Synthesis of 4′-*C*-alkylated-5-iodo-2′-deoxypyrimidine nucleosides

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Dedicated to Professor Richard R. Schmidt on the occasion of his 78th anniversary

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Abstract
Starting from available ribose-building blocks, the 4′-*C*-methyl-, 4′-*C*-ethyl- and the new 4′-*C*-propyl-substituted deoxyuridines were synthesized. Afterwards we converted 4′-*C*-alkylated-2′-deoxyuridines into the corresponding 4′-*C*-alkylated-5-iodo-2′-deoxyuridines **3a-c** and those in turn into the 4′-*C*-alkylated-5-iodo-2′-deoxycytidines **4a-c**.

Keywords: DNA replication, nucleoside analogues, 4′-*C*-alkylation, antiviral agents, carbohydrate, halogenation

Introduction

For a long time, chemically modified nucleoside analogues have been prominent life-saving drugs. This pharmacologically diverse family, which contains structural features of the skeleton of natural nucleosides, is used for treatment of cancer and viral infections.[1] Along with HIV (human immunodeficiency virus) and HV (hepatitis virus), HSV (herpes simplex virus) and VZV (varicella-zoster virus) are prominent pathogens. In addition to acyclovir and bromovinyldeoxyuridine, HSV and VZV are treated with the approved antiviral drug 2′-deoxy-5-iodouridine **1** (Figure 1).[1a,d,f,i,2] Compound **1**, marketed for example as Stoxil®, Herples®, Virodox® and Herpid®, targets the viral DNA replication. Thereby, **1** acts as an antagonist of thymidine, its natural nucleoside counterpart, and targets the thymidylate phosphorylase and the workhorse of the DNA replication, the viral DNA polymerase.[1a,f-h,2] As a general rule, 5-substituted deoxycytidines are appreciably more selective, but equally or slightly less potent in their anti-HSV activity than the accordant 5-substituted deoxyuridines.[1a,3] Thus, the antiviral spectrum of 2′-deoxy-5-iodocytidine **2** (Figure 1), launched as Cuterherpes® and Cebeviran®, is similar to **1** to which drug **2** is converted by enzymatic deamination.[1a,3a,c,4]

In addition to 5-halopyrimidine nucleosides, 4′-*C*-modified nucleosides gained significant interest, because several analogues of this class exhibited antiviral activity.[5] 4′-*C*-modified nucleosides act also as nucleoside reverse transcriptase inhibitors (NRTIs)[5g,h,6] and showed even activity against multi-drug resistant virus strains.[5c,6c] The evolution of viral resistance boosts the urgent requirements for new effective drugs and therapies against viral infections.[7] Because there is a great need for the development of novel medicines[7,8] and consequently also for NRTIs, we developed a synthetic route for 4′-*C*-alkylated-5-iodo-2′-deoxyuridines **3a-c** and 4′-*C*-alkylated-5-iodo-2′-deoxycytidines **4a-c**. We recently designed and synthesized a series of 4′-*C*-modified nucleosides and nucleotides.[6b,9] In this study we combined our knowledge with a literature known synthesis strategy for **1**[10] and **12a**[5b] to synthesize the compounds **3a-c** and converted those in turn into the 4′-*C*-alkylated-5-iodo-2′-deoxycytidines **4a-c**. These novel nucleoside entities are of great interest, because they combine the structural features of the marketed drug **1** or **2**, and 4′-*C*-modified nucleosides in one small molecule (Figure 1).

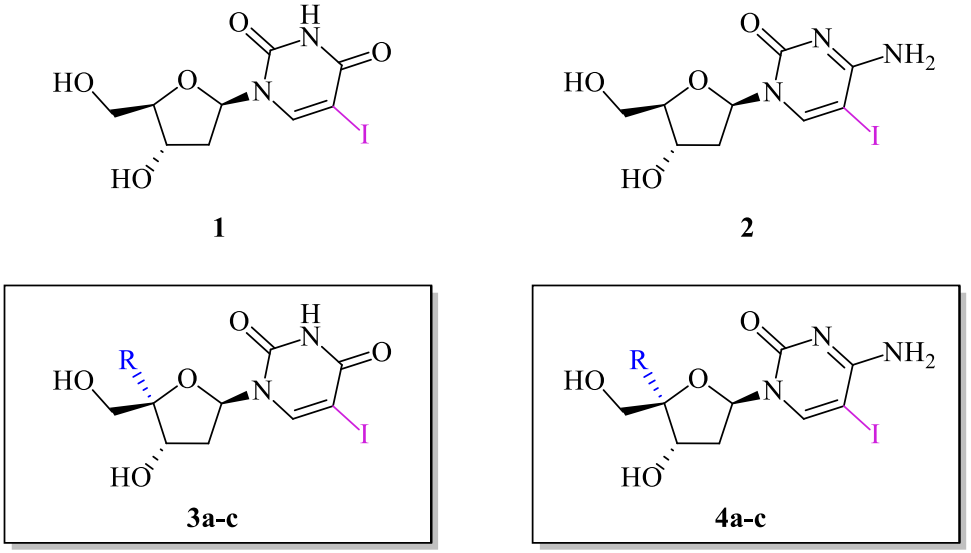
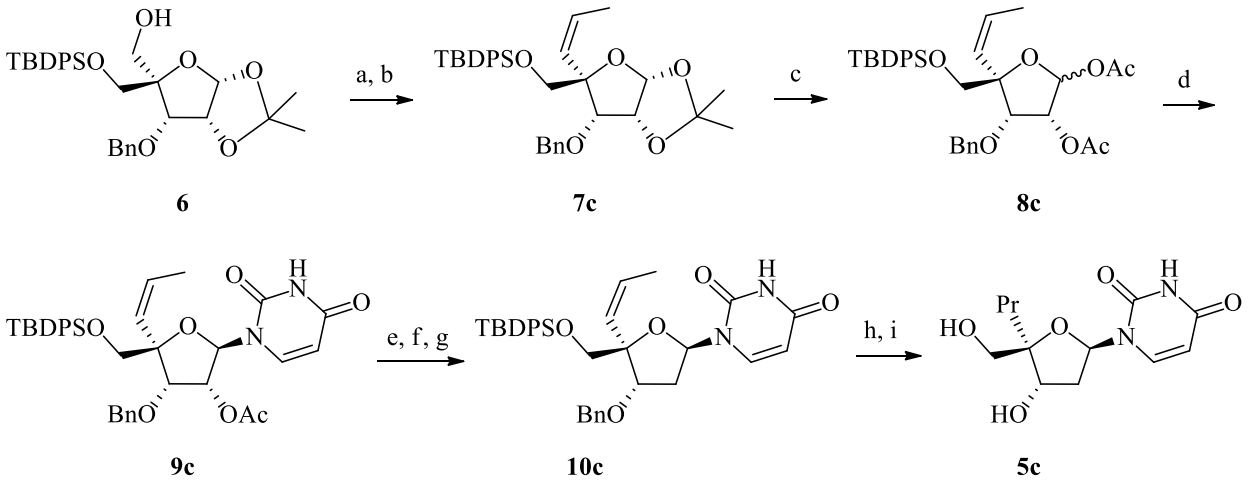


Figure 1. Chemical structures of 2′-deoxy-5-iodouridine **1**, 2′-deoxy-5-iodocytidine **2**, 4′-*C*-alkylated-5-iodo-2′-deoxyuridines **3a-c**, and 4′-*C*-alkylated-5-iodo-2′-deoxycytidines **4a-c**.

