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Synthesis of 6-Alkyluridines from 6-Cyanouridine via Zinc(II) Chloride-Catalyzed Nucleophilic Substitution with Alkyl Grignard Reagents

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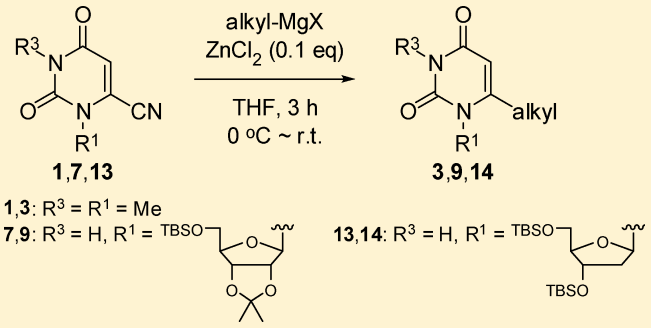
Supporting Information

ABSTRACT: 6-Cyanouracil derivatives underwent a direct nucleophilic substitution reaction with alkyl Grignard reagents in the presence of zinc(II) chloride as a catalyst to form the corresponding 6-alkyluracils. This methodology is applicable to sugar-protected 6-cyanouridine and 6-cyano-2′-deoxyuridine without the protection at the N^3-imide and provides a facile and general access to versatile 6-alkyluracil and 6-alkyluridine derivatives.



INTRODUCTION

C-Alkyl-substituted uridines are an important class of pyrimidine nucleoside analogues that have received substantial attention for decades. 5-Alkyluridines have been widely utilized as naturally occurring thymidine or 5-methyluridine analogues for a range of biological interests. There is also a growing interest in the 6-alkyluridine derivatives for their potential biological applications.[1,2] In particular, 6-alkyluridine derivatives represented spatial or regioisomeric analogues of thymidine and *syn*-conformation-constrained uridine/thymidine analogues which can be used to probe the interaction between nucleoside/nucleotide substrates and targeted proteins.[1−4] More recently, the introduction of alkyl-linkers at the 6-position of the uracil base has also been employed in the development of intramolecular and intermolecular base−sugar bridged uridine/thymidine analogues.[5,6]

Careful examination of literature revealed that the synthesis of 6-alkyluridines has mostly been achieved by four approaches (summarized in Scheme 1) with certain limitations: (A) specific 6-alkyluracils required multistep synthesis from acyclic precursors, and direct ribosylation of the 6-alkyluracils usually gave a mixture of N^1- and N^3-ribosides due to the steric and electronic effects.[2,7] (B) Lithiation at the 6-position of uridine followed by the reaction with electrophiles has been a straightforward approach for the synthesis of 6-substituted uridine derivatives.[8] However, the lithiated uridine could only react with less hindered alkyl halides to form simple 6-alkyluridines with concomitant alkylation at the α-carbon of the 6-alkyl substituent as byproducts.[5,9,10] (C) The palladium-catalyzed cross-coupling reactions of 6-halouridines are effective to introduce alkenyl (Csp^2) and alkynyl (Csp) substituents at the 6-position of uridine. Nevertheless, the Suzuki−Miyaura and Stille reactions have only limited success in the preparation of 6-alkyluridines.[11,12] (D) Reduction from 6-alkenyl- or 6-alkynyluridines was incompatible with unsaturated moieties in the same molecule.[6,13] The cross-coupling reactions have been restricted by the preparation of 6-halouridines, which suffered from lower yields and limited scales.[11] Thus, there is a need to develop a more general and effective process for the synthesis of 6-alkyluridines.

RESULTS AND DISCUSSION

In our attempt to prepare the 6-acyluracil derivatives by Grignard reaction, 6-cyano-1,3-dimethyluracil[14] (6-CN-1,3-DMU, **1**) was treated with methylmagnesium bromide in THF, but surprisingly the reaction did not afford the desired 6-Ac-1,3-DMU (**2**). Instead, 6-cyano-1,3-dimethyl-4-methylene-3,4-dihydropyrimidin-2-one (**4**, 31%) was obtained as the major product, and its structure was confirmed by X-ray crystallography. Another product was found to be 6-Me-1,3-DMU (**3a**, 20%), which was identical to the authentic compound prepared from the methylation of 6-methyluracil.[15] Products **4** and **3a** resulted from a 1,2- and 1,4-addition to the uracil ring carbons, respectively, followed by the elimination to retain their aromaticities. When the reaction was carried out with ethylmagnesium bromide, the substitution reaction took place predominantly to give 6-Et-1,3-DMU (**3b**) as the sole product in 66% yield (Scheme 2). We envisioned that the direct nucleophilic substitution reaction of 6-cyanouracil with the Grignard reagents would provide a feasible route for the synthesis of 6-substituted uridine derivatives.

The reaction of 6-CN-1,3-DMU (**1**) as a non-nucleoside model with EtMgBr was further investigated in order to

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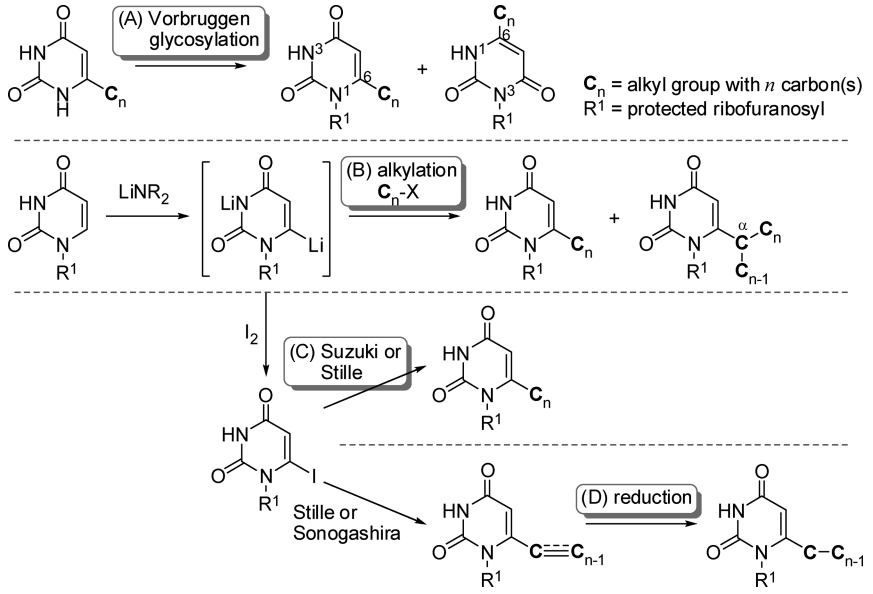
Scheme 1. Previous Strategies for the Synthesis of 6-Alkyluridine Derivatives



Scheme 2. Initial Reaction Outcome

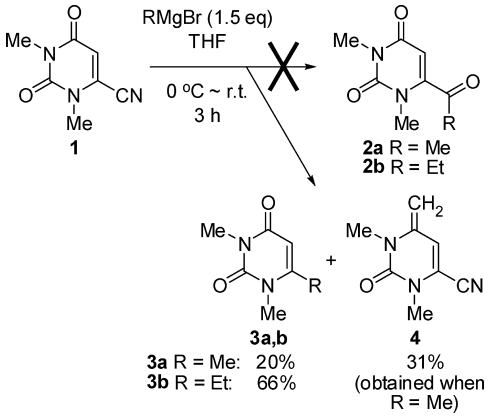
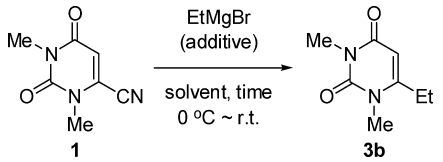


Table 1. Optimization for the Reaction of 6-CN-1,3-DMU (1) with EtMgBr



entry	EtMgBr[a] (equiv)	additive (0.1 equiv)	solvent[b]	time (h)	yield[c,d] (%)
1	1.5		THF	3	66[f]
2	2.0		THF	3	18
3	1.5		THF	1	72 (3)
4	1.5		toluene	3	45 (10)
5	1.5	$ZnCl_2$[e]	THF	1	55 (38)
6	1.5	$ZnCl_2$[e]	THF	3	90[f]
7	1.5	$ZnBr_2$	THF	3	80 (14)
8	1.5	CuCl	THF	3	59 (6)
9	1.5	$CuCl_2$	THF	3	52 (9)
10	1.5	$NiCl_2$	THF	3	67
11	1.5	CuI/$ZnCl_2$[e]	THF	3	59 (39)
12	1.5	Et_2Zn[g]	THF	3	89
13	g, h		THF	3	0 (83)
14	g, h	$MgCl_2$	THF	3	0 (82)

[a]0.9 M EtMgBr in THF. [b]Reaction concentration = 0.1 M. [c]Unless specified otherwise, the yields were determined by ^{1}H NMR analysis of the crude products using 1,3,5-trimethoxybenzene as an internal standard. [d]Numbers in parentheses represent the percentages for the unreacted substrate **1**. [e]$ZnCl_2$ (1 M) in Et_2O. [f]Isolated yield. [g]Et_2Zn (1.5 M) in toluene. [h]Et_2Zn (1.5 equiv) was used instead of EtMgBr in the reaction.

optimize the substitution reaction. Various conditions including different temperature, time, solvent, and the amount of the Grignard reagents were screened. The optimum conditions were to carry out the reaction with 1.5 equiv of the Grignard reagent in THF from 0 °C to room temperature, and the reaction could be completed within 3 h. Subsequently, a series of Lewis acids as additives were examined (entries 5−11 in Table 1), and it was found that the zinc salts effectively improved the yields (entries 6 and 7 in Table 1). The combination of the ethyl Grignard reagent and zinc salts raised the possibility that diethylzinc might be the reactive species in the reaction. Thus, a catalytic amount of Et_2Zn was employed, and the reaction yield was comparable to the results with zinc salts (entries 6, 7, and 12 in Table 1). However, only the starting material was recovered when a stoichiometric amount of Et_2Zn was used instead of EtMgBr in the reaction (entries 13 and 14 in Table 1). We postulated that the zinc adducts played the roles of Lewis acids to activate the carbonyl group at the 4-position to facilitate the substitution reaction.

