7 h and after addition of tds-Cl (5.37 ml, 27.35 mmole) stirring continued for another 17 h.to form a colorless precipitate.The solid was filtered off, washed with CH_2Cl_2 (100 ml).the organic phase treated with phosphate buffer (100 ml, pH 7.0) and dried over $MgSO_4$. After evaporation of the solvent at 40°C *in vacuo* the residue was purified by CC (silica-gel, 32 x 4.5 cm) analogously to a). In this experiment 0.35 g (2 %) of 5′-*O*-DMTr-2′,3′-di-*O*-tds-uridine (**14**) were eluted first with CH_2Cl_2 / EtOAc (8:1, 900 ml) followed by 12.27 g (85 %) of the 2′-isomer **12** and 0.87 g (6 %) of the 3′-isomer **13**, respectively. **12:** Mp 102-105° C. UV (MeOH): 264 (4.06), 234 (4.35), 203 (4.79). ^{1}H-NMR ($CDCl_3$): 8.85 (b, NH); 7.92 (d, H-C (6)); 7.40-7.20 (m, DMTr); 6.82 (d, H-o to OCH_3); 5.95 (d, H-C(1′)); 5.25 (d, H-C(5)); 4.35(m, H-C(2′)), H-C(3')); 4.08 (m, H-C(4′)); 3.78 (s, OCH_3); 3.45 (s, H-C(5′)); 2.55 (d, HO-C-(3′)); 1.68-1.55 (m, H-C(tds)); 0.90 (m, CH_3-C(tds)); 0.20 (d, CH_3-Si(tds)). Calc for $C_{38}H_{48}N_2O_8Si$ (688.9): C, 66.25; H, 7.03; N, 4.07. Found: C, 66.05; H, 7.03; N, 3.72. Rf on SiO_2 in CH_2Cl_2 / EtOAc (3:1) = 0.58. **13**: Mp 108-111°C . UV (MeOH): 264 (4.09), 234 (4.40), 203 (4.84). ^{1}H-NMR ($CDCl_3$): 9.10 (b,NH); 7.88 (d, H-C (6)); 7.40-7.20 (m, DMTr); 6.83 (d,H-o to OCH_3); 5.95 (d, H-C(1′)); 5.35 (dd, H-C(5)); 4.37 (t,H-C(2′)); 4.13 (q, H-C(3′)); 4.05 (m, H-C(4′)); 3.78 (s, OCH_3); 3.60, 3.30 (2 dd, H-C(5′)); 2.88 (dd, HO-C(2′)); 1.62-1.50 (m, H-C(tds)); 0.90-0.72 (m,CH_3-C(tds)); 0.12-0.05 (2s, CH_3-Si(tds)). Calc for $C_{38}H_{48}N_2O_8Si$ (688.9): C, 66.25; H, 7.03; N, 4.07. Found: C, 66.21; H, 7.15; N, 3.88. Rf on SiO_2 in CH_2Cl_2 / EtOAc (3:1) = 0.33. **14**: Mp 98-101°C. UV (MeOH): 264 (4.12), 234 (4.42), 203 (4.89). ^{1}H-NMR ($CDCl_3$)

:8.80 (b, NH); 8.18 (d, H-C (6)); 7.40-7.20 (m, DMTr); 6.82 (d, H-o to OCH_3); 5.85 (d,H-C(1′)); 5.25 (dd, H-C(5)); 4.12 (m, H-C(2′), H-C(3′), H-C(4′)); 3.80 (s, OCH_3); 3.68, 3.32 (2 dd, H-C(5′)); 1.65-1.55 (m, H-C(tds)); 0.85 (q,CH_3-C(tds)); 0.13 -0.08 (2s, CH_3-Si(tds)). Calc for $C_{46}H_{66}N_2O_8Si_2$ (831.2): C, 66.47; H, 8.00; N, 3.37. Found : C, 66.30; H 7.88; N 3.47. Rf on SiO_2 in CH_2Cl_2 / EtOAc (3:1) = 0.74.

2′-*O*-*Tert*-butyldimethylsilyl-5′-*O*-trityluridine (15). A mixture of 5′-*O*-trityluridine (**4**) (5g, 10.3 mmole) in CH_3CN (100 ml) and DBU (3.1 ml, 20.6 mmole) was treated with tbdms-Cl (2.02g, 13.4 mmole) and stirred at r.t. for 15 h. Solvent was removed *in vacuo* and the residue was taken up in $CHCl_3$ (200 ml) and washed with phosphate buffer (100 ml), and the organic phase was dried over Na_2SO_4. After removing of the solvent, the residue was purified by silicagel column chromatography to elute subsequently 2′,3′-di-*O*-tbdms-5′-*O*-Tr-uridine (**17**) (1.7 g, 23 %) with toluene / EtOAc (10:1, 100 ml), 2.6g (43 %) of the 2'-isomer **15** and 1.54 g (25 %) of the 3′-isomer **16** using toluene / EtOAc (5:1) and EtOAc, respectively.

15: Mp 104-107°C . UV (MeOH): 264 (3.97), 202 (4.74). ^{1}H-NMR ($CDCl_3$): 8.50 (b, NH); 7.93 (d, H-C (6)); 7.50-7.20 (m, Tr); 5.96 (d, H-C(1′)); 5.27 (d, H-C(5)); 4.38, 4.36 (m, H-C(2′), H-C(3′)); 4.11 (b, H-C (4′)); 3.50 (d, H-C(5′)); 0.90 (s, CH_3-C(tbdms)); 0.20 (2s, CH_3-Si(tbdms)). Calc for $C_{34}H_{41}N_2O_6Si \cdot 0.5\ H_2O$ (609.8): C, 66.97; H, 6.78; N, 4.59. Found: C, 67.00; H, 6.63; N, 4.55. Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.64. **16**: Mp 90-94°C. UV (MeOH): 262 (4.02), 202 (4.78). Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.35. **17**: Mp 96-97°C. UV (MeOH): 263 (4.00), 202 (4.73). Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.76.

5′-Di-*O*-thexyldimethylsilyluridine (18). A mixture of uridine (**3**) (5 g, 20.5 mmole), DBU (13.77 ml, 92.1 mmole) in CH_3CN (150 ml) was treated with tds-Cl (12.05 ml, 61.4 mmole) and after stirring at r.t. for 2 h the solvent removed *in vacuo*. The residue was taken up in $CHCl_3$ (200 ml) and washed with phosphate buffer (2 x 50 ml). The organic phase was dried over Na_2SO_4, evaporated to dryness (16 g) and the residue purified by CC (sillica gel 40 x 3.5 cm) to elute first 2′,3′,5′-tri-*O*-tds-uridine (**20**) with toluene / EtOAc (10:1, 300 ml) then 5.9 g (54 %) of the required 2′,5′-di-*O*-tds-derivative **18** with toluene / EtOAc (4:1, 750 ml) and finally 3.55 g (32 %) of the 3′,5′-isomer **19** with toluene / EtOAc (2:1, 400 ml).

18: Mp 110-112°C. UV (MeOH): 262 (4.05), 206 (3.96). ^{1}H-NMR ($CDCl_3$): 7.95 (d, H-C (6)); 5.98 (d, H-C(1′)); 5.70 (d, H-C(5)); 4.20 (m,H-C(2′)); 4.10 (m, H-

C(3′), H-C (4′)); 4.00, 3.80 (2d, H-C(5′)); 1.65 (q, H-C-(tds)); 0.85 (m, CH_3-C(tds)); 0.17, 0.16 (2s, CH_3-Si(tds)). Calc for $C_{25}H_{48}N_2O_6Si_2$ (528.8): C, 66.97; H, 6.78; N, 4.59. Found: C, 67.00; H, 6.63; N, 4.55. Rf on SiO_2 in CH_2Cl_2 /EtOAc (7:1) = 0.30. **19**: Mp 134-135°C. UV (MeOH): 261 (4.05), 207 (3.96). Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.12. **20:** UV (MeOH): 261 (3.88), 205 (3.86). Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.53.