Results and Discussion

It is noteworthy to mention that 4′-*C*-modification of nucleosides always contain the generation of quaternary carbon centers including the restraints associated with the respective chemistry. To our knowledge, three main methodologies have been evolved for the synthesis of 4′-*C*-modified nucleosides. In methodology one a 4′-*C*-branch is attached to 2′-*C*-deoxynucleosides;[11]

methodology two involves the asymmetric SAMP/RAMP-hydrazone α-alkylation and diastereoselective nucleophilic 1,2-addition;[12] and in methodology three, suitable 4-*C*-ribose glycosyl donors are synthesized for the nucleoside formation using Vorbrüggen`s method.[11b,13] Recently, we reported nine-steps reaction sequences (methodology three) for 4′-*C*-methyl-, 4′-*C*-ethyl-substituted deoxyuridines **5a-b**.[9f] According to these findings we obtained **5a-b** and investigated the synthesis of 2′-deoxy-4′-*C*-propyluridine **5c** (Scheme 1).



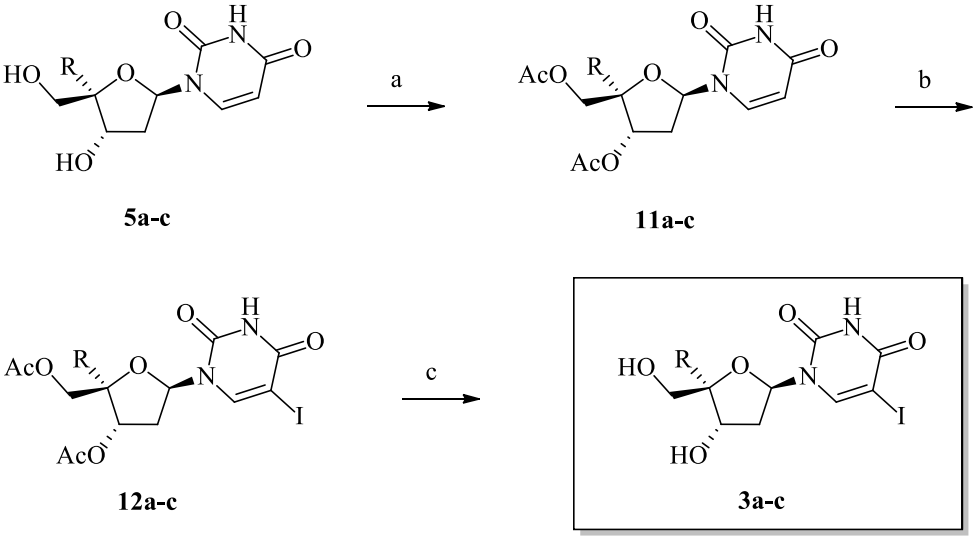
Scheme 1. Synthesis of 2′-deoxy-4′-*C*-propyluridine **5c.** *Reagents and conditions:* a) DMP, CH_2Cl_2, r.t., 91%;[9f] b) $EtPPh_3Br$, *t*-BuOK, THF, r.t., 84%; c) AcOH, Ac_2O, H_2SO_4, r.t., 64%; d) uracil, BSA, TMSOTf, MeCN, reflux, 71%; e) NaOMe, MeOH, r.t.; f) PhOCSCl, DMAP, MeCN, r.t.; g) *n*-Bu_3SnH, AIBN, toluene, reflux, 83% over 3 steps; h) 10% Pd/C, H_2, EtOH, r.t.; i) TBAF, THF, r.t., 65% over 2 steps.

Here our synthesis strategy of 4′-*C*-modified nucleosides starts with the selective silylated 4-*C*-hydroxymethyl substituted ribose building block **6**.[14] After conversion of **6**, with Dess-Martin periodinane (DMP)[15] to the corresponding aldehyde, Wittig reaction allowed us C-C-bond formation to yield the 4-*C*-(*Z*)-prop-1-enyl ribose analogue **7c**. Bulky alkoxides have previously been reported to be the bases of choice in Wittig reactions involving sterically encumbered substrates[9c,16] and so we performed the reaction with potassium *tert*-butoxide (*t*-BuOK) and ethyltriphenylphosphonium bromide ($EtPPh_3Br$) as C2-synthon. By protection group manipulations we converted **7c** to the substituted ribosyl acetate **8c**.

Next, according to Vorbrüggen glycosylation the nucleobase uracil was fused with the 4-*C*-modified glycosyl donor **8c**.[13] Reaction with bis(trimethylsilyl)uracil, which is formed as an intermediate by silylation of uracil with bis(trimethylsilyl)acetamide (BSA), and trimethylsilyl triflate (TMSOTf) as catalyst gave stereoselectively the β-configurated 4′-*C*-(*Z*)-prop-1-enyl substituted nucleoside **9c**. After deacetylation with sodium methoxide (NaOMe) and reaction with phenyl chlorothionoformate (PhOCSCl) in the presence of 4-dimethylaminopyridine

(DMAP) we obtained the thiocarbonate ester, which was subsequently reduced with tributyltin hydride (*n*-Bu_3SnH) to the 2′-deoxyuridine analogue **10c**. Catalytic hydrogenation with Pd/C followed by desilylation with tetrabutylammonium fluoride (TBAF) furnished the 2′-deoxy-4′-*C*-propyluridine **5c** (Scheme 1).

After we had the analogues **5a-c** in hand, we assigned a literature known synthesis strategy for **1**[10] and **12a**[5b] to our routes. We acetylated **5a-c** to yield compounds **11a-c**. Diammonium cerium (IV) nitrate (CAN) mediated iodination (**12a-c**), followed by deprotection furnished in good to excellent yields the 4′-*C*-methyl-, 4′-*C*-ethyl- and 4′-*C*-propyl-5-iodo-2′-deoxyuridine analogues **3a-c** (Scheme 2).