The reactions of 6-CN-1,3-DMU (**1**) with a variety of Grignard reagents, as shown in Table 2, were investigated to establish the scope and generality of the nucleophilic components. Both the uncatalyzed reaction and the reaction with zinc(II) chloride as an additive were examined for comparison purposes. Under the optimized conditions (entries 1 and 6 in Table 1), 6-CN-1,3-DMU (**1**) reacted with most of the alkylmagnesium halides (sp^3 Grignard reagents) to form the 6-alkyluracil derivatives (**3a−g,i**) in good yields (entries 1−7 and 9 in Table 2), except the allylmagnesium chloride did not afford the desired product (entry 8 in Table 2). Our investigation has shown that the reactivity of alkylmagnesium

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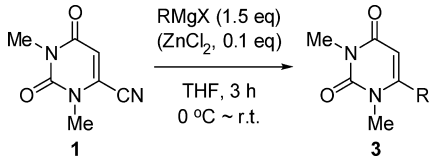
Table 2. Reactions of 6-CN-1,3-DMU (1) with Various Grignard Reagents



1 3

			yield[a] (%)	
entry	RMgX	product	$ZnCl_2$[b]	no additive
1	methyl[c]	**3a**	53	20[d]
2	ethyl[c]	**3b**	90	66
3	isopropyl[e]	**3c**	60	51
4	*tert*-butyl[e]	**3d**	32	49
5	*n*-butyl[f]	**3e**	81[g]	40
6	cyclopentyl[h]	**3f**	44	36
7	3-butenyl[c]	**3g**	87	45
8	allyl[e]	ND[i]		
9	benzyl[e]	**3i**	60	32
10	phenyl[c]	**3j**	24	16
11	vinyl[c,e]	NR[j]		
12	ethynyl[c]	NR[j]		

[a]Isolated yield. [b]$ZnCl_2$ (1 M) in Et_2O; [c]RMgBr in THF/MeMgBr (1 M), EtMgBr (0.9 M), 3-butenyl-MgBr (0.5 M), PhMgBr (1 M), vinyl-MgBr (0.7 M), ethynyl-MgBr (0.5 M); [d]20% of **3a** and 31% of **4** were obtained from the reaction as shown in Scheme 1; [e]RMgCl in THF/*i*-PrMgCl (2 M), *t*-BuMgBr (1.7 M), allyl-MgCl (1.7 M), BnMgCl (20 wt %), vinyl-MgCl (1.9 M). [f]20 wt % of *n*-BuMgCl in THF/toluene. [g]46% of **3e** under standard condition; 81% of **3e** when the reaction concentration was raised to 0.2 M. [h]Cyclopentyl-MgCl (2 M) in Et_2O. [i]ND = no desired product under both conditions. [j]NR = no reaction under both conditions.

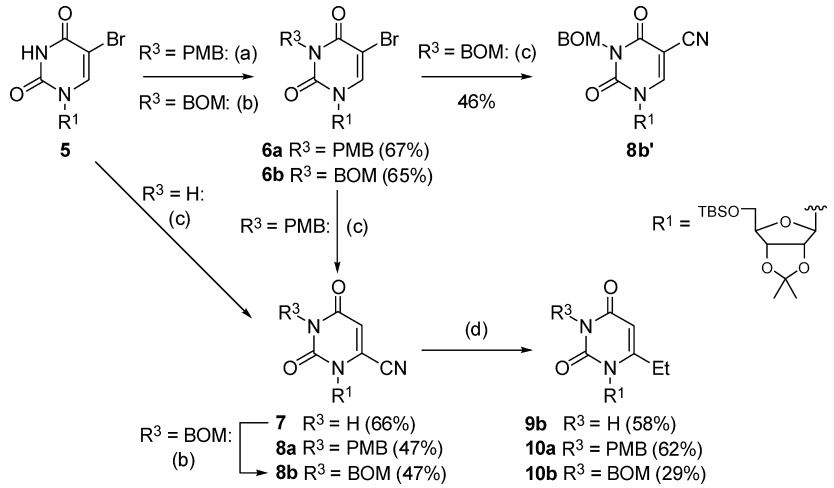
halides decreases with the increase of the steric hindrance, and in general, the yields were improved by the addition of $ZnCl_2$ as a catalyst. In the reactions with sp^2 and sp Grignard reagents, phenylmagnesium bromide was found to give the substitution product (**3j**) in low yields (entry 10 in Table 2), while vinyl and ethynyl Grignard reagents could not react with 6-CN-1,3-DMU (**1**) (entries 11 and 12 in Table 2). The survey of the reaction scope suggested that the nucleophilic substitution of 6-cyanouracils with alkyl Grignard reagents could be amenable for the synthesis of the 6-alkyluridine derivatives.

Since the model study demonstrated that the substitution reaction was applicable to the N^1,N^3-disubstituted 6-cyanouracil, we first considered that the introduction of an appropriate protecting group for the N^3-imide would be necessary when the reaction was intended to apply to the 6-cyanouridine derivatives. Both *p*-methoxybenzyl (PMB) and benzyloxymethyl (BOM) as protecting groups for the N^3-imide were anticipated to be stable toward the Grignard reagents, and thus, N^3-PMB- and N^3-BOM-5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-*O*-isopropylidene-6-cyanouridines (**8a**,**b**) were chosen as the nucleoside substrates in our initial trials.

N^3-Alkylation of 5′-*O*-TBS-2′,3′-*O*-isopropylidene-5-bromouridine[16] (**5**) with PMBCl or BOMCl in the presence of DBU as a base provided the corresponding N^3-PMB- and N^3-BOM-protected 5-bromouridines **6a**,**b**.[17] N^3-PMB-6-cyanouridine **8a** was then obtained from the addition−elimination reaction of **6a** with sodium cyanide in DMF. Nevertheless, under the same condition, the reaction of **6b** with NaCN only resulted in the N^3-BOM-5′-*O*-TBS-2′,3′-*O*-isopropylidene-5-cyanouridine (**8b′**).[14,18,19] Alternatively, the desired N^3-BOM 6-cyanouridine **8b** was obtained from the direct N^3-alkylation of 5′-*O*-TBS-2′,3′-*O*-isopropylidene-6-cyanouridine[16] (**7**) with BOMCl and DBU (Scheme 3).

The sugar- and N^3-protected 6-cyanouridines **8a** and **8b** were reacted with EtMgBr under the uncatalyzed condition (entry 1 in Table 1) and the corresponding N^3-protected 6-ethyluridines **10a** and **10b** were obtained in 62% and 29% yields, respectively. The low yield of **8b** was attributed to partial cleavage of the BOM group during the reaction. Furthermore, the removal of the N^3-protecting groups was also problematic. A global deprotection to remove the PMB, isopropylidene and TBS groups of **10a** with CAN followed by our previously developed workup protocol furnished the desired 6-ethyluridine (**11b**) in 10% yield.[11] Meanwhile, hydrogenolysis of the N^3-BOM of **10b** followed by the removal of TBS and isopropylidene groups with aqueous TFA gave 6-ethyluridine (**11b**) in 24% yield. Both synthetic routes suffered from lengthy steps and poor overall yields, and were impractical for the synthesis of the 6-alkyluridine derivatives.

Scheme 3. Synthesis of N^3-Protected 6-Ethyluridines[a]



[a]Reagents and conditions (a) PMBCl, DBU, CH_3CN, 60 °C, 3 h; (b) BOMCl, DBU, DMF, 0 °C to rt; (c) NaCN, DMF, rt, 2 h; (d) EtMgBr (0.9 M in THF; R^3 = PMB or BOM: 1.5 equiv; R^3 = H: 2.5 equiv), THF, 0 °C to rt, 3 h.

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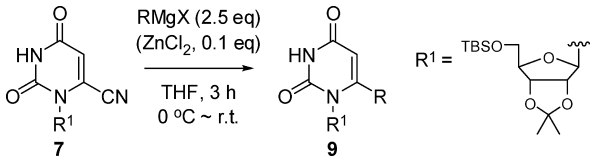
The unsatisfactory results have prompted us to make a bold attempt to subject the N^3-unprotected 6-cyanouridine to the Grignard reaction. Therefore, the sugar-protected 6-cyanouridine 7[16] was directly reacted with 2.5 equiv of EtMgBr under the uncatalyzed conditions. An additional equivalent of the Grignard reagent was used because the unprotected N^3-imide proton was expected to consume an equal amount of the Grignard reagent. It was beyond our expectations that the reaction proceeded to give 5′-*O*-TBS-2′,3′-*O*-isopropylidene-6-ethyluridine (**9b**) as the sole product in 58% yield. The result indicated that a protecting group for the reactive N^3-imide is unnecessary in this novel substitution reaction.

Afterward, the reaction of 7 with a series of alkyl Grignard reagents, as shown in Table 3, was explored in order to expand

Table 3. Reactions of Sugar-Protected 6-Cyanouridine 7 with Various Grignard Reagents



7 9

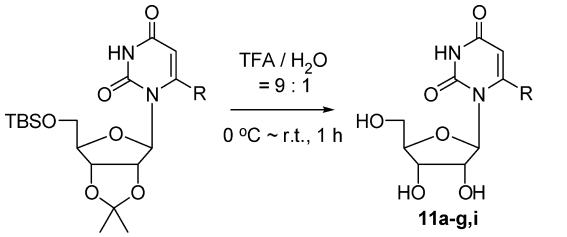
			yield[b] (%)	
entry	RMgX[a]	product	$ZnCl_2$[c]	no additive
1	methyl	**9a**	45[d]	trace
2	ethyl	**9b**	82	58
3	isopropyl	**9c**	57	52
4	*tert*-butyl	**9d**	44	42
5	*n*-butyl	**9e**	60[e]	29
6	cyclopentyl	**9f**	37	49
7	3-butenyl	**9g**	46	16
8	benzyl	**9i**	54	39

[a]Refer to footnotes *c*, *e*, *f*, and *h* in Table 2. [b]Isolated yield. [c]$ZnCl_2$ (1 M) in Et_2O; [d]No reaction under the standard conditions; 45% of **9a** from the reaction with 5 equiv of MeMgBr and 0.5 equiv of $ZnCl_2$. [e]34% of **9e** under the standard conditions; 60% of **9e** when the reaction concentration was raised to 0.2 M.

the reaction scope to the nucleoside derivatives. Under the uncatalyzed condition, the sugar-protected 6-cyanouridine **7** can react with the alkyl Grignard reagents to give the corresponding sugar-protected 6-alkyluridines **9** in reasonable yields. The reaction can also be facilitated by the addition of $ZnCl_2$ as the catalyst. (Table 3) Nonetheless, MeMgBr gave the desired product only in a trace amount under both conditions. Upon increasing the amounts of MeMgBr and $ZnCl_2$ to 5 and 0.5 equivalents, respectively, the desired sugar-protected 6-methyluridine **9a** was obtained in 45% yield. The acid-labile TBS and isopropylidene groups of **9a−g,i** were deprotected with aqueous TFA to give the targeted 6-alkyluridines **11a−g,i** in good yields (Scheme 4).