2′,5′-Di-*O*-*tert*-butyldimethylsilyluridine (21). A mixture of uridine (**3**) (2.44 g, 10 mmole) in CH_3CN (30 ml) and DBU (6.3 ml, 42 mmole) was stirred at r.t. for 2 h.The solvent was removed *in vacuo* and the residue was taken up in $CHCl_3$ (150 ml) and washed with phosphate buffer (100 ml), and the organic phase was dried over Na_2SO_4. After evaporation the residue was purified by silica-gel column chromatography eluting subsequently 2′,3′,5′-tri-*O*-tbdms uridine (**23**) (0.75 g, 16 %) with toluene / EtOAc (9:1, 100 ml), then 2.35 g (50 %) of the 2′,5'-di-*O*-silyl-isomer **21** and finally 1.54 g (26 %) of the 3′,5'- isomer **22** with toluene / EtOAc (4:1) and (3:1), respectively. The mp, UV and ^1H NMR data of these compounds were identical with those of the authentic samples.[19]

3′-*O*-Phenoxythiocarbonyl-2′,5′-di-*O*-protected uridine derivatives 24, 26, 28, 30, 32 and 34. General procedure: The starting uridine derivative (0.85 mmole) and 4-(dimethylamino)pyridine (2.5-4.5 equivalents) were dissolved in CH_3CN (15 ml), then phenoxythiocarbonyl chloride (1.1 mmole) added and srtirred at r.t. for 20 h. The mixture was diluted with EtOAc (20 ml), washed twice with H_2O (25 ml), the organic phase dried over Na_2SO_4 and evaporated. The residue was purified by silica-gel CC using toluene / EtOAc (10:1) in case of **24**, **26**, **28** and **30** and n-hexane / ether (2:1) for **32** and **34**, respectively, to give pure materials.

3'-*O*-Phenoxythiocarbonyl-2',5'-di-*O*-trityluridine (24). From 0.62 g of **5**. Yield: 0.35 g (52%) colorless crystals. Mp 212-216°C. UV (MeOH): 258 (4.08), 203 (5.02). ^1H-NMR ($CDCl_3$): 8.40 (b,NH); 7.70 (d,H-C (6)); 7.50-7.10 (m, m-H(ptc), p-H(ptc),Tr); 7.08 (d,o-H(ptc)); 6.67 (d,H-C(1′)); 5.20 (d, H-C(5)); 4.68 (m, H-C(2′)); 4.30 (d, H-C(2′)); 4.20 (s, H-C (4′)); 3.40, 3.10 (2d, H-C(5′)). Calc for $C_{54}H_{44}N_2O_7S \cdot 0.5\ H_2O$ (874.0): C, 74.21; H, 5.19; N, 3.21. Found: C, 74.31; H, 5.25; N, 3.11. Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.68.

3'-*O*-Phenoxythiocarbonyl-2'-*O*-thexyldimethylsilyl-5'-*O*-trityl-uridine (26). From 0.535 g of **8**. Yield: 0.348 g (65%) colorless foam. Mp 125-127°C. UV (MeOH): 259 (4.13), 203 (4.90). ^{1}H-NMR ($CDCl_3$): 8.35 (b, NH); 7.92 (d, H-C (6)); 7.50-7.10 (m, m-H(ptc), p-H(ptc),Tr); 7.07 (d, o-H(ptc)); 6.07 (d, H-C(1')); 5.93 (t, H-C(3')); 5.34 (d, H-C(5)); 4.68 (t, H-C(2')); 4.44 (d, H-C (4')); 3.59, 3.51 (2d, H-C(5')); 1.65 (q, H-C(tds)); 0.85 (m, CH_3-C(tds)); 0.20, 0.17 (2s, CH_3-Si(tds)). Calc for $C_{43}H_{48}N_2O_7$ SSi (765.0): C, 67.51; H, 6.32; N, 3.66. Found : C, 67.31; H, 6.45; N, 3.58. Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.85.

5'-*O*-Dimethoxytrityl-3'-*O*-phenoxythiocarbonyl-2'-*O*-thexyl-dimethylsilyluridine (28). From 0.585 g of **12**. Yield: 0.523 g (76%) colorless foam. Mp 92-97°C. UV (MeOH): 265 (4.15), 234 (4.49), 204 (4.90). ^{1}H-NMR ($CDCl_3$): 8.40 (bs, NH); 7.95 (d, H-C (6)); 7.50-7.20 (m, m-H(ptc), p-H(ptc),Tr); 7.08 (d, o-H(ptc)); 6.83 (d, H-o to OCH_3); 6.08 (d,H-C(1')); 5.90 (t, H-C(3')); 5.35 (d, H-C(5)); 4.68 (t, H-C(2')); 4.40 (d, H-C (4')); 3.55 (s, H-C(5')); 1.70-1.55 (m, H-C (tds)); 0.92-0.86 (m, CH_3-C(tds)); 0.18 (s, CH_3-Si(tds)). Calc for $C_{42}H_{52}N_2O_9$ SSi (825.0): C, 65.51; H, 6.35, N, 3.40. Found: C, 65.34; H, 6.35; N, 3.10. Rf on SiO_2 in CH_2Cl_2 / EtOAc (3:1) = 0.76.

5'-*O*-Dimethoxytrityl-2'-*O*-thexyldimethylsilyl-3'-deoxyuridine (29) A solution of **28** (3.75 g, 4.55 mmole) in dry toluene (100 ml) was treated with AIBN (0.5 g, 3 mmole) and Bu_3SnH (3.01 ml, 11.36 mmole) at 85°C under nitrogen atmosphere with stirring for 3 h. The solvent was removed in *vacuo* , the residue taken up in CH_2Cl_2 (100 ml), washed with H_2O (100 ml) and the organic phase dried over Na_2SO_4. After evaporation the residue was dissolved in CH_2Cl_2 (10 ml) and applied onto a silica gel column (25 x 3.5 cm) for chromatography with CH_2Cl_2 / EtOAc (6:1, 350 ml). The main fraction gave on evaporation a colorless amorphous solid. Yield: 2.70 g (88 %), mp 92-94°C. UV (MeOH): 265 (4.05), 234 (4.16), 205 (4.75). ^{1}H-NMR ($CDCl_3$): 8.10(d, H-C (6)); 7.40-7.20 (m, DMTr); 6.83 (d, H-o to OCH_3); 5.72 (d, H-C(1')); 5.25 (d, H-C(5)); 4.50 (m, H-C(2')); 4.38 (d, H-C (4')); 3.80 (s, OCH_3); 3.62, 3.35 (2 dd, C-H-C(5')); 2.15 (t, H-C(3')); 1.70-1.55 (m, H-C (tds)); 1.00-0.80 (m, CH_3-C(tds));. 0.23, 0.15 (2s, CH_3-Si(tds)). Calc for $C_{38}H_{48}N_2O_7$ Si (672.9): C, 67.83; H, 7.19; N, 4.16;. Found : C, 67.48; H, 7.23; N, 3.86. Rf on SiO_2 in CH_2Cl_2 / EtOAc (3:1) = 0.49.

3'-*O*-Phenoxythiocarbonyl-2'-*O*-*tert*-butyldimethylsilyl-5'-O-trityluridine (30). From 0.51 g of **15**. Yield: 0.44 g (71%) colorless solid. Mp 125-127°C. UV (MeOH): 257 (4.17), 204 (4.90). ^{1}H-NMR ($CDCl_3$): 8.30 (b, NH); 7.93 (d, H-C (6)); 7.50-7.20 (m, m-H(ptc), p-H-(ptc),Tr); 7.10 (d, o-H(ptc)); 6.03 (d, H-C(1')); 5.93 (t, H-C(3')); 5.34 (d, H-C(5)); 4.69 (t, H-C(2')); 4.48 (d, H-C (4')); 3.57 (s, H-C(5')); 0.90 (m, CH_3-C(tbdms)); 0.20 (s, CH_3-Si(tbdms)). Calc for $C_{41}H_{44}N_2O_7$ SSi (737.0): C, 66.82; H, 6.02; N, 3.80. Found: C, 66.60; H, 6.09; N, 3.75. Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.82.