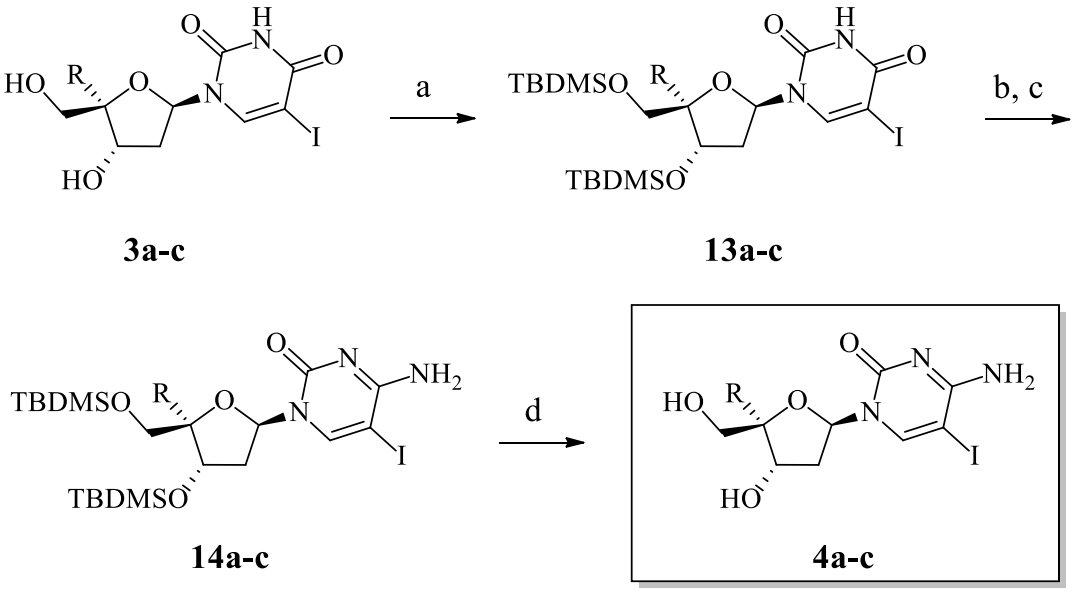


5a-c **11a-c** **12a-c** **3a-c**

R: Me (**a**), Et (**b**), *n*-Pr (**c**)

Scheme 2. Synthesis of 2′-deoxy-5-iodouridine analogues **3a-c.** *Reagents and conditions:* a) Et_3N, Ac_2O, DMAP, MeCN, r.t., 63% (**11a**), 74% (**11b**), 93% (**11c**); b) I_2, CAN, MeCN, reflux, 89% (**12a**), 98% (**12b**), 89% (**12c**); c) NaOMe, MeOH, r.t., 91% (**3a**), 97% (**3b**), 97% (**3c**).

Our convergent synthetic strategy to synthesize the 4′-*C*-alkylated-5-iodo-2′-deoxycytidines **4a-c** was based on the conversion of uridine or thymidine derivatives into the respective cytidine analogues.[9e,17] Thus, we silylated **3a-c** with *tert*-butyldimethylsilyl chloride (TBDMSCl) in the presence of imidazole to yield compounds **13a-c**. Afterwards **13a-c** was converted into **14a-c** by treatment with the 2,4,6-triisopropylbenzenesulfonyl chloride (TPSCl)-Et_3N-DMAP system, and followed by aminolysis with ammonium hydroxide (NH_4OH) to generate the exocyclic amino function. Finally, desilylation with TBAF yielded the 4′-*C*-methyl-, 4′-*C*-ethyl- and 4′-*C*-propyl-5-iodo-2′-deoxycytidine analogues **4a-c** (Scheme 3).



R: Me (**a**), Et (**b**), *n*-Pr (**c**)

Scheme 3. Synthesis of 2′-deoxy-5-iodocytidine analogues **4a-c.** *Reagents and conditions:* a) TBDMSCl, imidazole, DMF, r.t., 81% (**13a**), 90% (**13b**), 91% (**13c**); b) TPSCl, DMAP, Et_3N, MeCN, r.t.; c) 28% NH_4OH, 78% (14a), 77% (**14b**), 80% (**14c**) over 2 steps; d) TBAF, THF, r.t., 92% (**4a**), 89% (**4b**), 81% (**4c**).

Conclusions

In conclusion, we synthesized, starting from the available ribose-building block **6**, the 4′-*C*-methyl-, 4′-*C*-ethyl- and the new 4′-*C*-propyl-substituted deoxyuridines **5a-c**. Afterwards we synthesized starting with **5a-c** the corresponding 4′-*C*-alkylated-5-iodo-2′-deoxyuridines **3a-c** and converted those into the 4′-*C*-alkylated-5-iodo-2′-deoxycytidines **4a-c**. The novel nucleoside analogues **3a-c** and **4a-c** are 4′-*C*-alkylated derivatives of the approved antiviral drugs 2′-deoxy-5-iodouridine **1** and 2′-deoxy-5-iodocytidine **2**. Due to the fact, that several derivatives of 4′-*C*-modified nucleosides also showed antiviral activity, the here reported molecules are generally of great interest because of their potential antiviral activities. Additionally the herein reported molecules could act as useful synthetic building blocks for further 4′-*C*-modified nucleosides.

Experimental Section

General. All reagents are commercially available and used without further purification. MeCN was dried by distillation from CaH_2. All other solvents are dried over molecular sieves and used directly without further purification. All reactions were conducted under exclusion of air and

moisture. Petroleum ether (PE) used had a b.p. range of 35-80 °C. NMR spectra: Bruker Avance III 400 MHz spectrometer. ^{1}H and ^{13}C chemical shifts are reported relative to the residual solvent peak. Flash chromatography: Merck silica gel G60. TLC: Merck precoated plates (silica gel 60 F_{254}). ESI-IT: Bruker Esquire 3000 plus. HRMS: Bruker Daltronics micrOTOF-Q II ESI-Qq-TOF. The reported yield refers to the analytically pure substance and is not optimized. Building block **6** was synthesized according to literature.[14] Compounds **5a-b** were prepared as we described recently.[9f]

3-*O*-Benzyl-5-(*O*-*tert*-butyldiphenylsilyl)-4-*C*-(*Z*)-prop-1-enyl-1,2-*O*-isopropylidene-α-D-ribofuranose (**7c**). To a solution of compound **6** (20.0 g, 36.4 mmol) in CH_2Cl_2 (55 mL), was added DMP[15] (20.0 g, 47.2 mmol) and the mixture was stirred at r.t. over night. After completion of the reaction, the mixture was quenched with aq sat. $NaHCO_3$ solution (60 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (4×20 mL). The organic layers were combined, dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 1:9) as eluent to give the aldehyde intermediate as a white solid (yield 17.78 g, 91%).[9f]