The success in the synthesis of 6-alkyluridines has prompted us to broaden the scope of this strategy to the synthesis of 6-alkyl-2′-deoxyuridine derivatives. Therefore, 3′,5′-di-*O*-TBS-5-bromo-2′-deoxyuridine[20] (**12**) was treated with NaCN to give the sugar-protected 6-cyano-2′-deoxyuridine **13**. Subjection of **13** to the optimized $ZnCl_2$-catalyzed condition with the alkyl Grignard reagents afforded the corresponding sugar-protected 6-alkyl-2′-deoxyuridine derivatives (**14a,b,g**). Subsequent removal of the TBS group with TBAF gave the desired 6-alkyl-2′-deoxyuridines (**15a,b,g**) (Scheme 5).

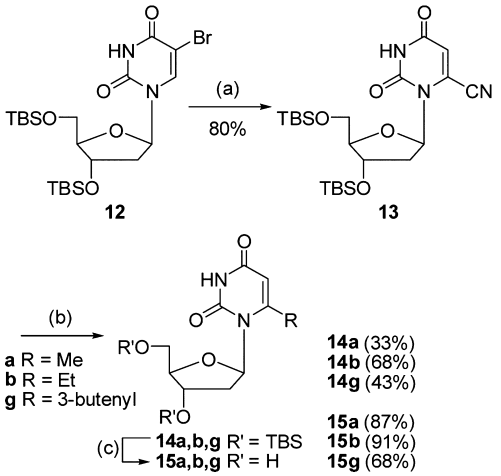
Scheme 4. Deprotection of Sugar-Protected 6-Alkyluridines



9a-g,i **11a** R = Me (89%) **11b** R = Et (91%) **11c** R = *i*-Pr (94%) **11d** R = *t*-Bu (89%) **11e** R = *n*-Bu (87%) **11f** R = cyclopentyl (62%) **11g** R = 3-butenyl (86%) **11i** R = Bn (83%)

11a-g,i

Scheme 5. Synthesis of 6-Alkyl-2′-deoxyuridines[a]



[a]Reagents and conditions: (a) NaCN (2.5 equiv), DMF, rt, 6 h, 80%; (b) RMgBr (R = Me: 5 equiv; R = Et or 3-butenyl: 2.5 equiv), $ZnCl_2$ (R = Me: 0.5 equiv; R = Et or 3-butenyl: 0.1 equiv), THF, 0 °C to rt, 3 h; (c) 1 M TBAF in THF with ca. 5% water.

CONCLUSION

In summary, we have discovered a novel substitution reaction of 6-cyanouracil derivatives with alkyl Grignard reagents, which illustrated the versatile reactivity of 6-cyanouracils.[14,18,19,21] Our investigation has successfully provided a facile and general synthesis of 6-alkyluridines from readily prepared 6-cyanouridines. Further application of this methodology will be amenable to the synthesis of a variety of 6-alkyluracil derivatives for biochemical applications.

EXPERIMENTAL SECTION

General Chemical Procedures. The chemical shift values are reported in δ values (parts per million, ppm) relative to the standard chemical shift for the hydrogen residue peak and carbon-13 peak in the deuterated solvent, $CDCl_3$, or DMSO-d_6.[22] The coupling constant (J) values are expressed in hertz (Hz). The numbers of protons directly attached to the individual carbons were determined by ^{13}C NMR DEPT experiments. Thin-layer chromatography (TLC) was performed on silica gel plates. Compounds on TLC were visualized by illumination under UV light (254 nm), or dipped into 10% ethanolic sulfuric acid followed by charring on a hot plate. Solvent systems are expressed as a percentage of the more polar component with respect to total volume (v/v %). Silica gel (230−400 mesh) was used for flash column chromatography and this technique has been described by Still et al.[23] Evaporations were carried out under reduced pressure (water aspirator or vacuum pump) with the bath temperature below 50 °C unless specified otherwise. Materials obtained from commercial suppliers were used without further purification.

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General Procedure for the Reaction of 6-Cyanouracil Derivatives with Grignard Reagents (for Compounds 3, 4, 9, 10, and 14). To a solution of 6-cyanouracil derivative in THF (0.1 M) was slowly added $ZnCl_2$ (0.1 equiv) and then the Grignard reagent (1.5 or 2.5 equiv) at 0 °C. After the addition was completed, the reaction mixture was stirred for 3 h, and the reaction temperature was allowed to rise to room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution, and the solvent was removed under reduced pressure. The residue was partitioned between $CHCl_3$ and H_2O, and the aqueous layer was further extracted with $CHCl_3$. The organic portions were combined, washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to dryness. The resulting residue was purified by flash column chromatography to give the product.

1,3,6-Trimethyluracil[15] (3a) and 6-Cyano-1,3-dimethyl-4-methylidene-3,4-dihydropyrimidin-2-one (4). The reaction was purified by flash column chromatography (Hex/EtOAc = 9:1 to 7:3 to 1:9) to give the products (**4**, solid, 0.2476 g, 31%, R_f = 0.20 (Hex/EtOAc = 9:1 and **3a**, white solid, 0.1509 g, 20%, R_f = 0.19 (Hex/EtOAc = 1: 9)). **3a**: mp 113−115 °C (lit.[15] mp 114−115 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.57 (s, 1 H), 3.36 (s, 3 H), 3.28 (s, 3 H), 2.20 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.3, 152.5, 151.3, 101.1 (CH), 31.6 (CH_3), 27.8 (CH_3), 20.1 (CH_3); MS (EI, 20 eV) *m*/*z* 56 (100), 69 (39), 82 (88), 97 (59), 125 (32), 154 (79) (M^+). **4**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.16 (s, 1 H), 4.07 (d, 1 H, *J* = 1.1 Hz), 4.01 (d, 1 H, *J* = 1.1 Hz), 3.27 (s, 3 H), 3.06 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.2, 140.3, 116.1 (CH), 114.9, 112.7, 89.3 (CH_2), 33.5 (CH_3), 30.5 (CH_3); MS (EI, 20 eV) *m*/*z* 163 (100) (M^+); MS (FAB) *m*/*z* 164 (100) (M + H); HRMS (FAB, magnetic sector) calcd for $C_8H_{10}N_3O$ 164.0824, found 164.0826.

1,3-Dimethyl-6-ethyluracil[24] (3b). The reaction was purified by flash column chromatography (Hex/EtOAc = 8:2 to 6:4) to give the product (**3b**, white solid, 0.1509 g, 90%, R_f = 0.18 (Hex/EtOAc = 5:5)): mp 50−52 °C (lit.[24] mp 46−47 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.63 (s, 1 H), 3.40 (s, 3 H), 3.34 (s, 3 H), 2.52 (q, 2 H, *J* = 7.3 Hz), 1.24 (t, 3 H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.4, 156.1, 152.4, 98.8 (CH), 30.8 (CH_3), 27.6 (CH_3), 25.4 (CH_2), 11.0 (CH_3); MS (EI, 20 eV) *m*/*z* 82 (40), 168 (100) (M^+); HRMS (EI, 70 eV, magnetic sector) calcd for $C_8H_{12}N_2O_2$ 168.0899, found 168.0903.

1,3-Dimethyl-6-isopropyluracil[25] (3c). The reaction was purified by flash column chromatography (Hex/EtOAc = 8.5:1.5 to 7.5:2.5) to give the product (**3c**, oil, 0.5471 g, 60%, R_f = 0.25 (Hex/EtOAc = 5: 5)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.61 (s, 1 H), 3.40 (s, 3 H), 3.28 (s, 3 H), 2.83 (sep, 1 H, *J* = 6.7 Hz), 1.19 (d, 6 H, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.9, 160.7, 152.7, 97.3 (CH), 30.9 (CH_3), 29.5 (CH), 27.8 (CH_3), 21.2 (CH_3); MS (EI, 70 eV) *m*/*z* 167 (46), 182 (100) (M^+); HRMS (EI, 70 eV, magnetic sector) calcd for $C_9H_{14}N_2O_2$ 182.1055, found 182.1055.

6-*tert*-Butyl-1,3-dimethyluracil[26] (3d). The reaction was purified by flash column chromatography (Hex/EtOAc = 8.5:1.5 to 7:3) to give the product (**3d**, foam, 0.0956 g, 49%, R_f = 0.3 (Hex/EtOAc = 5: 5)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.81 (s, 1 H), 3.55 (s, 3 H), 3.34 (s, 3 H), 1.40 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.9, 161.4, 153.4, 99.3 (CH), 35.7, 35.1 (CH_3), 29.7 (CH_3), 27.8 (CH_3); MS (EI, 70 eV) *m*/*z* 181 (55), 196 (100) (M^+); HRMS (EI, 70 eV, magnetic sector) calcd for $C_{10}H_{16}N_2O_2$ 196.1212, found 196.1218.