3'-*O*-Phenoxythiocarbonyl-2',5'-di-*O*-thexyldimethylsilyluridine (32). From 0.457 g of **18**. Yield: 0.38 g (67%) amorphous solid. Mp 94-97°C. UV (MeOH): 259 (4.00), 207 (4.07). ^{1}H-NMR ($CDCl_3$): 8.45 (b, NH); 7.94 (d, H-C (6)); 7.45 (m, m-H(ptc)); 7.35 (m, p-H(ptc)); 7.08 (d, o-H(ptc)); 6.10 (d, H-C-)(1')); 5.73 (d, H-C(5)); 5.60 (m, H-C(2')); 4.50 (m,H-C(3')); 4.40 (m, H-C (4')); 4.02-3.95 (2d, H-C(5')); 1.65 (q, H-C (tds)); 0.92-0.86 (m, CH_3-C(tds)); 0.22, 0.18 (2s, CH_3Si(tds)). Calc for $C_{32}H_{52}N_2O_7SSi_2$ (665.0): C, 57.80; H, 7.88; N, 4.21. Found: C, 57.91; H, 7.94; N, 4.20. Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.66.

3'-*O*-Phenoxythiocarbonyl-2',5'-di-*O*-*tert*-butyldimethylsilyl-uridine (34). From 0.4 g of **21**. Yield: 0.421 g (81%) colorless foam. Mp 92-95°C. UV (MeOH): 256 (4.09), 203 (4.27). ^{1}H-NMR ($CDCl_3$): 8.35 (b, NH); 7.93 (d, H-C (6)); 7.46 (m, m-H(ptc)); 7.36 (m, p-H(ptc)); 7.10 (d, o-H(ptc)); 6.05 (d, H-C(1')); 5.73 (d, H-C(5)); 5.60 (t,H-C(2')); 4.45, 4.40 (m, H-C(3'), H-C (4')); 4.09, 3.90 (2d, H-C(5')); 0.90 (m, CH_3-C-(tbdms)); 0.28, 0.16 (2s, CH_3-Si(tbdms)). Calc for $C_{28}H_{44}N_2O_7$ SSi_2 (608.9): C, 55.23; H, 7.28; N, 4.60. Found: C, 55.08; H, 7.36; N, 4.62. Rf on SiO_2 in CH_2Cl_2 / EtOAc (7:1) = 0.53.

3'-Deoxy-5'-*O*-trityluridine (36). A solution of either **26** (1.35 g, 1.77 mmole) or **30** (1.30 g, 1.77 mmole) in dry toluene (50 ml) was treated with AIBN (0.05 g, 0.3 mmole) and Bu_3SnH (0.65 ml, 2.4 mmole) at 85 °C with stirring for 3 h under nitrogen atmosphere.Subsequent desilylation was achieved by addition of tetrabutylammonium fluoride (0.94 g, 3 mmole) in THF (5 ml) and heating to 75°C for 4 h..The solvent was removed and the residue was extracted with EtOAc (50 ml), washed with H_2O and the organic phase dried over Na_2SO_4.After evaporation *in*

vacuo the crude product was applied onto a silica gel column (20 x 2 cm) for chromatography with $CHCl_3$ / EtOAc (1:1, 100 ml) to give a colorless foam. Yield: 0.68g (85 %) from **26** and 0.752 g (87%) from **30**, mp 115-119°C. UV (MeOH): 267 (3.97), 203 (4.72). ^{1}H-NMR ($CDCl_3$): 12.5 (bs, NH); 8.13 (d, H-C (6)); 7.50-7.20 (m, Tr); 5.77 (s, H-C(1′)); 5.31 (d, H-C(5)); 4.78 (bs, OH-C(2′)); 4.63 (m, H-C(2′)); 4.46 (d, H-C (4′)); 3.64, 3.37 (d, q, H-C(5′));.2.10 (m, H-C(3′)). Calc for $C_{28}H_{26}N_2O_5 \cdot H_2O$ (488.5): C, 68.84; H, 5.78; N, 5.73. Found: C, 69.31; H, 5.72; N, 5.68. Rf on SiO_2 in $CHCl_3$ / MeOH (4:1) = 0.84.

5'-*O*-Dimethoxytrityl-3'-deoxyuridine (37). A mixture of **29** (4.0 g, 5.94 mmole) and TBAF · 3 H_2O (3.18 g,10.1 mmole) in dry THF (10 ml) was stirred at r.t. for 24 h. The reaction solution was diluted with CH_2Cl_2 (100 ml), washed with 5% $NaHCO_3$ (100 ml), the organic phase dried over Na_2SO_4 and then the solvent was removed in *vacuo*. Purification was done by CC (silica-gel, 20 x 4 cm) by elution with EtOAc. After removal of the solvent the residue was dissolved in CH_2Cl_2 (5 ml) and added dropwise to petroleumether (50 ml) with vigorous stirring. A colorless amorphous solid was obtained which was dried in high vacuum at 40°C. Yield: 2.78 (88 %), mp 113-115°C. UV (MeOH): 264 (4.08), 233 (4.38), 204 (4.84). ^{1}H-NMR ($CDCl_3$): 8.17 (d, H-C (6)); 7.40-7.20 (m, DMTr); 6.81 (d, H-o to OCH_3); 5.75(d, H-C(1′)); 5.30 (d, H-C(5)); 4.90 (d, H-C (4′)); 4.62 (m, H-C(2′)); 3.78 (s, OCH_3); 3.65, 3.35 (2dd, H-C(5′)); 2.17, 1.95 (tt, dd, H-C(3′)). Calc for $C_{30}H_{30}N_2O_7$ 0.5 H_2O (539.6): C, 66.78; H, 5.79; N, 5.19. Found: C, 66.91; H, 5.62; N, 5.23. Rf on SiO_2 in $CHCl_3$ / MeOH (9:1) = 0.63.

N^4-Acetyl-2',5'-di-*O*-thexyldimethylsilylcytidine (41), N^4-acetyl-3',5'-di-*O*-thexyldimethylsilylcytidine (42) and N^4-acetyl-2',3',5'-tri-*O*-thexyldimethylsilylcytidine (43). a) A suspension of N^4-acetylcytidine (**38**)[29] was treated wth DBU (2.6 ml, 17.5 mmole), whereby a clear solution was obtained. Thexyldimethylsilyl chloride (2.05 ml, 9.3 mmole) was added and stirred at r.t. for 5 h. The solution was evaporated to dryness, the residue treated with CH_2Cl_2 (50 ml), and washed with phosphate buffer (pH 7, 100 ml). The organic phase was dried over Na_2SO_4, evaporated *invacuo* and then the product mixture separated by CC (silica gel, 30 x 12 cm) to give in the first product fraction **41** on elution with $CHCl_3$ / EtOAc (3:1, 200 ml) as a colorless foam. Yield: 1.04g (52 %). Compound **42** was isolated from the second fraction on evaporation. Yield: 0.74g