Next, $EtPPh_3Br$ (23.43 g, 63.1 mmol) and *t*-BuOK (10.78 g, 96.0 mmol) were suspended in THF (100 mL) and stirred at r.t. for 2 h. Then the synthesized aldehyde (15.00 g, 27.4 mmol) in THF (20 mL) was added and stirring was continued for 17 h. The reaction mixture was quenched with aq sat. $NaHCO_3$ solution (40 mL) and extracted with CH_2Cl_2 (3×60 mL). The combined organic layers were dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 1:6) to give **7c**. Yellow gum, yield 12.86 g, 84%, R_f 0.55 (EtOAc-PE, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (s, 9H), 1.29 (s, 3H), 1.51 (s, 3H), 1.65 (dd, *J* 7.2, 1.7 Hz, 3H), 3.49 (d, *J* 11.7 Hz, 1H), 3.69 (d, *J* 11.7 Hz, 1H), 4.36 (d, *J* 4.6 Hz, 1H), 4.60 (dd, *J* 4.6, 3.9, 1H), 4.67 (d, *J* 12.3 Hz, 1H), 4.83 (d, *J* 12.3 Hz, 1H), 5.52 (dq, *J* 11.9, 7.2 Hz, 1H), 5.74 (d, *J* 3.9 Hz, 1H), 5.80 (dd, *J* 11.8, 1.7 Hz, 1H), 7.25-7.42 (m, 11H), 7.60-7.68 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.79, 19.48, 25.58, 26.48, 27.01, 64.58, 72.76, 78.37, 86.54, 100.23, 103.91, 113.36, 126.97, 127.76, 127.87, 128.03, 128.05, 128.63, 128.65, 129.81, 129.81, 133.27, 133.94, 135.02, 135.75, 136.09, 138.21. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{34}H_{42}O_5Si$: 581.3; found: 581.1.

1,2-Di-*O*-acetyl-3-*O*-benzyl-5-(*O*-*tert*-butyldiphenylsilyl)-4-*C*-(*Z*)-prop-1-enyl-α,β-D-ribofuranose (**8c**). To a solution of compound **7c** (12.80 g, 22.9 mmol) in a mixture of AcOH (208 mL) and Ac_2O (32.4 mL, 247.7 mmol) was added concd H_2SO_4 (200 μL) and the mixture was stirred for 24 h at r.t. After completion of the reaction, the mixture was concentrated and coevaporated with toluene (2 × 100 mL). The residue was diluted with CH_2Cl_2 (100 mL) and washed with aq sat. $NaHCO_3$ (25 mL) and demin. H_2O (25 mL), dried over $MgSO_4$, concentrated, and purified by silica gel column chromatography (EtOAc-PE, 1:4) to give **8c**. Yellow gum, yield 8.91 g, 64%, R_f 0.68 (EtOAc-PE, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03 (s, 9H), 1.74 (dd, *J* 3.8, 1,5 Hz, 3H), 1.84 (s, 3H), 2.05 (s, 3H), 3.59 (d, *J* 11.4 Hz, 1H), 3.74 (d, *J* 11.4 Hz, 1H), 4.52 (d, *J* 11.6 Hz, 1H), 4.62 (d, *J* 4.9 Hz, 1H), 4.67 (d, *J* 11.6 Hz, 1H), 5.36 (d, *J* 4.9 Hz, 1H), 5.49-5.60 (m, 2H), 6.21 (s, 1H), 7.25-7.42 (m, 11H), 7.60-7.72 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ

14.45, 19.58, 20.98, 21.17, 27.05, 65.07, 73.55, 74.82, 76.69, 88.78, 98.24, 100.20, 126.35, 127.82, 127.86, 127.96, 128.01, 128.50, 128.60, 129.86, 129.97, 133.40, 135.01, 135.79, 135.84, 138.02, 169.71, 170.20. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{35}H_{42}O_7Si$: 625.3; found: 625.1.

2′-*O*-Acetyl-3′-*O*-benzyl-5′-(*O*-*tert*-butyldiphenylsilyl)-4′-*C*-(*Z*)-prop-1-enyluridine (**9c**). Compound **8c** (7.63 g, 12.8 mmol) and uracil (2.87 g, 25.6 mmol) were solved in MeCN (40 mL) and *N*,*O*-bis(trimethylsilyl)acetamide (18.4 mL, 76.8 mmol) was added. The mixture was refluxed for 1 h and after cooling to r.t. Me_3SiOTf (3.0 mL, 16.64 mmol) was added. After refluxing again for 1 h the mixture was quenched with aq sat. $NaHCO_3$ solution (10 mL), evaporated and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 3:7) to give **9c**. White foam, yield 5.72 g, 71%, R_f 0.13 (EtOAc-PE, 1:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07 (s, 9H), 1.69 (dd, *J* 7.1, 1.6 Hz, 3H), 2.07 (s, 3H), 3.66 (d, *J* 11.9 Hz, 1H), 3.90 (d, *J* 11.9 Hz, 1H), 4.44 (s, 1H), 4.44 (d, *J* 10.5 Hz, 1H), 4.64 (d, *J* 11.2 Hz, 1H), 5.23 (dd, *J* 8.1, 2.3 Hz, 1H), 5.33 (dd, *J* 6.1, 2.7 Hz, 1H), 5.48 (dd, *J* 11.9, 1.7 Hz, 1H), 5.57-5.69 (m, 1H), 6.07 (d, *J* 2.7 Hz, 1H), 7.25-7.46 (m, 11H), 7.53-7.65 (m, 4H), 7.68 (d, *J* 8.2 Hz, 1H), 8.15 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.05, 19.41, 20.74, 27.04, 64.13, 73.87, 74.19, 75.81, 77.21, 87.11, 87.98, 100.01, 102.63, 124.43, 127.72, 127.95, 128.01, 128.03, 128.48, 130.08, 130.12, 130.18, 132.13, 132.94, 135.34, 135.62, 137.31, 139.77, 149.75, 162.42, 169.94. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{37}H_{42}N_2O_7Si$: 677.3; found: 677.9.

3′-*O*-Benzyl-5′-(*O*-*tert*-butyldiphenylsilyl)-2′-deoxy-4′-*C*-(*Z*)-prop-1-enyluridine (**10c**). Compound **9c** (5.88 g, 9.0 mmol) was solved in MeOH (100 mL) and NaOMe (0.73 g, 13.5 mmol) was added. The mixture was stirred at r.t. for 2 h. After completion of the reaction, the mixture was treated with aq concd tartaric acid (50 mL) and extracted with CH_2Cl_2 (3×80 mL). The combined organic layers were dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 4:1). The resulting compound was dissolved in MeCN (65 mL), DMAP (3.31 g, 27.0 mmol) and PhOCSCl (1.5 mL, 10.8 mmol) were added and the mixture was stirred at r.t. for 1 h. After completion of the reaction the mixture was concentrated, diluted in CH_2Cl_2 (60 mL), washed with aq 5% citric acid (30 mL) and demin. H_2O (20 mL). The aqueous layer was extracted with CH_2Cl_2 (50 mL), the combined organic layers dried over $MgSO_4$ and evaporated. To a solution of the residue in toluene were added *n*-Bu_3SnH (12.57 g, 43.2 mmol) and a catalytic amount of AIBN. The mixture was refluxed for 1 h. After completion of the reaction the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (EtOAc-PE, 3:7) to give **10c**. White foam, yield 4.44 g, 83%, R_f 0.31 (EtOAc-PE, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07 (s, 9H), 1.73 (dd, *J* 7.2, 1.6 Hz, 3H), 2.12-2.24 (m, 1H), 2.38-2.47 (m, 1H), 3.73 (d, *J* 11.7 Hz, 1H), 3.94 (d, *J* 11.8 Hz, 1H), 4.46-4.55 (m, 2H), 4.59 (d, *J* 11.7 Hz, 1H), 5.21 (dd, *J* 8.2, 2.1 Hz, 1H), 5.53 (dd, *J* 11.9, 1.6 Hz, 1H), 5.69 (dq, *J* 11.9, 7.1 Hz, 1H), 6.12 (dd, *J* 7.3, 3.0 Hz, 1H), 7.26-7.46 (m, 11H), 7.51-7.67 (m, 4H), 7.92 (d, *J* 8.2 Hz, 1H), 8.14 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.30, 19.63, 27.26, 37.80, 64.50, 72.75, 75.66, 77.43, 83.20, 88.99, 100.21, 102.19, 124.68, 127.71, 128.15,