6-*n*-Butyl-1,3-dimethyluracil[11] (3e). The reaction was purified by flash column chromatography (Hex/EtOAc = 7:3) to give product (**3e**, oil, 0.790 g, 81%, R_f = 0.16 (Hex/EtOAc = 7: 3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.53 (s, 1 H), 3.33 (s, 3 H), 3.25 (s, 3 H), 2.40 (t, 2 H, *J* = 7.7 Hz), 1.56−1.47 (m, 2 H), 1.42−1.32 (m, 2 H), 0.90 (t, 3 H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.5, 155.0, 152.6, 99.9 (CH), 32.1 (CH_2), 31.1 (CH_3), 28.9 (CH_2), 27.7 (CH_3), 22.0 (CH_2), 13.5 (CH_3); MS (EI, 20 eV) *m*/*z* 55 (83), 69 (83), 82 (56), 97 (100), 127 (27), 154 (63), 196 (51) (M^+).

6-Cyclopentyl-1,3-dimethyluracil (3f). The reaction was purified by flash column chromatography (Hex/EtOAc = 8.7:1.3 to 8.5:1.5) to give the product (**3f**, foam, 0. 0925 g, 44%, R_f = 0.3 (Hex/EtOAc = 5:5)): mp 51−55 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.69 (s, 1 H), 3.45 (s, 3 H), 3.34 (s, 3 H), 2.97−2.89 (m, 1 H), 2.06−2.02 (m, 2 H), 1.80−1.79 (m, 2 H), 1.71−1.68 (m, 2 H), 1.63−1.59 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.9, 159.0, 152.9, 97.6 (CH), 41.1 (CH), 31.8 (CH_2), 31.6 (CH_3), 27.9 (CH_3), 25.0 (CH_2); MS (EI, 70 eV) *m*/*z* 167 (100), 208 (18) (M^+); HRMS (EI, 70 eV, magnetic sector) calcd for $C_{11}H_{16}N_2O_2$ 208.1212, found 208.1218.

6-(3-Butenyl)-1,3-dimetyluracil (3g). The reaction was purified by flash column chromatography (Hex/EtOAc = 9:1 to 8:2) to give the product (**3g**, foam, 0.1562 g, 87%, R_f = 0.3 (Hex/EtOAc = 5:5)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.86−5.76 (m, 1 H), 5.61 (s, 1 H), 5.14−5.08 (m, 2 H), 3.40 (s, 3 H), 3.33 (s, 3 H), 2.57 (t, 2 H, *J* = 7.6 Hz), 2.38−2.33 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.4, 154.1, 152.6, 135.2 (CH), 116.8 (CH_2), 100.2 (CH), 31.7 (CH_2), 31.2 (CH_3), 30.7 (CH_2), 27.8 (CH_3); MS (EI, 20 eV) *m*/*z* 179 (100), 194 (44) (M^+); HRMS (EI, 70 eV, magnetic sector) calcd for $C_{10}H_{14}N_2O_2$ 194.1055, found 194.1061.

6-Benzyl-1,3-dimethyluracil[27] (3i). The reaction was purified by flash column chromatography (Hex/EtOAc = 7:3 to 6:4) to give the product (**3i**, solid, 0.2754 g, 60%, R_f = 0.3 (Hex/EtOAc = 5:5)): mp 95−97 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.30 (m, 3 H), 7.18 (d, 2 H, *J* = 7.2 Hz), 5.55 (s, 1 H), 3.82 (s, 2 H), 3.35 (s, 3 H), 3.32 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.5, 153.2, 152.7, 134.1, 129.2 (CH), 128.6 (CH), 127.7 (CH), 102.6 (CH), 39.2 (CH_2), 31.6 (CH_3), 28.0 (CH_3); MS (EI, 70 eV) *m*/*z* 230 (100) (M^+); HRMS (EI, 70 eV, magnetic sector) calcd for $C_{13}H_{14}N_2O_2$ 230.1055, found 230.1054.

6-Phenyl-1,3-dimethyluracil[28,29] (3j). The reaction was purified by flash column chromatography (Hex/EtOAc = 9.5:0.5 to 8.5:1.5) to give the product (**3j**, solid, 0.0526 g, 24%, R_f = 0.25 (Hex/EtOAc = 5:5)): mp 104−106 °C (lit.[28,29] mp 86−88 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47−7.44 (m, 3 H), 7.31−7.29 (m, 2 H), 5.66 (s, 1 H), 3.37 (s, 3 H), 3.19 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.3, 154.5, 152.6, 133.3, 130.1 (CH), 128.9 (CH), 127.6 (CH), 102.3 (CH), 34.5 (CH_3), 27.9 (CH_3); MS (EI, 20 eV) *m*/*z* 216 (100) (M^+).

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(*p*-methoxybenzyl)-5-bromouridine (6a). To a solution of 5′-*O*-*tert*-butyldimethylsilyl-2′,3′-*O*-isopropylidene-5-bromouridine[16] (**5**, 5.3147 g, 11.13 mmol) in CH_3CN (50 mL) were added DBU (3.36 mL, 22.26 mmol, 2 equiv) and PMBCl (2.26 mL, 16.70 mmol, 1.5 equiv).[17] The reaction mixture was stirred at 60 °C for 3 h. The solvent was removed under reduced pressure. The residue was partitioned between EtOAc and H_2O. The aqueous layer was further extracted with EtOAc. The organic portions were combined, washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to dryness. The residue was purified by flash column chromatography (Hex/EtOAc = 9:1) to give the product (**6a**, solid, 4.4276 g, 67%, R_f = 0.38 (Hex/EtOAc = 8:2)): mp 118−120 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (s, 1 H), 7.48 (d, 2 H, *J* = 8.6 Hz), 6.81 (d, 2 H, *J* = 8.7 Hz), 5.86 (d, 1 H, *J* = 2.5 Hz), 5.13 (d, 1 H, *J* = 13.5 Hz), 5.05 (d, 1 H, *J* = 13.5 Hz), 4.72−4.68 (m, 2 H), 4.42−4.41 (m, 1 H), 3.91 (dd, 1 H, *J* = 2.0 and 11.7 Hz), 3.77 (dd, 1 H, *J* = 2.9 and 11.6 Hz), 3.77 (s, 3 H), 1.59 (s, 3 H), 1.37 (s, 3 H), 0.85 (s, 9 H), 0.08 (s, 3 H), 0.077 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.3, 158.9, 150.2, 137.6 (CH), 131.2 (CH), 128.4, 113.9, 113.7 (CH), 96.4, 94.1 (CH), 87.2 (CH), 86.0 (CH), 80.7 (CH), 63.4 (CH_2), 55.2 (CH_3), 45.0 (CH_2), 27.2 (CH_3), 25.9 (CH_3), 25.2 (CH_3), 18.3, −5.3 (CH_3), −5.5 (CH_3); MS (ESI) *m*/*z* 595 (100) (M − H), 597 (89) (M + H); HRMS (ESI, TOF) calcd for $C_{26}H_{37}BrN_2O_7Si$·Na (M + Na) 619.1451, found 619.1406.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(benzyloxymethyl)-5-bromouridine (6b). To a solution of 5′-*O*-*tert*-butyldimethylsilyl-2′,3′-*O*-isopropylidene-5-bromouridine[16] (**5**, 2.6083 g, 5.46 mmol) in DMF (6 mL) were added DBU (1.7 mL, 10.92 mmol, 2.0 equiv) and BOMCl (1.14 mL, 8.19 mmol, 1.5 equiv) at 0 °C.[17] The reaction temperature was allowed to rise to room temperature, and the reaction mixture was stirred for 2 days. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography (Hex/EtOAc = 9:1) to give the product (**6b**, foam, 2.1338 g, 65%, R_f = 0.50 (Hex/EtOAc = 7: 3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (s, 1 H), 7.36−7.25 (m, 5 H), 5.86