(37 %). b). A suspension of N^4-acetylcytidine (**38**) (3 g, 10.5 mmole) and imidazole (2.9 g, 42 mmole) in dry DMF (100 ml) was dissolved by gentle warming, then tds-Cl (6.2 ml, 31.6 mmole) added and stirred at r.t. for 3 days. The work up was done analogous to method a). Separation of the crude mixture was done by silica-gel column chromatography, (35 x 3.5 cm) whereby the N^4-acetyl-2′,3′,5 -tri-*O*-thexyl-dimethylsilylcytidine (**43**) was eluted first with toluene / EtOAc (5:2, 350 ml) in a yield of 0.3 g (4%), followed by compound **41** yielding 4.2 g (70 %) and finally of **42** with toluene / EtOAc (2:1) to give 1.42 g (24%) of compound **42**. **41**: Colorless foam, mp 78-82°C. UV (MeOH): 298 (3.89), 247 (4.17), 212 (4.27). ^{1}H-NMR ($CDCl_3$): 9.10 (b, NH); 8.45 (d, H-C(6)); 7.35 (d, H-C (5)); 5.92 (d, H-C(1′)); 4.42 (m, H-C(2′), H-C(3′), H-C(4′)); 3.86 (dd, H-C(5′)); 2.42 (d, OH-C(3′)) 2.26 (s, CH_3CO); 1.65 (s, H-C(tds)); 0.90 (m, CH_3-C(tds)); 0.40-0.20 (m, CH_3-Si-(tds)). Calc for $C_{27}H_{51}N_3O_6Si_2 \cdot 0.5\ H_2O$ (578.9): C, 56.02; H, 9.05; N,7.26. Found: C, 56.21; H, 9.14; N, 7.33. Rf on SiO_2 in toluene / EtOAc (1:1) = 0.40. **42:** Colorless solid, mp 92-95°C. UV (MeOH): 298 (3.92), 247(4.19), 212 (4.28). ^{1}H-NMR ($CDCl_3$): 9.20 (bs, NH); 8.25 (d, H-C(6)); 7.40 (d, H-C (5)); 5.98 (d, H-C(1′)); 4.25 (m, H-C(2′)), 4.55-3.95 (m, H-C(3′), H-C(4′)); 3.75 (dd, H-C(5′); 3.07 (d, OH-C(2′)); 2.25 (s, CH_3CO); 1.75-1.55 (m, H-C(tds)); 0.90 (m, CH_3-C-(tds)); 0.15 (q, CH_3-Si(tds)). Calc for $C_{27}H_{51}N_3O_6Si_2$ (569.9): C, 56.91; H, 9.02; N, 7.37. Found: C, 56.68; H, 8.92; N, 7.37. Rf on SiO_2 in toluene / EtOAc(1:1) = 0.11. **43**: Colorless amorphous solid, mp 98-101°C. UV (MeOH): 299 (3.91), 248 (4.19), 215 (4.39). ^{1}H-NMR ($CDCl_3$) :10.0 (bs, NH); 8.50 (d, H-C(6)); 7.38 (d, H-C (5)); 5.80 (d, H-C(1′)); 3.95-4.20 (m, H-C(2′), H-C(3′), H-C(4′)); 3.78 (dd, H-C(5′)); 2.28 (s, CH_3CO); 1.75-1.55 (m, H-C(tds)); 0.7-1.0 (m, CH_3-C(tds)); 0.05-0.30 (m, CH_3-Si(tds)). Calc for $C_{35}H_{69}N_3O_6Si_3 \cdot 0.5\ H_2O$ (721.2): C, 58.29; H, 9.78; N, 5.78. Found: C, 58.49; H, 9.65; N, 5.78. Rf on SiO_2 in $CHCl_3$ / EtOAc (1:1) = 0.58.

N^4-Acetyl-3′-*O*-phenoxythiocarbonyl-2′,5′-di-*O*-thexyldimethyl-silylcytidine (45). A suspension of **41** (5.79 g, 10 mmole) and 4-(dimethylamino) pyridine (6.0 g, 49 mmole) in dry CH_3CN was dissolved by slight warmig and then treated with ptc-Cl (3.3 ml, 24.5 mmole) whereby a precipitate was formed.The reaction mixture was stirred overnight at r.t., diluted with EtOAc (200 ml), washed with H_2O (200 ml), dried over Na_2SO_4 and evaporated to dryness.The purification of the

crude product was achieved by CC (silica-gel 25 x 1.6 cm) with toluene / EtOAc (1:1, 600 ml) to give a colorless foam. Yield: 6.29 g (88%), mp 104-108°C. UV (MeOH): 298 (3.90), 246 (4.28), 206 (4.43). ^{1}H-NMR ($CDCl_3$): 9.10 (bs, NH); 8.45 (d, H-C(6)); 7.40-7.30 (m, H-C(5), m-H(ptc), p-H(ptc)); 7.03 (d, o-H-ptc); 5.98 (d, H-C(1′)); 5.42 (q, H-C(2′)),4.65 (m, H-C(3′)); 4.55 (d, H-C(4′)); 4.20, 3.90 (2d, H-C-(5′)); 2.25 (s, CH_3CO); 1.72-1.58 (m, H-C(tds)); 0.90 (m, CH_3-C(tds)); 0.30-0.10 (m, CH_3-Si(tds)). Calc for $C_{34}H_{55}N_3O_7SSi_2 \cdot 0.5\ H_2O$ (715.0): C, 57.11; H, 7.89, N, 5.88. Found: C, 56.76; H, 7.75; N, 5.87. Rf on SiO_2 in toluene / EtOAc (1:1) = 0.53.

N^4-Acetyl-3′-*O*-phenoxythiocarbonyl-2′-5′-di-*O*-*tert*-butyldimethylsilylcytidine (46). From **44** (5.14 g, 10 mmole) analogous to the proceeding procedure. Isolation by CC with n-hexane / acetone (4:1) to give on evaporation a colorless foam. Yield: 4.68 g (72%), mp 110-112°C. UV (MeOH): 298 (3.88), 246 (4.29), 207 (4.41). ^{1}H-NMR ($CDCl_3$): 9.67 (bs, NH); 8.50 (d, H-C(6)); 7.40 (d, m, H-C(5), m-H(ptc)); 7.32 (d, pH(ptc)); 7.05 (d, o-H(ptc)); 5.95 (d,H-C(1′)); 5.46 (q, H-C(2′)); 4.62 (m, H-C(3′)); 4.55 (d, H-C(4′)); 4.20, 3.95 (2dd, H-C-(5′)); 2.36 (s, CH_3CO); 0.93 (s, CH_3-C(tbdms)); 0.15-0.10 (q, CH_3-Si-(tbdms)).
Calc for $C_{30}H_{47}N_3O_7SSi_2$ (649.9): C, 55.44; H, 7.29; N, 6.47. Found: C, 55.35; H, 7.34; N, 6.43. Rf on SiO_2 in CH_2C_2 / EtOAc(1:1) = 0.53.

N^4-Acetyl-2′,5′-di-*O*-thexyldimethylsilyl-3′-deoxycytidine (47)
A solution of **45** (6.1 g, 8.5 mmole) in dry toluene (100 ml) was treated with Bu_3SnH (5.64 ml, 21.1 mmole) and AIBN (0.05 g) with stirring at 85°C under nitrogen atmosphere for 24 h. After cooling, the reaction mixture was evaporated and diluted with CH_2Cl_2 (200 ml). The organic phase was washed with H_2O, dried over Na_2SO_4 and evaporated again to dryness. The residue was purified by CC (silica gel, 35 x 2.5 cm) with a gradient of toluene / EtOAc 4:1 - 2:3 to elute the product with the last fraction. Evaporation gave a colorless solid. Yield: 3.9 g (82 %), mp 72-78°C. UV (MeOH) :269 (4.07), 245 (4.21), 212 (4.07). ^{1}H-NMR ($CDCl_3$): 9.40 (bs, NH); 8.51 (d, H-C(6)); 7.30 (d, H-C(5)); 5.72 (d, H-C(1′)); 4.50 (dd, H-C(2′)); 4.32 (d, H-C(4′)); 4.18, 3.72 (2d, H-C-(5′)); 2.23 (s, CH_3CO); 1.90,1.60 (t, d, H-C(3′)); 1.72-1.55 (m, H-C(tds)); 0.90- 0.70 (m, CH_3-C(tds)); 0.30-0.15 (s, t, CH_3-Si--(tds)). Calc for $C_{27}H_{51}N_3O_5Si_2$ (553.9): C, 57.11; H, 7.89; N, 5.88. Found: C, 56.76; H, 7.75, N, 5.87. Rf on SiO_2 in toluene / EtOAc(1:1) = 0.50.

N^4-Acetyl-2′,5′-di-*O*-*tert*-butyldimethylsilyl-3′-deoxycytidine (48). Analogous to the proceeding procedure from **46** (5.52 g, 8.5 mmole) after chromatographical work-up with n-hexane / acetone (8:1 - 5:1) to give an amorphous solid. Yield: 2.89 g (58%), mp 93-96°C. UV (MeOH): 298 (3.86), 248 (4.24). ^{1}H-NMR ($CDCl_3$) : 9.85 (bs, NH); 8.55 (d, H-C(6)); 7.30 (d, H-C(5)); 5.75 (d, H-C(1′)); 4.54 (dd, H-C(2′)); 4.32 (d, H-C(4′)); 4.22, 3.72 (2dd, H-C-(5′)); 2.20 (s, CH_3CO); 1.95, 1.62 (dt, td, H-C-(3′)); 0.90 (s, CH_3-C(tbdms)); 0.20, 0.05 (s, d, CH_3-Si-(tbdms)). Calc for $C_{23}H_{43}N_3O_5Si_2$ (497.8): C, 55.50; H. 8.71; N, 8.44. Found: C, 55.43; H, 8.65; N, 8.05. Rf on SiO_2 in n-hexane / acetone (2:1) = 0.50.