128.18, 128.21, 128.75, 130.25, 130.34, 131.65, 132.46, 133.20, 135.55, 135.79, 137.79, 140.43, 150.17, 162.96. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{35}H_{40}N_2O_5Si$: 619.3; found: 619.6.

2′-Deoxy-4′-*C*-propyluridine (**5c**). To a solution of compound **10c** (4.06 g, 7.1 mmol) in EtOH (50 mL) was added an equivalent weight amount of 10% Pd/C and the mixture was stirred at r.t. for 8 h under H_2 atmosphere (balloon). After completion of the reaction the mixture was filtered through Celite on a sintered funnel and washed thoroughly. The solvent was removed and the residue was dissolved in THF (40 mL) and a 1 M solution of TBAF (9.1 mL, 9.1 mmol) was added. The mixture was stirred at r.t. for 16 h, concentrated and purified by silica gel column chromatography (EtOAc→MeOH-EtOAc, 1:9) to give **5c**. White foam, yield 1.25 g, 65%, R_f 0.48 (MeOH-EtOAc, 1:9). ^{1}H NMR (400 MHz, MeOD): δ 0.92 (t, *J* 7.1 Hz, 3H), 1.31-1.70 (m, 4H), 2.28-2.34 (m, 2H), 3.55 (d, *J* 11.7 Hz, 1H), 3.63 (d, *J* 11.7 Hz, 1H), 4.40 (t, *J* 5.5 Hz, 1H), 5.65 (d, *J* 8.1 Hz, 1H), 6.16 (t, *J* 6.5 Hz, 1H), 8.03 (d, *J* 8.1 Hz, 1H). ^{13}C NMR (101 MHz, MeOD): δ 15.41, 18.28, 35.00, 41.81, 65.55, 72.96, 85.76, 91.12, 102.50, 142.83, 152.43, 166.51. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{12}H_{18}N_2O_5$: 293.1; found: 293.3. HRMS: *m/z* $[M+H]^+$ calcd for $C_{12}H_{18}N_2O_5$: 271.12885; found: 271.12864.

General synthetic procedure, exemplified by 3′,5′-di-*O*-acetyl-2′-deoxy-4′-*C*-methyluridine (**11a**)

To a suspension of compound **5a** (0.62 g, 2.56 mmol) in MeCN (14 mL) was added NEt_3 (1.43 mL, 10.2 mmol), Ac_2O (0.96 mL, 10.2 mmol) and a catalytic amount of DMAP. The mixture was stirred at r.t. for 20 h and then diluted with CH_2Cl_2 (40 mL) and washed with demin. H_2O (3×30 mL). The organic layer was dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 6:1).

11a. White foam, yield 0.55 g, 63%, R_f 0.30 (EtOAc-PE, 6:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 2.33 (dt, *J* 14.2, 7.1 Hz, 1H), 2.52 (ddd, *J* 14.3, 6.1, 3.6 Hz, 1H), 4.12 (d, *J* 11.9 Hz, 1H), 4.18 (d, *J* 11.9 Hz, 1H), 5.31 (dd, *J* 6.8, 3.6 Hz, 1H), 5.76 (d, *J* 7.4 Hz, 1H), 6.24 (t, *J* 6.7 Hz, 1H), 7.55 (d, *J* 8.2 Hz, 1H), 9.35 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 18.40, 20.92, 20.95, 38.71, 67.98, 73.82, 84.21, 85.08, 102.84, 139.02, 150.44, 163.19, 170.21. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{14}H_{18}N_2O_7$: 349.1; found: 349.3.

3′,5′-Di-*O*-acetyl-2′-deoxy-4′-*C*-ethyluridine (**11b**). White foam, yield 1.18 g, 74%, R_f 0.31 (EtOAc-PE, 6:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, *J* 7.5 Hz, 3H), 1.60 (dq, *J* 14.8, 7.4 Hz, 1H), 1.74 (dq, *J* 15.1, 7.6 Hz, 1H), 2.09 (s, 3H), 2.10 (s, 3H), 2.32 (dt, *J* 14.3, 7.1 Hz, 1H), 2.47 (ddd, *J* 14.3, 6.1, 3.5 Hz, 1H), 4.16 (s, 2H), 5.37 (dd, *J* 6.9, 3.5 Hz, 1H), 5.75 (d, *J* 8.2 Hz, 1H), 6.17 (t, *J* 6.6 Hz, 1H), 7.55 (d, *J* 8.2 Hz, 1H), 9.65 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 7.98, 20.94, 24.83, 38.92, 66.02, 74.01, 84.24, 86.80, 102.81, 139.04, 150.52, 163.38, 170.07, 170.27. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{15}H_{20}N_2O_7$: 363.1; found: 363.3.

3′,5′-Di-*O*-acetyl-2′-deoxy-4′-*C*-propyluridine (**11c**). White foam, yield 1.21 g, 93%, R_f 0.67 (EtOAc-PE, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, *J* 7.1 Hz, 3H), 1.27-1.69 (m, 4H), 2.09 (s, 3H), 2.11 (s, 3H), 2.30 (dt, *J* 14.2, 7.1 Hz, 1H), 2.47 (ddd, *J* 14.3, 6.1, 3.5 Hz, 1H), 4.16 (s, 2H), 5.35 (dd, *J* 6.8, 3.5 Hz, 1H), 5.74 (dd, *J* 8.2, 2.0 Hz, 1H), 6.20 (dd, *J* 7.0, 6.5 Hz, 1H), 7.53

(d, *J* 8.2 Hz, 1H), 8.61 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.87, 17.12, 21.07, 21.09, 34.36, 39.05, 66.49, 74.10, 84.37, 86.81, 102.88, 139.09, 150.28, 162.82, 170.17, 170.32. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{16}H_{22}N_2O_7$: 377.1; found: 377.3.