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(d, 1 H, J = 2.6 Hz), 5.55 (d, 1 H, J = 9.8 Hz), 5.51 (d, 1 H, J = 9.8 Hz), 4.73−4.62 (m, 4 H), 4.43−4.40 (m, 1 H), 3.92 (dd, 1 H, J = 1.9 and 11.6 Hz), 3.78 (dd, 1 H, J = 2.7 and 11.6 Hz), 1.59 (s, 3 H), 1.37 (s, 3 H), 0.89 (s, 9 H), 0.11 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.0, 150.1, 138.4 (CH), 137.8, 128.2 (CH), 127.62 (CH), 127.55 (CH), 113.9, 96.2, 93.9 (CH), 87.1 (CH), 85.8 (CH), 80.7 (CH), 72.5 (CH_2), 71.6 (CH_2), 63.4 (CH_2), 27.2 (CH_3), 25.9 (CH_3), 25.2 (CH_3), 18.3, −5.3 (CH_3), −5.5 (CH_3); MS (ESI) m/z 619 (100) (M + Na), 621 (89) (M + Na + 2); HRMS (ESI, TOF) calcd for $C_{26}H_{37}Br_1N_2O_7Si$·Na (M + Na) 619.1451, found 619.1449.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(*p*-methoxybenzyl)-6-cyanouridine (8a). To a solution of **6a** (4.0204 g, 6.73 mmol) in DMF (60 mL) was added NaCN (0.4908 g, 10.1 mmol, 1.5 equiv), and the reaction mixture was stirred at room temperature for 2.5 h.[16] The solvent was removed under reduced pressure. The residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was further extracted with $CHCl_3$. The organic portions were combined, washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to dryness. The residue was purified by flash column chromatography (Hex/EtOAc = 9:1) to give the product (**8a**, oil, 1.7037 g, 3.13 mmol, 47%, R_f = 0.43 (Hex/EtOAc = 8:2)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, 2 H, J = 8.6 Hz), 6.82 (d, 2 H, J = 8.7 Hz), 6.31 (s, 1 H), 6.04 (d, 1 H, J = 2.1 Hz), 5.11 (dd, 1 H, J = 2.1 and 6.7 Hz), 4.98 (s, 2 H), 4.82 (dd, 1 H, J = 4.6 and 6.6 Hz), 4.19−4.15 (m, 1 H), 3.86 (dd, 1 H, J = 5.2 and 10.9 Hz), 3.81−3.77 (m, 3 H), 3.77 (s, 3 H), 1.57 (s, 3 H), 1.35 (s, 3 H), 0.89 (s, 9 H), 0.051 (s, 3 H), 0.048 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.7, 159.4, 149.3, 130.9 (CH), 127.6, 125.6, 114.7, 113.8 (CH), 112.6 (CH), 110.9, 94.5 (CH), 88.7 (CH), 83.7 (CH), 81.5 (CH), 63.4 (CH_2), 55.2 (CH_3), 44.2 (CH_2), 27.1 (CH_3), 25.9 (CH_3), 25.4 (CH_3), 18.4, −5.35 (CH_3), −5.38 (CH_3); MS (ESI) m/z 566 (100) (M + Na). HRMS (ESI, TOF) calcd for $C_{27}H_{37}N_3O_7Si$·Na (M + Na) 566.2298, found 566.2260.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(benzyloxymethyl)-6-cyanouridine (8b). To a solution of 5′-*O*-*tert*-butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-cyanouridine[16] (**7**, 0.9221 g, 2.18 mmol) in DMF (10 mL) was added DBU (0.66 mL, 4.36 mmol, 2.0 equiv) and then BOMCl (0.45 mL, 3.27 mmol, 1.5 equiv) at 0 °C. After the addition was completed, the reaction mixture was stirred for 3.5 h, and the reaction temperature was allowed to rise to room temperature. The solvent was removed under reduced pressure. The residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was further extracted with $CHCl_3$. The organic portions were washed with saturated aqueous NaCl solution, combined, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to dryness. The resulting residue was purified by flash column chromatography (Hex/EtOAc = 8:2) to give the product (**8b**, foam, 0.5619 g, 1.03 mmol, 47%, R_f = 0.40 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.28 (m, 5 H), 6.25 (s, 1 H), 6.01 (d, 1 H, J = 1.7 Hz), 5.45 (d, 1 H, J = 9.8 Hz), 5.40 (d, 1 H, J = 9.9 Hz), 5.10 (dd, 1 H, J = 1.7 and 6.5 Hz), 4.82−4.79 (m, 1 H), 4.67 (s, 2 H), 4.20−4.15 (m, 1 H), 3.89−3.81 (m, 2 H), 1.58 (s, 3 H), 1.36 (s, 3 H), 0.89 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.8, 149.3, 137.4, 128.4 (CH), 127.9 (CH), 127.6 (CH), 126.4, 114.8, 112.5 (CH), 110.7, 94.5 (CH), 88.7 (CH), 83.6 (CH), 81.4 (CH), 72.7 (CH_2), 70.8 (CH_2), 63.5 (CH_2), 27.2 (CH_3), 25.9 (CH_3), 25.4 (CH_3), 18.4, −5.31 (CH_3), −5.33 (CH_3); MS (ESI) m/z 566 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{27}H_{38}N_3O_7Si$ (M + H) 544.2479, found 544.2466.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(benzyloxymethyl)-5-cyanouridine (8b′). Compound **8b′** was obtained from the reaction of **6b** (0.7374 g, 1.23 mmol) with NaCN (0.0604 g, 1.23 mmol, 1 equiv) in DMF (15 mL) at 0 °C to room temperature as described for **8a**. The reaction was purified by flash column chromatography (Hex/EtOAc = 8:2) to give the product (**8b′**, foam, 0.3049 g, 46%, R_f = 0.25 (Hex/EtOAc = 7:3)). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.21 (s, 1 H), 7.35−7.26 (m, 5 H), 5.81 (d, 1 H, J = 2.4 Hz), 5.51 (d, 1 H, J = 10.1 Hz), 5.47 (d, 1 H, J = 9.8 Hz), 4.69−4.68 (m, 3 H), 4.65−4.64 (m, 1 H), 4.54−4.52 (m, 1 H), 3.95 (dd, 1 H, J = 1.7 and 11.8 Hz), 3.78 (dd, 1 H, J = 2.3 and 11.9 Hz), 1.60 (s, 3 H), 1.37 (s, 3 H), 0.88 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.9, 149.3, 146.6 (CH), 137.5, 128.3 (CH), 127.8 (CH), 127.7 (CH), 113.8, 113.0, 95.1 (CH), 88.0 (CH), 86.3 (CH), 80.9 (CH), 72.7 (CH_2), 70.9 (CH_2), 63.5, 27.1 (CH_3), 25.8 (CH_3), 25.1 (CH_3), 18.2, −5.4 (CH_3), −5.6 (CH_3); MS (ESI) m/z 566 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{27}H_{37}N_3O_7Si$·Na (M + Na) 566.2298, found 566.2303.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-methyluridine[5] (9a). To a solution of **7**[16] (0.5808 g, 1.3713 mmol) in THF (13.7 mL) were slowly added $ZnCl_2$ (1 M solution in Et_2O, 0.69 mL, 0.69 mmol, 0.5 equiv) and MeMgBr (1 M solution in THF, 6.86 mL, 6.86 mmol, 5 equiv) at 0 °C. After the addition was completed, the reaction mixture was stirred for 3 h and the reaction temperature was allowed to rise to room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution, and the solvent was removed under reduced pressure. The residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was further extracted with $CHCl_3$. The organic portions were washed with saturated aqueous NaCl solution, combined, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to dryness. The reaction was purified by flash column chromatography (Hex/ether = 5:5) to give the product (**9a**, oil, 0.2551 g, 0.6183 mmol, 45%, R_f = 0.11 (Hex/ether = 5:5)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.54 (bs, 1 H), 5.70 (s, 1 H), 5.56 (s, 1 H), 5.21 (d, 1 H, J = 6.4 Hz), 4.82 (dd, 1 H, J = 4.6 and 6.1 Hz), 4.15−4.11 (m, 1 H), 3.82−3.78 (m, 2 H), 2.33 (s, 3 H), 1.53 (s, 3 H), 1.33 (s, 3 H), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.9, 153.2, 150.5, 113.7, 103.0 (CH), 91.7 (CH), 89.5 (CH), 84.2 (CH), 82.0 (CH), 64.2 (CH_2), 27.2 (CH_3), 25.9 (CH_3), 25.3 (CH_3), 20.4 (CH_3), 18.4, −5.28 (CH_3); MS (ESI) m/z 435 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{19}H_{31}N_2O_6Si$ (M − H) 411.1951, found 411.1943.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-ethyluridine[30] (9b). The reaction was purified by flash column chromatography (Hex/EtOAc = 9:1 to 8:2) to give the product (**9b**, oil, 0.9115 g, 58%, R_f = 0.13 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.20 (bs, 1 H), 5.72 (s, 1 H), 5.58 (s, 1 H), 5.19 (dd, 1 H, J = 0.6 and 6.2 Hz), 4.81 (dd, 1 H, J = 4.6 and 6.3 Hz), 4.15−4.11 (m, 1 H), 3.82−2.80 (m, 2 H), 2.62 (q, 2 H, J = 7.3 Hz), 1.54 (s, 3 H), 1.33 (s, 3 H), 1.28 (t, 3 H, J = 7.3 Hz), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.0, 158.2, 150.6, 113.7, 101.0 (CH), 91.2 (CH), 89.5 (CH), 84.3 (CH), 82.1 (CH), 64.2 (CH_2), 27.2 (CH_3), 26.1 (CH_2), 25.9 (CH_3), 25.3 (CH_3), 18.4, 12.1 (CH_3), −5.3 (CH_3); MS (ESI) m/z 449 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{20}H_{34}N_2O_6Si$·Na (M + Na) 449.2084, found 449.2097.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-isopropyluridine (9c). The reaction was purified by flash column chromatography (Hex/EtOAc = 9:1 to 8.5:1.5) to give the product (**9c**, foam, 0.2406 g, 52%, R_f = 0.20 (Hex/EtOAc = 7: 3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.30 (bs, 1 H), 5.80 (s, 1 H), 5.64 (s, 1 H), 5.19 (dd, 1 H, J = 0.8 and 6.6 Hz), 4.81 (dd, 1 H, J = 4.7 and 6.4 Hz), 4.15−4.11 (m, 1 H), 3.83−3.81 (m, 2 H), 3.01−2.94 (m, 1 H), 1.54 (s, 3 H), 1.33 (s, 3 H), 1.29 (d, 3 H, J = 6.7 Hz), 1.26 (d, 3 H, J = 6.7 Hz), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.3, 162.6, 150.8, 113.8, 98.9 (CH), 90.8 (CH), 89.5 (CH), 84.5 (CH), 82.1 (CH), 64.3 (CH_2), 29.6 (CH), 27.3 (CH_3), 25.9 (CH_3), 25.3 (CH_3), 22.1 (CH_3), 21.2 (CH_3), 18.4, −5.24 (CH_3), −5.25 (CH_3); MS (ESI) m/z 463 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{21}H_{37}N_2O_6Si$ (M + 1) 441.2421, found 441.2434.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-*tert*-butyluridine (9d). The reaction was purified by flash column chromatography (Hex/EtOAc = 9:1 to 8.5:1.5) to give the product (**9d**, foam, 0.9043 g, 42%, R_f = 0.23 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.03 (bs, 1 H), 6.17 (s, 1 H), 5.76 (s, 1 H), 5.17 (d, 1 H, J = 6.6 Hz), 4.82−4.80 (m, 1 H), 4.11 (dd, 1 H, J = 5.8 and 11.1 Hz), 3.85−3.83 (m, 2 H), 1.54 (s, 3 H), 1.45 (s, 9 H), 1.33 (s, 3 H), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.7, 163.4, 151.4, 113.8, 100.6 (CH), 92.5 (CH), 89.3 (CH), 84.7 (CH), 82.4 (CH), 64.3 (CH_2), 36.0, 30.5 (CH_3), 27.3 (CH_3), 25.9 (CH_3), 25.4 (CH_3), 18.4, −5.19 (CH_3), −5.23 (CH_3); MS (ESI) m/z