N^4-Acetyl-3′-deoxycytidine (49). A solution of **47** and **48** (1 mmole), respectively, in dry THF (15 ml) was stirred with TBAF.$3H_2O$ (3 mmole) at 80°C for 1 h and then at r.t. for 24 h. The solvent was removed *in vacuo* and the residue dissolved in little MeOH and then applied onto a silca-gel column (20 x 1.5 cm). Elution with $CHCl_3$ / MeOH (95:5) and evaporation of the product fraction gave a colorless solid. Yield: 0.21 g (78%), mp 171-174°C. UV (MeOH): 286 (3.78), 245 (4.12), 212 (4.26), 206 (4.24). ^{1}H-NMR (DMSO-D_6): 9.85 (bs, NH); 8.48 (d, H-C(6)); 7.12 (d, H-C-(5)); 5.68 (d, H-C(1′)); 5.62 (bs, HO-C(2′)); 5.15 (bs, HO-C(3′)); 4.38 (b, H-C(2')); 4.17 (d, H-C(4′)); 3.83, 3.57(2d, H-C(5′)); 2.10 (s, CH_3CO); 1.85, 1.68 (td, dd, H-C(3′)). Calc for $C_{11}H_{14}N_3O_5 \cdot 0.5\ H_2O$ (497.8): C, 47.49; H, 5.80; N, 15.10. Found: C, 47.24; H, 5.85; N, 14.73. Rf on SiO_2 in $CHCl_3$ /MeOH (9:1) = 0.53.

1,2-*O*-Isopropylidene-α-D-xylofuranose (51).[39]

Anhydrous D-xylose (**50**) (30 g, 0.2 mole) was stirred in dry acetone (900 ml) for 20 min and then conc. H_2SO_4 (20 ml, 0.38 mole) added slowly dropwise whereby the suspension became clear within 3 h. The brown solution was carefully neutralized by KOH (50 g) in H_2O (50ml) to pH 7 separating a precipitate of K_2SO_4 which was collected, washed with acetone and then the united filtrates evaporated to a sirup. The oily residue was dissolved in H_2O (500 ml), extracted three times with n-hexane (250 ml) and then the aqueous layer again evaporated to a sirup which was coevaporated twive with toluene / EtOH (1:1, 100 ml). Yield: 25 g (66%). Rf on SiO_2 in $CHCl_3$ / MeOH (9:1) = 0.35. The n-hexane fraction contains the 1,2,3,5-di-*O*-isopropylidene-α-D-xylose. Yield: 9.7 g (21%).

1,2-*O*-Isopropylidene-5-*O*-(methylbenzoyl)-α-D-xylofuranose (52). A solution of the crude product **51** (25 g, 0.13 mole) in dry pyridine (80 ml) was cooled to 0°C and then 4-methylbenzoyl chloride (17.4 ml, 0.13 mole) in pyridine (20 ml) added dropwise with stirring whereby the temperature should not raise. After addition the mixture was stirred for another 1 h and then poured onto crushed ice (900 g) with vigorous stirring. The resulting precipitate was collected, washed several times with H_2O and then dried in a vacuum desiccator. The crude material was purified by silica-gel column chromatography (300 g, 5.5 x 35 cm) with toluene / AcOEt (3:1).The main fraction was evaporated and gave on crystallization from ether / n-hexane (3:1, 200 ml) colorless crystals. Yield: 26.4 g (66%), mp 74-75°C. Lit.[39] 73-74°C. UV (MeOH): 238 (4.21), 201 (4.42). ^{1}H-NMR ($CDCl_3$): 7.95, 7.25 (2 d, H-C(tol)); 5.95 (d, H-C(1)); 5.80 (m, H-C(2)); 4.60 (d, H-C(4)); 4.35 (m, H-C(5)); 4.18 (s, H-C(3)); 2.40 (s, H_3C-C(tol)); 1.50, 1.30 (2s, $(H_3C)_2C$). Rf on SiO_2 in toluene / EtOAc (3:1) = 0.21.

3-Deoxy-1,2-*O*-isopropylidene-5-*O*-(4-methylbenzoyl)-α-D-xylofuranose (54). A solution of 1,2-*O*-isopropylidene-5-*O*-(4-methylbenzoyl)-α-D-xylofuranose (**52**) in dry CH_3CN was treated with 4-(dimethylamino)pyridine (5 g, 40 mmole) and after 20 min stirring, phenoxythiocarbonyl chloride (3.2 ml, 24 *mmole*) added and stirred for 2 h at r.t. The precipitate was filtered off and the filtrate evaporated to dryness. The residue was taken up in EtOAc (100 ml) , washed subsequently with H_2O (100 ml), with cold 1N HCl (50 ml), saturated $NaHCO_3$ and NaCl solution, then dried over Na_2SO_4 and evaporated *in vacuo*. The yellowish solid (**53**) was dissolved in anhydrous toluene (50 ml) and treated with AIBN (0.05 g, 0.3 mmole) and Bu_3SnH (6.4 ml, 24 mmole) under nitrogen atmosphere. The reaction mixture was kept at 80 °C for 6 h and after cooling to r.t. evaporated to dryness.The residue was taken up in $CHCl_3$ (100 ml) and washed with H_2O (4 x 100 ml) and again evaporated. The resulting oil was purified by silica-gel column chromatography (20 x3.5 cm) by elution first with n-hexane / ether and then with ether (650 ml) to give on evaporation *in vacuo* a colorless viscous oil.. Yield: 4.21 g (72 %). UV (MeOH): 238 (4.18), 202 (4.42). ^{1}H-NMR ($CDCl_3$) : 7.95 (d, H o-tol); 7.25 (d, H m-tol); 5.90 (d, H-C(1)); 4.80 (t, H-C(2)); 4.50 (m, H-C(5)); 2.43 (s, CH_3 (tol)); 2.20 (dd, H-C(2)); 1.80 (t, H-C(3)); 1.55, 1.35 (2s, CH_3-isopropylidene). Rf on SiO_2 in toluene / EtOAc (4:1)=0.41.

1,2-Di-*O*-acetyl-3-deoxy-5-*O*-(4-methylbenzoyl)-D-α,β-xylofuranose (55) A solution of **54** (4.8 g,16.4 mmole) in 75 % HCOOH (200 ml) was stirred at 50°C for 2 h the solvent was removed *in vacuo* and then the residue coevaporated with 1-butanol (100 ml) and toluene (100 ml). The colorless oil was dissolved in dry pyridine (85 ml) and acetylated with Ac_2O (55ml, 0.58 mol) at r.t. for 2 h. The precipitate was filtered off and washed with H_2O. The syrupy residue was taken up in $CHCl_3$ (100 ml) and washed with saturated $NaHCO_3$ and H_2O (100 ml). The organic phase was dried over Na_2SO_4, evaporated and the residue purified by CC (silica-gel, 22 x 3.5 cm) using n-hexane / ether (1:1) for elution. The product fraction gave on evaporation a colorless viscous oil. Yield: 4.47g (81 %). UV (MeOH): 238 (4.26), 202 (4.39). ^{1}H-NMR ($CDCl_3$) : 7.95 (d, H o-tol); 7.25 (d, H m-tol); 6.32 (d, H-C(1)); 5.38, 5.25 (2d, H-C(4)); 4.82 (m, H-C(2)); 4.60-4.30 (m, H-C(5)); 2.43 (s,CH_3(tol)); 2.40 - 2.20 (m, H-C(3)); 2.13, 2.00 (2s, CH_3CO). Rf on SiO_2 in n-hexane / ether (1:1) = 0.30, 0.34 (both isomers).