General synthetic procedure, exemplified by 3′,5′-di-*O*-acetyl-2′-deoxy-5-iodo-4′-*C*-methyluridine (**12a**)

Compound **11a** (0.46 g, 1.40 mmol), iodine (0.21 g, 0.84 mmol) and CAN (0.38 g, 0.70 mmol) were solved in MeCN (23 mL) and refluxed for 1 h. After completion of the reaction the solvent was removed under reduced pressure and the residue was partitioned between EtOAc (40 mL), aq sat. NaCl (20 mL) and aq 5% $NaHSO_4$ (5 mL). The aqueous layer was extracted with EtOAc (2×40 mL) and the combined organic layers were washed first with aq 5% $NaHSO_4$ (5 mL) and then with aq sat. NaCl (25 mL) and demin. H_2O (2×15 mL), dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 2:1).

12a. White foam, yield 0.56 g, 89%, R_f 0.57 (EtOAc-PE, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (s, 3H), 2.12 (s, 3H), 2.21 (s, 3H), 2.36 (dt, *J* 14.2, 7.0 Hz, 1H), 2.53 (ddd, *J* 14.3, 6.2, 3.8 Hz, 1H), 4.13 (d, *J* 12.1 Hz, 1H), 4.21 (d, *J* 12.0 Hz, 1H), 5.32 (dd, *J* 6.9, 3.8 Hz, 1H), 6.21 (t, *J* 6.6 Hz, 1H), 8.02 (s, 1H), 9.44 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 18.42, 20.89, 21.32, 39.09, 67.90, 68.79, 73.51, 84.44, 85.39, 143.98, 150.13, 159.96, 170.21. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{14}H_{17}IN_2O_7$: 475.0; found: 475.1.

3′,5′-Di-*O*-acetyl-2′-deoxy-5-iodo-4′-*C*-ethyluridine (**12b**). White foam, yield 1.56 g, 98%, R_f 0.71 (EtOAc-PE, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, *J* 7.5 Hz, 3H), 1.60 (dq, *J* 14.8, 7.4 Hz, 1H), 1.75 (dq, *J* 15.1, 7.6 Hz, 1H), 2.11 (s, 3H), 2.21 (s, 3H), 2.38 (dd, *J* 14.3, 7.1 Hz, 1H), 2.50 (ddd, *J* 14.4, 6.2, 3.8 Hz, 1H), 4.19 (d, *J* 12.2 Hz, 1H), 4.22 (d, *J* 12.2 Hz, 1H), 5.38 (dd, *J* 7.0, 3.8 Hz, 1H), 6.20 (t, *J* 6.6 Hz, 1H), 8.02 (s, 1H), 9.65 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 8.01, 20.92, 21.36, 24.95, 39.27, 66.19, 68.86, 73.60, 84.43, 87.10, 143.98, 150.20, 160.04, 170.08, 170.32. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{15}H_{19}IN_2O_7$: 489.0; found: 489.1.

3′,5′-Di-*O*-acetyl-2′-deoxy-5-iodo-4′-*C*-propyluridine (**12c**). White foam, yield 1.53 g, 89%, R_f 0.63 (EtOAc-PE, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, *J* 7.1 Hz, 3H), 1.26-1.69 (m, 4H), 2.09 (s, 3H), 2.19 (s, 3H), 2.33 (dt, *J* 14.3, 7.0 Hz, 1H), 2.47 (ddd, *J* 14.4, 6.2, 3.8 Hz, 1H), 4.16 (d, *J* 12.4 Hz, 1H), 4.19 (d, *J* 12.4 Hz, 1H), 5.34 (dd, *J* 7.0, 3.8 Hz, 1H), 6.17 (t, *J* 6.6 Hz, 1H), 7.99 (s, 1H), 9.41 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.83, 17.10, 21.01, 21.46, 34.42, 39.35, 66.61, 68.91, 73.69, 84.50, 87.06, 144.05, 150.22, 160.03, 170.16, 170.38. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{16}H_{21}IN_2O_7$: 503.0; found: 503.4.

General synthetic procedure, exemplified by 2′-deoxy-5-iodo-4′-*C*-methyluridine (**3a**)

Compound **12a** (0.08 g, 0.17 mmol) was stirred with 0.1 M NaOMe/MeOH (8 mL) at r.t. for 1 h. After the reaction was completed, addition of 2 mL of demin. H_2O was followed by neutralization (pH 6) with Amberlite IR-120 (H^+ form) ion-exchange resin. The resin was filtered and washed with 50% aq MeOH (20 mL). The combined filtrate and washings were evaporated and purified by silica gel column chromatography (EtOAc).

3a. White foam, yield 0.057g, 91%, R_f 0.35 (EtOAc). ^{1}H NMR (400 MHz, MeOD): δ 1.16 (s, 3H), 2.30-2.44 (m, 2H), 3.57 (d, *J* 11.7 Hz, 1H), 3.62 (d, *J* 11.7 Hz, 1H), 4.40 (t, *J* 6.2 Hz, 1H), 6.14 (t, *J* 6.0 Hz, 1H), 8.64 (s, 1H). ^{13}C NMR (101 MHz, MeOD): δ 18.01, 41.55, 67.01, 67.82, 71.82, 85.73, 89.51, 147.47, 152.02, 162.92. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{10}H_{13}IN_2O_5$: 391.0; found: 391.1. HRMS: *m/z* $[M+H]^+$ calcd for $C_{10}H_{13}IN_2O_5$: 368.99419; found: 368.99329.

2′-Deoxy-5-iodo-4′-*C*-ethyluridine (**3b**). White foam, yield 0.093 g, 97%, R_f 0.43 (EtOAc). ^{1}H NMR (400 MHz, MeOD): δ 0.97 (t, *J* 7.6 Hz, 3H), 1.58 (dq, *J* 14.8, 7.5 Hz, 1H), 1.72 (dq, *J* 15.1, 7.6 Hz, 1H), 2.30-2.42 (m, 2H), 3.58 (d, *J* 11.6 Hz, 1H), 3.71 (d, *J* 11.6 Hz, 1H), 4.46 (t, *J* 5.9 Hz, 1H), 6.14 (t, *J* 6.2 Hz, 1H), 8.63 (s, 1H). ^{13}C NMR (101 MHz, MeOD): δ 8.52, 25.15, 41.96, 64.68, 67.86, 72.23, 85.93, 91.30, 147.47, 152.03, 162.91. ESI-MS: *m/z* $[M+Na]^+$ calcd for: $C_{11}H_{15}IN_2O_5$: 405.0; found: 405.1. HRMS: *m/z* $[M+H]^+$ calcd for $C_{11}H_{15}IN_2O_5$: 383.00984; found: 383.00858.