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477 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{22}H_{38}N_2O_6Si$·Na (M + Na) 477.2397, found 477.2412.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-*n*-butyluridine (9e). The reaction was purified by flash column chromatography (Hex/EtOAc = 8:2) to give the product (**9e**, oil, 1.4454 g, 60%, R_f = 0.19 (Hex/EtOAc = 7: 3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.73 (bs, 1 H), 5.68 (s, 1 H), 5.56 (s, 1 H), 5.18 (d, 1 H, J = 6.3 Hz), 4.80 (dd, 1 H, J = 4.6 and 6.2 Hz), 4.14 (dd, 1 H, J = 6.0 and 10.9 Hz), 3.82−3.80 (m, 2 H), 2.55 (t, 2 H, J = 7.7 Hz), 1.66−1.58 (m, 2 H), 1.53 (s, 3 H), 1.47−1.38 (m, 2 H), 1.32 (s, 3 H), 0.96 (t, 3 H, J = 7.3 Hz), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.3, 157.0, 150.8, 113.7, 101.8 (CH), 91.5 (CH), 89.6 (CH), 84.3 (CH), 82.1 (CH), 64.3 (CH_2), 32.6 (CH_2), 29.5 (CH_2), 27.2 (CH_3), 25.9 (CH_3), 25.3 (CH_3), 22.1 (CH_2), 18.4, 13.6 (CH_3), −5.25 (CH_3), −5.28 (CH_3); MS (ESI) m/z 477 (M + Na); HRMS (ESI, TOF) calcd for $C_{22}H_{37}N_2O_6Si$ (M − H) 453.2421, found 453.2417.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-cyclopentyluridine (9f). The reaction was purified by flash column chromatography (Hex/EtOAc = 7.5:2.5) to give the product (**9f**, foam, 0.5257 g, 49%, R_f = 0.23 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.39 (bs, 1 H), 5.84 (s, 1 H), 5.66 (s, 1 H), 5.18 (d, 1 H, J = 6.4 Hz), 4.81 (dd, 1 H, J = 4.9 and 6.1 Hz), 4.13 (dd, 1 H, J = 5.8 and 11.2 Hz), 3.82−3.81 (m, 2 H), 3.03−2.96 (m, 1 H), 2.13−2.02 (m, 2 H), 1.85−1.77 (m, 2 H), 1.76−1.56 (m, 4 H), 1.53 (s, 3 H), 1.33 (s, 3 H), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.4, 160.7, 150.8, 113.7, 98.9 (CH), 91.3 (CH), 89.6 (CH), 84.5 (CH), 82.2 (CH), 64.3 (CH_2), 41.2 (CH), 32.6 (CH_2), 31.8 (CH_2), 27.3 (CH_3), 25.9 (CH_3), 25.3 (CH_3), 24.8 (CH_2), 24.7 (CH_2), 18.4, −5.23 (CH_3), −5.24 (CH_3); MS (ESI) m/z 489 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{23}H_{39}N_2O_6Si$ (M + 1) 467.2580, found 467.2577.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-(3-butenyl)uridine[5] (9g). The reaction was purified by flash column chromatography (Hex/EtOAc = 9:1 to 8.5:1.5) to give the product (**9g**, oil, 0.1236 g, 16%, R_f = 0.23 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.31 (bs, 1 H), 5.85−5.75 (m, 1 H), 5.68 (s, 1 H), 5.56 (s, 1 H), 5.19 (d, 1 H, J = 6.4 Hz), 5.15−5.08 (m, 2 H), 4.81 (dd, 1 H, J = 4.7 and 6.2 Hz), 4.16−4.12 (m, 1 H), 3.82−3.80 (m, 2 H), 2.67 (t, 2 H, J = 7.6 Hz), 2.44−2.38 (m, 2 H), 1.54 (s, 3 H), 1.33 (s, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.7, 156.0, 150.6, 135.1 (CH), 117.1 (CH_2), 113.8, 102.2 (CH), 91.5 (CH), 89.5 (CH), 84.3 (CH), 82.1 (CH), 64.2 (CH_2), 32.3 (CH_2), 31.4 (CH_2), 27.2 (CH_3), 25.9 (CH_3), 25.4 (CH_3), 18.4, −5.24 (CH_3), −5.26 (CH_3); MS (ESI) m/z 453 (100) (M + H); HRMS (ESI, TOF) calcd for $C_{22}H_{36}N_2O_6Si$·Na (M + Na) 475.2240, found 475.2256.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-6-benzyluridine (9i). The reaction was purified by flash column chromatography (Hex/EtOAc = 7.5:2.5 to 7:3) to give the product (**9i**, foam, 0.6495 g, 54%, R_f = 0.18 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.57 (bs, 1 H), 7.37−7.28 (m, 3 H), 7.17 (d, 2 H, J = 6.9 Hz), 5.80 (s, 1 H), 5.31 (s, 1 H), 5.16 (d, 1 H, J = 6.4 Hz), 4.78 (dd, 1 H, J = 4.5 and 6.2 Hz), 4.12 (dd, 1 H, J = 6.0 and 10.8 Hz), 3.90 (s, 2 H), 3.81 (d, 2 H, J = 6.3 Hz), 1.46 (s, 3 H), 1.28 (s, 3 H), 0.88 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.0, 155.8, 150.6, 133.8, 129.2 (CH), 129.1 (CH), 127.8 (CH), 113.6, 103.9 (CH), 91.5 (CH), 89.5 (CH), 84.1 (CH), 82.0 (CH), 64.2 (CH_2), 38.7 (CH_2), 27.1 (CH_3), 25.9 (CH_3), 25.4 (CH_3), 18.5, −5.2 (CH_3); MS (ESI) m/z 511 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{25}H_{36}N_2O_6Si$·Na (M + Na) 511.2240, found 511.2234.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(*p*-methoxybenzyl)-6-ethyluridine (10a). The reaction was purified by flash column chromatography (Hex/EtOAc = 9.5:0.5 to 9:1) to give the product (**10a**, oil, 0.8612 g, 62%, R_f = 0.18 (Hex/EtOAc = 8:2)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40 (d, 2 H, J = 8.6 Hz), 6.81 (d, 2 H, J = 8.6 Hz), 5.71 (s, 1 H), 5.62 (s, 1 H), 5.17 (dd, 1 H, J = 0.8 and 6.4 Hz), 5.01 (d, 1 H, J = 13.7 Hz), 4.95 (d, 1 H, J = 13.7 Hz), 4.88 (dd, 1 H, J = 4.4 and 6.3 Hz), 4.15−4.11 (m, 1 H), 3.83 (dd, 1 H, J = 5.4 and 10.7 Hz), 3.77 (s, 3 H), 3.77−3.72 (m, 1 H), 2.58 (q, 2 H, J = 7.3 Hz), 1.53 (s, 3 H), 1.34 (s, 3 H), 1.25 (t, 3 H, J = 7.3 Hz), 0.88 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.2, 159.0, 155.5, 151.2, 130.6 (CH), 128.9, 113.7 (CH), 113.6, 100.9 (CH), 91.9 (CH), 89.6 (CH), 84.4 (CH), 82.4 (CH), 64.2 (CH_2), 55.2 (CH_3), 43.4 (CH_2), 27.3 (CH_3), 25.93 (CH_3), 25.85 (CH_2), 25.4 (CH_3), 18.5, 12.0 (CH_3), −5.27 (CH_3), −5.31 (CH_3); MS (ESI) m/z 569 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{28}H_{42}N_2O_7Si$·Na (M + Na) 569.2659, found 569.2651.

5′-*O*-*tert*-Butyldimethylsilyl-2′,3′-*O*-isopropylidene-N^3-(benzyloxymethyl)-6-ethyluridine (10b). The reaction was purified by flash column chromatography (Hex/EtOAc = 8:2) to give the product (**10b**, foam, 0.1543 g, 29%, R_f = 0.30 (Hex/EtOAc = 8: 2)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.24 (m, 5 H), 5.70 (s, 1 H), 5.58 (s, 1 H), 5.46 (d, 1 H, J = 9.9 Hz), 5.38 (d, 1 H, J = 9.9 Hz), 5.17 (d, 1 H, J = 6.5 Hz), 4.86 (dd, 1 H, J = 4.7 and 6.2 Hz), 4.67 (s, 2 H), 4.15−4.11 (m, 1 H), 3.86−3.78 (m, 2 H), 2.59 (q, 2 H, J = 7.3 Hz), 1.54 (s, 3 H), 1.34 (s, 3 H), 1.26 (t, 3 H, J = 7.3 Hz), 0.86 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.3, 156.5, 151.2, 137.9, 128.3 (CH), 127.7 (CH), 127.6 (CH), 113.6, 100.7 (CH), 91.6 (CH), 89.5 (CH), 84.3 (CH), 82.1 (CH), 72.2 (CH_2), 70.1 (CH_2), 64.2 (CH_2), 27.2 (CH_3), 26.0 (CH_2), 25.9 (CH_3), 25.4 (CH_3), 18.4, 12.0 (CH_3), −5.27 (CH_3), −5.29 (CH_3); MS (ESI) m/z 569 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{28}H_{42}N_2O_7Si$·Na (M + Na) 569.2659, found 569.2661.

6-Methyluridine[4,31] (11a). Compound **9a** (1.0011 g, 2.4266 mmol) was dissolved in aqueous trifluoroacetic acid (H_2O/TFA = 1 mL:11 mL) at 0 °C and then stirred at room temperature for 1 h. The solvents were removed under reduced pressure. The residue was coevaporated with a small amount of MeOH and then purified by flash column chromatography ($CHCl_3$/MeOH = 9:1, R_f = 0.21) to give the product (**11a**, solid, 0.5594 g, 2.1663 mmol, 89%). The compound was recrystallized from MeOH/EtOAc to give an analytical sample (**11a**, white solid, 0.2526 g, 0.9782 mmol, 40%): mp 171−173 °C (lit.[31] mp 177−178 °C); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.23 (s, 1 H), 5.56 (s, 1 H), 5.46 (d, 1 H, J = 4.2 Hz), 5.19 (d, 1 H, J = 5.4 Hz), 4.93 (d, 1 H, J = 6.4 Hz), 4.66 (t, 1 H, J = 5.8 Hz), 4.54 (dd, 1 H, J = 5.4 and 10.2 Hz), 4.06 (dd, 1 H, J = 6.1 and 12.2 Hz), 3.72−3.68 (m, 1 H), 3.63−3.58 (m, 1 H), 3.47−3.41 (m, 1 H), 2.26 (s, 3 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.8, 154.0, 151.2, 102.9 (CH), 92.2 (CH), 85.2 (CH), 71.4 (CH), 70.1 (CH), 62.3 (CH_2), 20.2 (CH_3); MS (ESI) m/z 281 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{10}H_{14}N_2O_6$·Na (M + Na) 281.0750, found 281.0742.