N^4,2′-Di-*N*,*O*-acetyl-3′-deoxy-5′-*O*-(4-methylbenzoyl)-cytidine (57). A mixture of N^4-acetylcytosine (**56**) (1.4 g, 8.92 mmole), hexamethyldisilazane (35 ml) and a catalytic amount of $(NH_4)_2SO_4$ was heated overnight under reflux. Evaporation *in vacuo* led to a brownish sirup which was then taken up in a solution of 1,2-di-*O*-acetyl-3-deoxy-5-*O*-(4-methylbenzoyl)-D-xylofuranose (**55**) (3 g, 8.92 mmole) in 1,2-dichloroethane (30 ml) and then treated with trimethylsilyl triflate (1.8 ml) in 1,2-dichloroethane (20 ml). After stirring at r.t. for 1.5 h, the reaction mixture was poured onto an ice cold saturated solution of $NaHCO_3$ and extracted with $CHCl_3$ (3 x 100 ml). The organic phase was dried over Na_2SO_4, evaporated and then the crude product purified by CC (silica-gel ,18 x 3.5 cm) with $CHCl_3$ / MeOH (98:2) to give on evaporation of the product fraction a colorless solid. Yield: 2.64g (70 %), mp 210-212°C. UV (MeOH): 271 (3.93), 230 (3.90), 212 (4.01). ^{1}H-NMR ($CDCl_3$): 8.10 (d, H-C(6)); 7.95 (2d, H o-tol); 7.32 (d, H m-tol); 7.30 (m, H-C(5)); 5.95 (s, H-C(1′)); 5.40 (b, H-C(2′)); 4.80, 4.58 (m, H-C(4′), H-C(5′)); 2.43 (s, CH_3(tol)); 2.20 (m, H-C-(3′)). Calc for $C_{21}H_{23}N_3O_7$ (429.4): C, 58.74; H, 5.40; N, 9.79. Found: C, 58.71; H, 5.65; N, 9.38. Rf on SiO_2 in $CHCl_3$ / MeOH (15:1) = 0.33.

2′,5′-Di-*O*-acetyl-3′-deoxyuridine (58). A solution of 3′-deoxyuridine (**1**) (2 g, 8.76 mmole) in Ac_2O (15 ml, 0.16 M) and few drops of pyridine was stirred at r.t. for 20 h and then the clear solution diluted with MeOH (15 ml) and concentrated to 3 - 5 ml.The light yellow solution was stirred in H_2O (20 ml), neutralised with

$NaHCO_3$ and kept overnight in the refrigerator. The precipitate was filtered off, washed with Et_2O (30 ml) and dried *in vacuo* at 60°C for 24 h to give of colorless crystals. Yield: 2.2 g (80%), mp 248-252°C. UV (MeOH): 259 (3.99), 203 (3.94). ^{1}H-NMR ($CDCl_3$): 9.28 (bs, NH); 7.42 (d, H-C(6)); 5.78 (s, H-C(1′)); 5.70 (d, H-C(5)); 5.32 (d, H-C(2′)); 4.35, 4.25 (2 dd, H-C(5′)); 4.03 (m, H-C(4′)); 2.30, 2.00 (m, H-C(3′)); 2.13 (s, CH_3CO). Calc for $C_9H_{13}N_3O_4$ (227.2): C, 47.57; H, 5.72; N, 18.49. Found: C, 47.41; H, 5.72; N, 18.21. Rf on SiO_2 in CH_2Cl_2 / EtOAc(1:1) = 0.22.

1-(2,5-Di-*O*-acetyl-3-deoxy-ß-D-*erythro*-pentofuranosyl)-4-(1,2,4-triazol-1-yl)-2(1H)-pyrimidone (59) A solution of the compound **58** (1.0 g, 3.2 mmole) in dry pyridine (20 ml) was treated with 1H-1,2,4-triazole (1.16 g 16.6 mmole) and o-chlorophenylphosphorodichloridate (1.32 ml, 8.1 mmole), and stirred at r.t. for 48 h. The dark brown reaction mixture was diluted with CH_2Cl_2 (100 ml), washed with 2 % $NaHCO_3$ (100 ml) solution, the organic phase dried over Na_2SO_4, and then the solvent removed *in vacuo* . The resulting residue was recrystallized from H_2O / MeOH to give colorless crystals. Yield: 0.79 g (69%), mp 198 - 201°C. UV (MeOH): 311 (3.91), 248 (4.15), 213 (4.26). ^{1}H-NMR ($CDCl_3$): 9.25 (s, H-C(3), triazole); 8.12 (s, H-C(5), triazole); 8.32 (d, H-C(6)); 7.06 (d, H-C(5)); 5.92 (s, H-C(1′)); 5.43 (m, H-C(2′)); 4.42, (s, H-C-(5′)); 4.67 (q, H-C(4′)); 2.25 - 2.15 (m, H-C(3′)); 2.15 (s, CH_3CO). Calc for $C_{15}H_{17}N_5O_6$ (363.3): C, 49.59; H, 4.72; N 19.28. Found: C, 49.92; H, 4.90; N, 18.74. Rf on SiO_2 in EtOAc = 0.40.

1-(2,5-Di-*O*-*tert*-butyldimethylsilyl-3-deoxy-ß-D-*erythro*-pentofuranosyl)-4-(1,2,4-triazol-1-yl)-2-(1H)-pyrimidone (60). Analogous to the proceeding procedure **35** (2.4 g, 5.25 mmole) and 1H-1,2,4-triazole (1.82 g, 26.3 mmole) in dry pyridine (20 ml) were treated with chlorophenylphosphorodichloridate (2.2 ml, 13,1 mmole) for 48 h at r.t. Purification was achieved by CC on silicagel (90 g, 3.5 x 23 cm) with a gradient of toluene / EtOAc (10:1 - 3:1) eluting the product in the last fraction. Evaporation gave a colorless amorphos solid. Yield: 1.84 g (70%), mp 48-52°C. UV (MeOH): 312 (3.91), 248 (4.12), 215 (4.22). ^{1}H-NMR ($CDCl_3$): 9.20 (s, H-C(3), triazole); 8.90 (d, H-C(6)); 8.10(s, H-C(5), triazole); 5.76 (s, H-C(1′)); 6.90 (d, H-C-5)); 4.62 (dd, H-C(2′)); 4.25, 3.75, (2d, H-C-(5′)); 4.42 (d, H-C(4′)); 1.98, 1.65 (td, dd,H-C(3′)); 0.90 (d, CH_3-C(tbdms)); 0.23, 0.12 (d, s, CH_3-Si(tbdms)). Calc for $C_{23}H_{41}N_4O_5Si_2$ (507.2): C, 54.40; H, 8.13; N, 13.79. Found: C, 54.48; H, 8.02; N, 14.07. Rf on SiO_2 in EtOAc = 0.84.

1-(5-*O*-Dimethoxytrityl-2-*O*-thexyldimethylsilyl-3-deoxy-ß-D-*erythro*-pentofuranosyl)-4-(1,2,4-triazol-1-yl)-(1H)-2-pyrimidone (61). A suspension of **29** (2.5 g, 3.72 mmole) and 1H-1,2,4,-triazole (1.28 g, 18.6 mmole) in dry pyridine (12 ml) was stirred with o-chlorophenylphosphorodichloridate (1.5 ml, 9.3 mmole) at r.t. for 3 days. The reaction mixture was diluted with CH_2Cl_2 (50 ml), washed with H_2O (50 ml) and with 2% aqueous $NaHCO_3$ solution, then the organic phase was dried over Na_2SO_4 followed by evaporation to dryness. The crude product was purified by CC (silica-gel, 18 x 4 cm) with toluene / EtOAc (3:1) to give after evaporation and drying in high vacuum at 40°C a colorless solid. Yield: 1.9 g (71 %), mp 78-81°C. UV (MeOH): 314 (3.87), 235 (4.45), 205 (4.81). ^{1}H-NMR ($CDCl_3$): 9.21 (s, H-C(3), triazole); 8.87 (d, H-C(6)); 8.05(s, H-C(5) triazole); 7.40-7.20 (m, H-C(DMTr)); 6.85 (d,H o-to OCH_3); 5.80 (s, H-C(1′)); 5.65 (dd, H-C(2′)); 4.50 (d, H-C(4′)); 3.80 (s, OCH_3); 3.70, 3.40 (2dd, H-C(5′)); 2.20-1.78 (td, dd, H-C-(3′)); 1.70-1.55 (m, H-C(tds)); 0.87(m, CH_3-C(tds)); 0.32, 0.15 (2s, CH_3Si-(tds)). Calc for $C_{40}H_{49}N_5O_6Si$ (723.9): C, 66.36; H, 6.82; N, 9.67. Found: C, 66.72; H, 6.95; N, 8.94. Rf on SiO_2 in toluene / EtOAc (3:7) = 0.68.