2′-Deoxy-5-iodo-4′-*C*-propyluridine (**3c).** White foam, yield 0.089 g, 97%, R_f 0.63 (EtOAc). ^{1}H NMR (400 MHz, MeOD): δ 0.95 (t, *J* 7.0 Hz, 3H), 1.28-1.69 (m, 4H), 2.29-2.43 (m, 2H), 3.58 (d, *J* 11.6 Hz, 1H), 3.70 (d, *J* 11.6 Hz, 1H), 4.45 (t, *J* 5.9 Hz, 1H), 6.14 (t, *J* 6.2 Hz, 1H), 8.62 (s, 1H). ^{13}C NMR (101 MHz, MeOD): δ 15.40, 18.27, 35.13, 42.07, 65.26, 68.02, 72.43, 86.07, 91.33, 147.62, 152.18, 163.05. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{12}H_{17}IN_2O_5$: 419.0; found: 419.2. HRMS: *m/z* $[M+H]^+$ calcd for $C_{12}H_{17}IN_2O_5$: 397.02549; found: 397.02489.

General synthetic procedure, exemplified by 3′,5′-di-(*O*-*tert*-butyldimethylsilyl)-2′-deoxy-5-iodo-4′-*C*-methyluridine (**13a**)

To a solution of **3a** (0.463 g, 1.26 mmol) in DMF (3 mL) TBDMSCl (1.22 g, 8.1 mmol) and imidazole (0.81 g, 11.6 mmol) were added. The clear solution was stirred at r.t. for 60 h. Demin. H_2O (15 mL) was added, the aqueous layer was extracted with EtOAc (4×50 mL), dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 1:4).

13a. White foam, yield 0.605 g, 81%, R_f 0.30 (EtOAc-PE, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.15 (s, 3H), 0.15 (s, 3H), 0.91 (s, 9H), 0.95 (s, 9H), 1.15 (s, 3H), 2.18 (ddd, *J* 13.4, 7.4, 6.2 Hz, 1H), 2.33 (ddd, *J* 13.2, 5.9, 3.1 Hz, 1H), 3.55 (d, *J* 10.9 Hz, 1H), 3.71 (d, *J* 10.9 Hz, 1H), 4.33 (dd, *J* 6.1, 3.1 Hz, 1H), 6.18 (dd, *J* 7.3, 6.0 Hz, 1H), 8.13 (s, 1H), 8.17 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ -5.03, -4.94, -4.93, -4.53, 18.21, 18.50, 18.72, 25.87, 26.36, 42.63, 68.04, 68.24, 73.08, 84.94, 89.15, 144.77, 149.74, 159.82. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{22}H_{41}IN_2O_5Si_2$: 619.2; found: 619.0.

3′,5′-Di-(*O*-*tert*-butyldimethylsilyl)-2′-deoxy-5-iodo-4′-*C*-ethyluridine (**13b**). White foam, yield 1.670 g, 90%), R_f 0.31 (EtOAc-PE, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.15 (s, 3H), 0.16 (s, 3H), 0.90 (s, 9H), 0.94 (t, *J* 7.5 Hz, 3H), 0.95 (s, 9H), 1.47 (dq, *J* 14.8, 7.5 Hz, 1H), 1.74 (dq, *J* 15.1, 7.6 Hz, 1H), 2.11-2.21 (m, 1H), 2.31 (ddd, *J* 13.2, 5.9, 2.9 Hz, 1H), 3.57 (d, *J* 10.8 Hz, 1H), 3.74 (d, *J* 10.8 Hz, 1H), 4.40 (dd, *J* 6.2, 2.9 Hz, 1H), 6.16 (dd, *J* 7.5, 6.0 Hz, 1H), 8.11 (s, 1H), 8.26 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ -5.06, -4.95, -4.92, -4.44, 8.41, 18.17, 18.68, 24.96, 25.88, 26.35, 42.69, 66.34, 68.14, 73.38, 84.98, 90.62, 144.76, 149.79, 159.87. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{23}H_{43}IN_2O_5Si_2$: 633.2; found: 633.1.

3′,5′-Di-(*O*-*tert*-butyldimethylsilyl)-2′-deoxy-5-iodo-4′-*C*-propyluridine (**13c**). White foam, yield 1.13g, 91%, R_f 0.39 (EtOAc-PE, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.15 (s, 3H), 0.15 (s, 3H), 0.90 (s, 9H), 0.91 (t, *J* 2.9 Hz, 3H) 0.94 (s, 9H), 1.23-1.51 (m, 2H), 1.63 (dt, *J* 9.5, 5.8 Hz, 2H), 2.05-2.23 (m, 1H), 2.31 (ddd, *J* 13.2, 5.9, 2.9 Hz, 1H), 3.56 (d, *J* 10.9 Hz, 1H), 3.74 (d, *J* 10.9 Hz, 1H), 4.38 (dd, *J* 6.2, 2.9 Hz, 1H), 6.16 (dd, *J* 7.5, 6.0 Hz, 1H), 8.11 (s, 1H), 8.59 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ -5.06, -4.95, -4.93, -4.45, 14.95, 17.24, 18.17, 18.68, 25.79, 25.87, 26.35, 34.75, 42.68, 66.72, 68.20, 73.42, 84.99, 90.53, 144.75, 149.93, 160.05. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{45}IN_2O_5Si_2$: 647.2; found: 647.0.

General synthetic procedure, exemplified by 3′,5′-di-(*O*-*tert*-butyldimethylsilyl)-2′-deoxy-5-iodo-4′-*C*-methylcytidine (**14a**)

The solution of DMAP (0.113 g, 0.93 mmol), TPSCl (0.282 g, 0.86 mmol) and compound **13a** (0.191 g, 0.32 mmol) in MeCN (9 mL) was treated with freshly distilled Et_3N (0.65 mL, 4.67 mmol). After the yellow mixture was stirred for 50 h at room temperature, a 28% aq solution of NH_4OH (14 mL) was added and stirring was maintained for 3 h. MeCN was removed under vacuum and the aqueous layer was extracted with EtOAc (4×50 mL). The organic layer was dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc-PE, 4:1).

14a. White foam, yield 0.148 g, 78%, R_f 0.17 (EtOAc-PE, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.12 (s, 3H), 0.13 (s, 3H), 0.89 (s, 9H), 0.93 (s, 9H), 1.15 (s, 3H), 2.12 (dt, *J* 13.2, 6.5 Hz, 1H), 2.49 (ddd, *J* 13.4, 6.1, 4.0 Hz, 1H), 3.54 (d, *J* 10.8 Hz, 1H), 3.68 (d, *J* 10.8 Hz, 1H), 4.29 (dd, *J* 6.3, 4.0 Hz, 1H), 5.55 (s, 1H), 6.12 (t, *J* 6.3 Hz, 1H), 8.10 (s, 1H), 8.63 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ -5.06, -5.01, -4.98, -4.45, 18.16, 18.32, 18.66, 25.87, 26.32, 42.84, 55.91, 67.83, 72.50, 85.78, 88.82, 146.79, 154.88, 163.84. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{22}H_{42}IN_3O_4Si_2$: 618.2; found: 618.2.