6-Ethyluridine[32] (11b). Compound **11b** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9.5:0.5 to 9:1) to give the product (**11b**, foam, 0.4389 g, 91%, R_f = 0.18 ($CHCl_3$/MeOH = 9:1)): mp 62−72 °C (lit.[32] mp 119−121 °C); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.25 (s, 1 H), 5.52 (s, 1 H), 5.39 (d, 1 H, J = 3.8 Hz), 5.19 (d, 1 H, J = 5.3 Hz), 4.94 (d, 1 H, J = 6.3 Hz), 4.63 (t, 1 H, J = 5.7 Hz), 4.55 (dd, 1 H, J = 5.2 and 9.6 Hz), 4.07 (dd, 1 H, J = 6.0 and 12.0 Hz), 3.73−3.69 (m, 1 H), 3.63−3.58 (m, 1 H), 3.47−3.41 (m, 1 H), 2.56 (q, 2 H, J = 7.3 Hz), 1.17 (t, 3 H, J = 7.3 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.5, 158.3, 150.7, 100.7 (CH), 91.6 (CH), 84.8 (CH), 71.0 (CH), 69.8 (CH), 62.1 (CH_2), 25.4 (CH_2), 12.4 (CH_3); MS (ESI) m/z 295 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{11}H_{16}N_2O_6$·Na (M + Na) 295.0906, found 295.0915.

6-Isopropyluridine[2] (11c). Compound **11c** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9.7:0.3 to 9:1) to give the product (**11c**, solid, 0.2524 g, 94%). The compound was recrystallized from MeOH/H_2O to give an analytical sample (**11c**, white solid, 0.1356 g, 50%, R_f = 0.15 ($CHCl_3$/MeOH = 9:1)): mp 161−163 °C (lit.[2] mp 204−206 °C); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.27 (s, 1 H), 5.50−5.49 (m, 2 H), 5.20 (d, 1 H, J = 5.2 Hz), 4.93 (d, 1 H, J = 6.6 Hz), 4.64 (t, 1 H, J = 5.7 Hz), 4.52 (dd, 1 H, J = 5.3 and 9.6 Hz), 4.08 (dd, 1 H, J = 6.4 and 12.7 Hz), 3.72−3.68 (m, 1 H), 3.63−3.58 (m, 1 H), 3.47−3.41 (m, 1 H), 2.98−2.91 (m, 1 H), 1.19 (d, 6 H, J = 6.6 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 163.2, 162.9, 151.3, 98.9 (CH), 91.6 (CH), 85.2 (CH), 71.7 (CH), 70.2 (CH), 62.6 (CH_2), 29.4 (CH), 22.4 (CH_3), 21.6 (CH_3); MS (ESI) m/z 309 (100) (M +

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Na); HRMS (ESI, TOF) calcd for $C_{12}H_{18}N_2O_6$·Na (M + Na) 309.1063, found 309.1051. Anal. Calcd for $C_{12}H_{18}N_2O_6$: C, 50.35; H, 6.34; N, 9.79. Found: C, 50.51; H, 6.38; N, 9.43.

6-*tert*-Butyluridine (11d). Compound **11d** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9.5:0.5 to 9:1) to give the product (**11d**, 0.4754 g, 89%). The compound was recrystallized from MeOH/H_2O to give an analytical sample (**11d**, white solid, 0.2425 g, 47%, R_f = 0.13 ($CHCl_3$/MeOH = 9:1)): mp 181−183 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.34 (s, 1 H), 5.78 (d, 1 H, J = 2.9 Hz), 5.55 (s, 1 H), 5.15 (d, 1 H, J = 5.0 Hz), 4.92 (d, 1 H, J = 6.8 Hz), 4.59 (t, 1 H, J = 5.7 Hz), 4.52−4.48 (m, 1 H), 4.12 (dd, 1 H, J = 6.8 and 13.5 Hz), 3.69−3.59 (m, 2 H), 3.49−3.42 (m, 1 H), 1.38 (s, 9 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.9, 162.7, 151.3, 100.1 (CH), 92.8 (CH), 84.5 (CH), 71.9 (CH), 69.8 (CH), 62.2 (CH_2), 35.6, 30.1 (CH_3); MS (ESI) m/z 323 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{13}H_{20}N_2O_6$·Na (M + Na) 323.1219, found 323.1202. Anal. Calcd for $C_{13}H_{20}N_2O_6$: C, 51.99; H, 6.71; N, 9.33. Found: C, 51.92; H, 6.75; N, 9.54.

6-*n*-Butyluridine[11] (11e). Compound **11e** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9:1, R_f = 0.24) to give the product (**11e**, oil, 0.5746 g, 87%): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.25 (s, 1 H), 5.52 (s, 1 H), 5.37 (d, 1 H, J = 3.8 Hz), 5.21 (d, 1 H, J = 5.3 Hz), 4.95 (d, 1 H, J = 6.1 Hz), 4.65 (t, 1 H, J = 5.6 Hz), 4.54 (dd, 1 H, J = 5.2 and 9.5 Hz), 4.07 (dd, 1 H, J = 5.8 and 11.6 Hz), 3.73−3.69 (m, 1 H), 3.63−3.58 (m, 1 H), 3.47−3.40 (m, 1 H), 2.55−2.50 (m, 2 H), 1.59−1.52 (m, 2 H), 1.39−1.30 (m, 2 H), 0.90 (t, 3 H, J = 7.3 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.6, 157.0, 150.8, 101.6 (CH), 91.9 (CH), 84.9 (CH), 71.1 (CH), 69.9 (CH), 62.1 (CH_2), 31.8 (CH_2), 29.5 (CH_2), 21.6 (CH_2), 13.6 (CH_3); MS (ESI) m/z 323 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{13}H_{20}N_2O_6$·Na (M + Na) 323.1219, found 323.1210.

6-Cyclopentyluridine (11f). Compound **11f** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9.9:0.1 to 9:1) to give the product (**11f**, foam, 0. 3949 g, 62%, R_f = 0.18 ($CHCl_3$/MeOH = 9:1)): mp 63−70 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.27 (s, 1 H), 5.53−5.52 (m, 2 H), 5.17 (d, 1 H, J = 5.2 Hz), 4.93 (d, 1 H, J = 6.2 Hz), 4.64 (t, 1 H, J = 5.6 Hz), 4.51 (dd, 1 H, J = 5.3 and 9.0 Hz), 4.08 (dd, 1 H, J = 6.0 and 12.0 Hz), 3.72−3.68 (m, 1 H), 3.63−3.58 (m, 1 H), 3.47−3.41 (m, 1 H), 3.02−2.95 (m, 1 H), 2.09−1.99 (m, 1 H), 1.99−1.90 (m, 1 H), 1.76−1.46 (m, 6 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.6, 160.2, 150.8, 98.6 (CH), 91.6 (CH), 84.7 (CH), 71.2 (CH), 69.8 (CH), 62.1 (CH_2), 40.7 (CH), 32.3 (CH_2), 31.4 (CH_2), 24.4 (CH_2), 24.3 (CH_2); MS (ESI) m/z 335 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{14}H_{20}N_2O_6$·Na (M + Na) 335.1219, found 335.1216.

6-(3-Butenyl)uridine (11g). Compound **11g** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9.9:0.1 to 9:1) to give the product (**11g**, oil, 0.4593 g, 86%, R_f = 0.15 ($CHCl_3$/MeOH = 9:1)): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.26 (s, 1 H), 5.87−5.77 (m, 1 H), 5.53 (s, 1 H), 5.38 (d, 1 H, J = 3.4 Hz), 5.22 (bs, 1 H), 5.12−5.02 (m, 2 H), 4.95 (bs, 1 H), 4.65 (bs, 1 H), 4.56−4.54 (m, 1 H), 4.07 (t, 1 H, J = 6.0 Hz), 3.71 (dd, 1 H, J = 5.9 and 9.3 Hz), 3.60 (dd, 1 H, J = 3.1 and 11.7 Hz), 3.46−3.42 (m, 1 H), 2.64 (t, 2 H, J = 7.3 Hz), 2.40−2.32 (m, 2 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.3, 155.9, 150.7, 136.3 (CH), 116.1 (CH_2), 101.9 (CH), 91.7 (CH), 84.8 (CH), 71.0 (CH), 69.8 (CH), 62.0 (CH_2), 31.3 (CH_2), 31.1 (CH_2); MS (ESI) m/z 321 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{13}H_{17}N_2O_6$ (M − H) 297.1087, found 297.1091.

6-Benzyluridine (11i). Compound **11i** was prepared by the method described for **11a**. The reaction was purified by flash column chromatography ($CHCl_3$/MeOH = 9.5:0.5 to 9:1) to give the product (**11i**, foam, 0.2342 g, 83%, R_f = 0.20 ($CHCl_3$/MeOH = 9:1)): mp 64−72 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.33 (s, 1 H), 7.39−7.35 (m, 2 H), 7.31−7.25 (m, 3 H), 5.50 (d, 1 H, J = 3.7 Hz), 5.28 (s, 1 H), 5.05 (d, 1 H, J = 5.5 Hz), 4.91 (d, 1 H, J = 6.5 Hz), 4.62 (t, 1 H, J = 5.7 Hz), 4.50 (dd, 1 H, J = 5.5 and 9.7 Hz), 4.06 (dd, 1 H, J = 6.2 and 12.4 Hz), 3.99 (d, 1 H, J = 16.6 Hz), 3.93 (d, 1 H, J = 16.7 Hz), 3.65−3.55 (m, 2 H), 3.45−3.39 (m, 1 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.2, 155.6, 150.7, 135.5, 128.9 (CH), 128.8 (CH), 127.1 (CH), 103.3 (CH), 91.8 (CH), 84.7 (CH), 71.1 (CH), 69.7 (CH), 61.9 (CH_2), 37.5 (CH_2); MS (ESI) m/z 357 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{16}H_{17}N_2O_6$ (M − H) 333.1087, found 333.1084.