2′,5′-Di-*O*-acetyl-3′-deoxycytidine (62). A solution of **59** (0.5 g, 1.38 mmole) in 25 % NH_4OH (5 ml) and dioxane (25 ml) was stirred at r.t. for 2.5 h. The solvents were removed in *vacuo* to give an oily residue.Purification was achieved by CC (silica-gel , 20 x 2 cm) with $CHCl_3$ / MeOH (95:5) to give on evaporation of the product fraction a colorless solid. Yield: 0.32 g (75 %), mp 110-112°C. UV (MeOH): 269 (3.95), 239 (sh, 3.92), 202 (4.09). ^{1}H-NMR ($CDCl_3$): 7.60 (d, H-C(6)); 7.25 (d, NH_2); 5.75 (s, H-C(1′)); 5.72 (d, H-C(5)); 5.17 (d, H-C(2′)); 4.25, 4.15 (2dd, H-C-(5′)); 4.36 (m, H-C(4′)); 2.35-1.95 (m, H-C-(3′)); 2.05 (s, CH_3CO). Calc for $C_{13}H_{17}N_3O_6$ (311.3): C, 50.16; H, 5.50; N, 13.50. Found: C, 50.02; H, 5.43; N, 13.22. Rf on SiO_2 in CH_2Cl_2 / MeOH (9:1) = 0.42.

2′,5′-Di-*O*-*tert*-butyldimethylsilyl-3′-deoxycytidine (63). A solution of **60** (0.75 g, 1.48 mmole) in conc. ammonia / dioxane (25 ml, 5:1) was stirred at r.t. overnight, then evaporated and the residue was treated with CH_2Cl_2 (30 ml) and H_2O (30 ml). The organic phase was dried over $MgSO_4$ and after partial evaporation to a small volume put onto a silica-gel column (40 g, 2.5 x 25 cm) for chromatography with CH_2Cl_2 / MeOH (95:5) leading to a colorless amorphous solid. Yield: 0.51 g (76%), mp 106-112°C. UV (MeOH): 273 (3.93), 235 (sh, 3.86), 216 (sh, 4.00), 203 (4.28). ^{1}H-NMR ($CDCl_3$): 8.18 (d, H-C(6)); 5.73 (s, H-C(1′));

5.51 (d, H-C(5)); 4.45(dd, H-C(2′)); 4.32 (d, H-C(4′)); 4.16, 3.70 (2dd, H-C(5′)); 1.92, 1.49 (dd, td, H-C(3′)); 0.88 (d, CH_3-C(tbdms)); 0.17-0.09 (s, d, CH_3-Si(tbdms)). Calc for $C_{21}H_{41}N_3O_4Si_2$ (455.7): C, 55.34; H, 9.07; N, 9.22. Found: C, 55.05; H, 9.05; N, 9.13. Rf on SiO_2 in CH_2Cl_2 / MeOH (95:5) = 0.34.

5′-*O*-Dimethoxytrityl-2′-*O*-thexyldimethylsilyl-3′-deoxycytidine (64). A solution of **61** (1.5 g,2.07 mmole) in 25 % NH_4OH / dioxane solution (1:5, 60 ml) was stirred at r.t. for 24 h, then evaporated *in vacuo* to an oily residue which was purified by silica-gel column chromatography (18 x 3.5 cm) with CH_2Cl_2 / MeOH (95 / 5). The main fraction gave an amorphous colorless solid. Yield: 1.2 g (86 %), mp 126-131°C. UV (MeOH): 274 (3.99), 233 (4.41), 204 (4.78). ^{1}H-NMR (DMSO-D_6): 7.80 (d, H-C(6)); 7.26 (bs,NH_2); 7.40-7.20 (m, H-C(DMTr)); 6.82 (d, H o-to OCH_3); 5.65 (s, H-C(1′)); 4.35 (m, H-C(2′)); 4.25 (d, H-C(4′)); 3.80 (s, OCH_3); 3.40-3.10 (q, H-C(5′)); 2.05, 1.70 (dd, td, H-C-(3′)); 1.65-1.55 (q, H-C(tds)); 0.85(q, CH_3-C(tds)); 0.13, 0.08 (2s, CH_3Si-(tds)). Calc for $C_{38}H_{48}N_3O_6$ Si (670.9): C, 68.03; H, 7.21; N, 6.26. Found: C, 68.41; H, 7.40; N, 5.54. Rf on SiO_2 in CH_2Cl_2 / MeOH (9:1) = 0.91.

5′-*O*-Dimethoxytrityl-3′-deoxycytidine (65). A solution of **64** (1.8 g, 2.68 mmole) in dry THF (6 ml) was stirred with TBAF.$3H_2O$ (1.5 g, 4.75 mmole) and kept at r.t. for 24 h. The solvent was removed in *vacuo* and the crude product was purified by CC (silica-gel, 30 x 3.5 cm) with CH_2Cl_2 / MeOH (95:5, 500 ml). The product fraction gave a colorless foam. Yield: 1.25g (88 %), m.p. 178-182°C. UV (MeOH): 273 (3.98), 232 (4.38), 204 (4.75). ^{1}H-NMR (DMSO-D_6): 7.80 (d, H-C(6)); 7.40-7.20 (m, H-C(DMTr)); 7.08 (bd, NH_2); 6.85 (d, H o to OCH_3); 5.70 (s, H-C(1′)); 5.52 (d, HO-C(2′)); 4.40 (m, H-C(2')); 4.12 (m, H-C(4′)); 3.70 (s, OCH_3); 3.30, 3.20 (2 dd, H-C(5′)); 2.00, 1.72 (dd, td, H-C-(3′)). Calc for $C_{30}H_{31}N_3O_6 \cdot 0.5\ H_2O$ (538.6): C, 66.90; H, 5.99; N, 7.80. Found: C, 67.08; H, 6.00; N, 7.33. Rf on SiO_2 in CH_2Cl_2 / MeOH (9:1) = 0.48.

5'-*O*-Dimethoxytrityl-N^4-[2-(4-nitrophenyl)ethoxycarbonyl]-2'-*O*-thexyldimethylsilyl-3'-deoxycytidine (66). A solution of **64** (1.0 g, 1.49 mmole) in CH_2Cl_2 was treated with 1-methyl-3-(4-nitrophenyl)ethoxycarbonyl-imidazolium chloride (0.61 g, 1.94 mmole) and stirred for 1 h at r.t. It was diluted with CH_2Cl_2 (50 ml), washed with a solution of 5% $NaHCO_3$, the organic phase was dried over Na_2SO_4, evaporated to dryness and the residue put onto to a silica-gel

column (2.5 x 35 cm) for chromatography with first with CH_2Cl_2 and second with CH_2Cl_2 / MeOH (49:1). The product fraction was evaporated again, then the residue was dissoved in little ether and dropped into n-hexane (200 ml) with stirring to give an amorphous solid. Yield: 1.06 g (82%), mp 101-106°C. UV (MeOH): 281 (4.22), 236 (4.50), 203 (4.83). ^{1}H-NMR ($CDCl_3$): 8.52 (d, H-C(6)); 8.18 (d, o-H (npeoc)); 7.72 (bs, H-N); 7.2-7.4 (m, m-H(npeoc), H-C(DMTr)); 6.82 (d, o-H(DMTr)); 5.75 (s, H-C(1')); 4.38 (m, H-C(2'), α-CH_2(npeoc)); 3.80 (s, OCH_3)); 3.65, 3.30 (m, H-C(5')); 3.07 (t, ß-CH_2 (npeoc));2.05 (m, H-C(3')); 1.70 (dd, H-C(3')); 1.65 (m, H-C-(tds)); 0.85 (m, H_3C-C(tds)); 0.30, 0.15 (2s, H_3C-Si).
Calc. for $C_{47}H_{57}N_4O_{10}Si$ (866.1): C, 65.18; H, 6.63; N, 6.47. Found: C, 64.76, H, 6.51; N, 6.46. Rf on SiO_2 in CH_2Cl_2/MeOH (95:5) = 0.52.