3′,5′-Di-(*O*-*tert*-butyldimethylsilyl)-2′-deoxy-5-iodo-4′-*C*-ethylcytidine (**14b**). White foam, yield 0.150 g, 77%, R_f 0.18 (EtOAc-PE, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.12 (s, 3H), 0.12 (s, 3H), 0.88 (s, 9H), 0.92 (s, 9H), 0.93 (t, *J* 7.72 Hz, 3H), 1.48 (dq, *J* 14.8, 7.4 Hz, 1H), 1.73 (dq, *J* 15.1, 7.6 Hz, 1H), 2.09 (dt, *J* 13.3, 6.6 Hz, 1H), 2.46 (ddd, *J* 13.4, 6.1, 3.8 Hz, 1H), 3.54 (d, *J* 10.8 Hz, 1H), 3.71 (d, *J* 10.8 Hz, 1H), 4.37 (dd, *J* 6.5, 3.8 Hz, 1H), 5.56 (s, 1H), 6.10 (t, *J* 6.4 Hz, 1H), 8.07 (s, 1H), 8.63 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ -5.09, -5.01, -4.37, 8.31, 18.11, 18.61, 24.63, 25.87, 26.30, 42.96, 56.11, 65.83, 72.87, 85.78, 90.28, 146.73, 154.91, 163.89. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{23}H_{44}IN_3O_4Si_2$: 632.2; found: 632.2.

3′,5′-Di-(*O*-*tert*-butyldimethylsilyl)-2′-deoxy-5-iodo-4′-*C*-propylcytidine (**14c**). White foam, yield0.160 g, 80%, R_f 0.21 (EtOAc-PE, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.11 (s, 3H), 0.12 (s, 3H), 0.88 (s, 9H), 0.90-0.95 (m, 12H), 1.21-1.50 (m, 3H), 1.57-1.67 (m, 1H), 2.01-2.13 (m, 1H), 2.45 (ddd, *J* 13.4, 6.0, 3.7 Hz, 1H), 3.54 (d, *J* 10.8 Hz, 1H), 3.71 (d, *J* 10.8 Hz, 1H), 4.35 (dd, *J* 6.5, 3.7 Hz, 1H), 5.56 (s, 1H), 6.10 (t, *J* 6.4 Hz, 1H), 8.06 (s, 1H), 8.84 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ -5.11, -5.02, -5.01, -4.39, 14.95, 17.15, 18.11,

18.60, 25.86, 26.29, 34.42, 42.97, 56.20, 66.23, 72.59, 85.79, 90.21, 146.68, 154.93, 163.94. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{46}IN_3O_4Si_2$: 646.2; found: 646.1.

General synthetic procedure, exemplified by 2′-deoxy-5-iodo-4′-*C*-methylcytidine (**4a**)
Compound **14a** (0.148 g, 0.25 mmol) was dissolved in THF (10 mL), and a 1 M solution of TBAF (1.0 mL, 1.0 mmol) was added. The mixture was stirred at r.t. for 16 h, concentrated and purified by silica gel column chromatography (EtOAc→MeOH-EtOAc, 1:9).
4a. White foam, yield 0.84 g, 92%, R_f 0.15 (MeOH-EtOAc, 1:10). ^{1}H NMR (400 MHz, MeOD) δ 1.20 (s, 3H), 2.29 (ddd, *J* 13.7, 6.8, 4.9 Hz, 1H), 2.50 (dt, *J* 13.2, 6.5 Hz, 1H), 3.61 (d, *J* 11.7 Hz, 1H), 3.66 (d, *J* 11.7 Hz, 1H), 4.39 (t, *J* 6.6 Hz, 1H), 6.11 (dd, *J* 6.5, 5.0 Hz, 1H), 8.69 (s, 1H). ^{13}C NMR (101 MHz, MeOD) δ 17.93, 41.93, 56.46, 66.75, 71.29, 86.54, 89.42, 149.40, 157.37, 165.88. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{10}H_{14}IN_3O_4$: 390.0; found: 390.0. HRMS: *m/z* $[M+H]^+$ calcd for $C_{10}H_{14}IN_3O_4$: 368.01018; found: 368.00950.
2′-Deoxy-5-iodo-4′-*C*-ethylcytidine (**4b**). White foam, yield 0.85 g, 89%), R_f 0.16 (MeOH-EtOAc, 1:10). ^{1}H NMR (400 MHz, MeOD): δ 1.01 (t, *J* 7.6 Hz, 3H), 1.62 (dq, *J* 14.8, 7.5 Hz, 1H), 1.77 (dq, *J* 15.2, 7.6 Hz, 1H), 2.28 (ddd, *J* 13.7, 6.8, 5.4 Hz, 1H), 2.49 (ddd, *J* 13.7, 6.8, 5.4 Hz, 1H), 3.60 (d, *J* 11.6 Hz, 1H), 3.76 (d, *J* 11.6 Hz, 1H), 4.32-4.63 (m, 1H), 6.12 (dd, *J* 6.3, 5.6 Hz, 1H), 8.67 (s, 1H). ^{13}C NMR (101 MHz, MeOD): δ 8.48, 24.97, 42.41, 56.53, 64.38, 71.81, 86.83, 91.26, 149.41, 157.37, 165.86. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{11}H_{16}IN_3O_4$: 404.0; found: 404.0. HRMS: *m/z* $[M+H]^+$ calcd for $C_{11}H_{16}IN_3O_4$: 382.02583; found: 382.02489.
2′-Deoxy-5-iodo-4′-*C*-propylcytidine (**4c**). White foam, yield 0.80 g, 81%, R_f 0.17 (MeOH-EtOAc, 1:10). ^{1}H NMR (400 MHz, MeOD) δ 0.99 (t, *J* 7.1 Hz, 3H), 1.40-1.61 (m, 3H), 1.61-1.73 (m, 1H), 2.28 (ddd, *J* 13.6, 6.7, 5.5 Hz, 1H), 2.49 (dt, *J* 13.6, 6.2 Hz, 1H), 3.60 (d, *J* 11.6 Hz, 1H), 3.75 (d, *J* 11.6 Hz, 1H), 4.46 (t, *J* 6.2 Hz, 1H), 6.12 (dd, *J* 6.4, 5.6 Hz, 1H), 8.67 (s, 1H). ^{13}C NMR (101 MHz, MeOD) δ 15.26, 18.09, 34.81, 42.38, 56.55, 64.83, 71.84, 86.82, 91.13, 149.41, 157.36, 165.84. ESI-MS: *m/z* $[M+Na]^+$ calcd for $C_{12}H_{18}IN_3O_4$: 418.0; found: 418.0. HRMS: *m/z* $[M+H]^+$ calcd for $C_{12}H_{18}IN_3O_4$: 396.04148; found: 396.04016.

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