3′,5′-Di-*O*-*tert*-butyldimethylsilyl-6-cyano-2′-deoxyuridine (13). Compound **13** was prepared from 3′,5′-di-*O*-*tert*-butyldimethylsilyl-5-bromo-2′-deoxyuridine[20] (**12**) by the method described for **8a**. The reaction was purified by flash column chromatography (Hex/EtOAc = 8:2, R_f = 0.23) to give the product (**13**, white solid, 1.0719 g, 2.2251 mmol, 80%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.59 (bs, 1 H), 6.40 (t, 1 H, J = 7.1 Hz), 6.31 (s, 1 H), 4.43−4.40 (m, 1 H), 3.88−3.83 (m, 3 H), 2.63−2.55 (m, 1 H), 2.28−2.21 (m, 1 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.07 (s, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.2, 148.7, 126.5, 113.8 (CH), 111.2, 88.1 (CH), 85.9 (CH), 71.7 (CH), 63.0 (CH_2), 39.2 (CH_2), 26.0 (CH_3), 25.7 (CH_3), 18.5, 17.8, −4.7 (CH_3), −4.9 (CH_3); MS (ESI) m/z 504 (100) (M + Na); HRMS (ESI, TOF) Calcd for $C_{22}H_{38}N_3O_5Si_2$ (M − H) 480.2350, found 480.2350.

3′,5′-Di-*O*-*tert*-butyldimethylsilyl-6-methyl-2′-deoxyuridine[33] (14a). To a solution of **13** (0.6756 g, 1.4024 mmol) in THF (13.7 mL) were slowly added $ZnCl_2$ (1 M solution in Et_2O, 0.70 mL, 0.70 mmol, 0.5 equiv) and MeMgBr (1 M solution in THF, 7.01 mL, 7.01 mmol, 5 equiv) at 0 °C. After the addition was completed, the reaction mixture was stirred for 3 h, and the reaction temperature was allowed to rise to room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution, and the solvent was removed under reduced pressure. The solvent was removed under reduced pressure. The residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was further extracted with $CHCl_3$. The organic portions were combined, washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to dryness. The resulting residue was purified by flash column chromatography (Hex/EtOAc = 7:3, R_f = 0.17) to give the product (**14a**, white solid, 0.1021 g, 0.2169 mmol, 33%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (bs, 1 H), 6.09 (t, 1 H, J = 7.0 Hz), 5.52 (s, 1 H), 4.55−4.50 (m, 1 H), 3.84−3.73 (m, 3 H), 2.87−2.81 (m, 1 H), 2.32 (s, 3 H), 2.10−2.04 (m, 1 H), 0.89 (s, 18 H); 0.07 (s, 6 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.5, 153.7, 150.3, 103.2 (CH), 87.4 (CH), 85.2 (CH), 71.7 (CH), 63.1 (CH_2), 38.4 (CH_2), 26.0 (CH_3), 25.7 (CH_3), 20.7 (CH_3), 18.5, 17.9, −4.7 (CH_3), −4.8 (CH_3), −5.3 (CH_3); MS (ESI) m/z 493 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{22}H_{43}N_2O_5Si_2$ (M − H) 471.2711, found 471.2716.

3′,5′-Di-*O*-*tert*-butyldimethylsilyl-6-ethyl-2′-deoxyuridine (14b). The reaction was purified by flash column chromatography (Hex/EtOAc = 7:3, R_f = 0.24) to give the product (**14b**, oil, 0.7066 g, 68%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.51 (bs, 1 H), 5.97 (dd, 1 H, J = 5.9 and 7.8 Hz), 5.54 (s, 1 H), 4.54−4.50 (m, 1 H), 3.82−3.73 (m, 3 H), 2.98−2.91 (m, 1 H), 2.63−2.56 (m, 2 H), 2.05−1.99 (m, 1 H), 1.23 (t, 3 H, J = 7.3 Hz), 0.88 (s, 18 H); 0.07 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.3, 158.7, 150.4, 101.1 (CH), 87.9 (CH), 85.1 (CH), 72.4 (CH), 63.7 (CH_2), 38.2 (CH_2), 26.1 (CH_2), 26.0 (CH_3), 25.7 (CH_3), 18.4, 17.8, 12.4 (CH_3), −4.7 (CH_3), −4.8 (CH_3), −5.28 (CH_3), −5.31 (CH_3); MS (ESI) m/z 507 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{23}H_{44}N_2O_5Si_2$·Na (M + Na) 507.2686, found 507.2683.

3′,5′-Di-*O*-*tert*-butyldimethylsilyl-6-(3-butenyl)-2′-deoxyuridine (14g). The reaction was purified by flash column chromatography (Hex/EtOAc = 8.5:1.5 to 5:5) to give the product (**14g**, oil, 0.1355 g, 43%, R_f = 0.275 (Hex/EtOAc = 7:3)): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.94 (bs, 1 H), 5.92−5.89 (m, 1 H), 5.82−5.72 (m, 1 H), 5.52 (s, 1 H), 5.11−5.05 (m, 2 H), 4.53−4.49 (m, 1 H), 3.83−3.72 (m, 3 H), 2.99−2.93 (m, 1 H), 2.70−2.56 (m, 2 H), 2.38−2.31 (m, 2 H), 2.04−1.98 (m, 1 H), 0.87 (s, 18 H), 0.064 (s, 3 H), 0.055 (s, 3 H), 0.03 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.4, 156.4, 150.4, 135.2 (CH), 116.8 (CH_2), 102.2 (CH), 88.0 (CH), 85.4 (CH), 72.5 (CH), 63.8 (CH_2), 38.1 (CH_2), 32.5 (CH_2), 31.8 (CH_2), 25.9 (CH_3), 25.7 (CH_3), 18.4, 17.8, −4.8 (CH_3), −4.9 (CH_3), −5.28 (CH_3), −5.32

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(CH_3); MS (ESI) m/z 533 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{25}H_{45}N_2O_5Si_2$ (M − 1) 509.2867, found 509.2897.

6-Methyl-2′-deoxyuridine[9] (15a). To a solution of **14a** (0.0839 g, 0.1782 mmol) in THF (1.7 mL) was added TBAF (1 M in THF, 0.39 mL, 2.2 equiv) at room temperature. The solution was stirred at room temperature for 5 h. The solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography ($CHCl_3$/MeOH = 9:1, R_f = 0.11) to give the product (**15a**, oil, 0.0375g, 0.1548 mmol, 87%): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.16 (s, 1 H), 6.05 (dd, 1 H, J = 6.1 and 8.0 Hz), 5.50 (s, 1 H), 5.13 (d, 1 H, J = 5.0 Hz), 4.65 (t, 1 H, J = 5.6 Hz), 4.29−4.23 (m, 1 H), 3.64−3.57 (m, 2 H), 3.50−3.44 (m, 1 H), 2.72−2.65 (m, 1 H), 2.28 (s, 3 H), 2.04−1.98 (m, 1 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.3, 153.7, 150.6, 102.3 (CH), 87.1 (CH), 84.7 (CH), 70.3 (CH), 61.7 (CH_2), 37.6 (CH_2), 19.8 (CH_3); MS (ESI) m/z 265 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{10}H_{13}N_2O_5$ (M − H) 241.0824, found 241.0828.

6-Ethyl-2′-deoxyuridine[9,32] (15b). Compound **15b** was prepared by the method described for **15a**. The reaction was purified by flash column chromatography ($CHCl_3$/EtOH = 95:5, R_f = 0.05) to give the product (**15b**, oil, 0.2067 g, 91%): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.16 (s, 1 H), 5.97 (dd, 1 H, J = 5.7 and 8.1 Hz), 5.46 (s, 1 H), 5.14 (d, 1 H, J = 5.0 Hz), 4.61 (t, 1 H, J = 5.6 Hz), 4.31−4.25 (m, 1 H), 3.63−3.57 (m, 2 H), 3.50−3.43 (m, 1 H), 2.74−2.69 (m, 1 H), 2.63−2.56 (m, 2 H), 2.06−2.00 (m, 1 H), 1.13 (t, 1 H, J = 7.3 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 163.1, 159.0, 151.1, 100.9 (CH), 87.9 (CH), 85.2 (CH), 71.1 (CH), 62.5 (CH_2), 38.1 (CH_2), 25.8 (CH_2), 12.9 (CH_3); MS (ESI) m/z 255 (M − H); HRMS (ESI, TOF) calcd for $C_{11}H_{15}N_2O_5$ (M − H) 255.0981, found 255.0983.

6-(3-Butenyl)-2′-deoxyuridine (15g). Compound **15g** was prepared by the method described for **15a**. The reaction was purified by flash column chromatography ($CHCl_3$/EtOH = 9.5:0.5 to 8:2) to give the product (**15g**, oil, 0.0139 g, 68%, R_f = 0.23 ($CHCl_3$/EtOH = 9:1)): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.18 (bs, 1 H), 6.00−5.94 (m, 1 H), 5.88−5.74 (m, 1 H), 5.48 (s, 1 H), 5.15−5.01 (m, 3 H), 4.61 (t, 1 H, J = 5.6 Hz), 4.31−4.24 (m, 1 H), 3.68−3.56 (m, 2 H), 3.50−3.42 (m, 1 H), 2.75−2.65 (m, 3 H), 2.34−2.26 (m, 2 H), 2.09−2.00 (m, 1 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.4, 156.2, 150.6, 136.5 (CH), 116.2 (CH_2), 101.7 (CH), 87.4 (CH), 84.8 (CH), 70.6 (CH), 62.0 (CH_2), 37.8 (CH_2), 31.4 (CH_2), 31.2 (CH_2); MS (ESI) m/z 305 (100) (M + Na); HRMS (ESI, TOF) calcd for $C_{13}H_{18}N_2O_5$·Na (M + Na) 305.1113, found 305.1115.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all synthesized compounds and X-ray structural data of compounds **4** and **11d** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

This paper is dedicated to Professor Leroy B. Townsend on the occasion of his 80th birthday.

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