5′-*O*-Dimethoxytrityl-N^4-2-(4-nitrophenyl)ethoxycarbonyl-3′-deoxycytidine (67). a) A solution of 5′-*O*-dimethoxytrityl-3′-deoxycytidine (**65**) (1.8 g, 3.4 mmole) in dry DMF (30 ml) was stirred with 3-methyl-1-[2-(4-nitrophenylethoxycarbonyl]-imidazolium chloride (1.27 g, 4.08 mmole) for 2h at r.t. The solvent was removed in high vacuum at 40°C, the residue was taken up in CH_2Cl_2 (50 ml) and washed with 5% $NaHCO_3$ solution (50 ml). The organic phase was dried over Na_2SO_4 and after removal of the solvent the residue was dissolved in CH_2Cl_2 and applied onto a silica-gel column (20 x 3.5 cm) and product **67** was eluted with CH_2Cl_2 / MeOH (98:2, 500 ml) The residue after evaporation was dissolved in CH_2Cl_2 (5 ml) and added dropwise into n-hexane / ether (1:1) with vigorous stirring to give an amorphous solid. Yield: 2.19 g (89 %), mp 172°C (sintering), 188-190°C (decomp.). UV (MeOH): 275 (4.26), 235 (4.55), 211 (4.70). ^{1}H-NMR ($CDCl_3$): 8.42 (d, H-C(6)); 8.40 (bs, H-N); 8.18 (d , o-H(npe)); 7.42-7.20 (m, H-C(DMTr)); 7.12, 7.03 (2bs, NH_2); 6.93 (d, H-C(5)); 6.83 (d, o-H to OCH_3); 5.78 (s ,H-C (1')); 4.54 (bs , HO-C(2′)); 4.70 (m, H-C(2')); 4.45 (m, H-C(4′)); 4.45 (t, α-CH_2(npe)); 3.70 (s, OCH_3); 3.60, 3.30 (2dd, H-C(5′)); 3.11 (t, ß-CH_2(npe)); 2.22-1.92 (m, H-C-(3′)). Rf on SiO_2 in $CHCl_3$ / MeOH (95:5) = 0.47.
b) Compound **68** (0.7 g, 1.7 mmole) was twice coevaporated with dry pyridine (10 ml), then dissolved in the same solvent (20 ml) and after addition of dimethoxytrityl chloride (0.85 g, 2.5 mmole) was stirred for 3 h at r.t. The reaction was stopped by addition of MeOH (5 ml), diluted by CH_2Cl_2 (50 ml) and then washed with sodium phosphate buffer (pH 7, 50 ml). The organic phase was dried over $MgSO_4$, evaporated to dryness and coevaporated twice with dry toluene (30 ml). The resulting solid

foam was purified by silica-gel column chromatography (30 g, 2 x 30 cm) with CH_2Cl_2 / MeOH (49:1). The product fraction was evaporated and the residue reprecipitated by dissolving in little CH_2Cl_2 and dropwise addittion into n-hexane (250 ml) with stirring to give an amorphous powder. Yield: 0.93 g (76%). The material is chromatographically and spectroscopically identical with product **67** from procedure a).

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl)-3'-deoxycytidine (68). A mixture of 3'-deoxycytidine (**2**) (0.61 g, 2.5 mmole), hexamethyldisilazane (HMDS) (7.5 ml) and dioxane (97.5 ml) was heated under reflux with exclusion of moisture for 12 h.The solution was evaporated to dryness, coevaporated with dry toluene, the residue was dissolved in CH_2Cl_2 (25 ml), 1-methyl-3-[2-(4-nitrophenyl)-ethoxycarbonyl]imidazolium chloride (1.02 g, 3.3 mmole) was added, stirred overnight and then evaporated to dryness. The solid was dissolved in MeOH (25 ml), triethylamine (5 ml) added and again stirred for 12 h at r.t. forming a precipitate which was collected and dried *in vacuo* to give a colorless powder. Yield: 0.85 g (81%), mp 116-118°C. UV (MeOH): 280 (4.15), 241 (4.20), 213 (4.37). ^{1}H-NMR (DMSO-D_6): 8.45 (d, H-C(6)); 8.13 (d, o-H(npe)); 7.55 (d, m-H(npe)); 6.90 (d, H-C(5)); 5.60 (m, H-C(1'), H-O(2')); 5.13 (t, H-O(5')); 4.34 (t, α-CH_2 (npe)); 4.15 (m, H-C(4')); 3.80, 3.55 (2 dd, H-C(5')); 3.05 (t, ß-CH_2(npe)); 1.85, 1.65 (2 m, H-C(3')). Rf on SiO_2 in $CHCl_3$ / MeOH (9:1) = 0.84.

N^4-Benzoyl-3'-deoxycytidine (69). A mixture of 3'-deoxycytidine (**2**) (0.454 g, 2 mmole) and benzoic anhydride (2.26 g, 10 mmole) was heated in dry MeOH (50 ml) for 4 h. After 2 h another portion of benzoic anhydride (1.13 g, 1 mmole) was added to complete the reaction. It was evaporated to dryness, the residue was treated with H_2O (30 ml) and ether (3 x 50 ml), the solid was collected and recrystallized from H_2O (15 ml) to give colorless crystals. Yield: 0.51 g (77%), mp 206-208°C. UV (MeOH): 303 (4.13), 257 (4.45), 202 (4.44). ^{1}H-NMR (DMSO-D_6): 8.65 (d, H-C(6)); 7.97 (m, o-H(bz); 7.5 (m, m,p-H(bz)); 7.30 (d, H-C(5)); 5.68 (s, H-C(1')); 5.67 (d, H-O(2')); 5.20 (t, H-O(5')); 4.38 (m, H-C(2')); 4.20 (m, H-C(4')); 3.85, 3.65 (2 dd, H-C(5')); 1.90, 1.70 (2 m, H-C(3')).

Calc. for $C_{16}H_{17}N_3O_5 \cdot 0.5\ H_2O$ (340.3): C, 56.47; H, 5.33; N, 12.35.
Found: C, 56.84; H, 5.22; N, 12.16. Rf on SiO_2 in $CHCl_3$ / MeOH (9:1) = 0.5.

N^4-Benzoyl-5'-*O*-dimethoxytrityl-3'-deoxycytidine (70).

A solution of **69** (0.248 g, 0.75 mmole) in dry pyridine (10 ml) was treated with dimethoxytrityl chloride (0.34 g, 1 mmole) and stirred for 2 h. The reaction was stopped by addition of MeOH (5 ml), then diluted with CH_2Cl_2 (50 ml) and washed with phosphate buffer (pH 7, 50 ml). The organic phase was dried over Na_2SO_4 evaporated and the residue was purified by silica-gel column chromatography (15 g, 1.5 x 40 cm) subsequently with CH_2Cl_2 (300 ml) and CH_2Cl_2 / MeOH (49:1). The product fraction was evaporated and then the residue reprecipitated from CH_2Cl_2 by dropwise addition into n-hexane with stirring giving an amorphous solid. Yield: 0.37 g (78%), mp 150-153°C. UV(MeOH): 303 (4.22), [256] (4.56), 235 (4.69), 204 (5.06). ^{1}H-NMR ($CDCl_3$): 8.75 (bs, H-N); 8.42 (d, H-C(6)); 7.88 (m, o-H (bz)); 7.53 (m, m,p-H (bz)); 7.45-7.20 (m, H-C(DMTr)); 6.85 (d, o-H to OCH_3)); 5.70 (d, H-C (1')); 4.70 (m, H-C(2')); 4.52 (bs, H-C(4')); 3.70 (s, OCH_3); 3.54, 3.30 (2 d, H-C(5')); 2.22, 2.05 (2 m, H-C(3')). Calc. for $C_{37}H_{35}N_3O_7 \cdot 0.5\ H_2O$ (642.7): C, 69.15; H, 5.64; N, 6.54. Found: C, 69.13, H, 5.64; N,6.56. Rf on SiO_2 in $CHCl_3$ / MeOH (95:5) = 0.60.

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Received 12/6/93
Accepted 1/10/94