Divergent and Stereocontrolled Approach to the Synthesis of Uracil Nucleosides Branched at the Anomeric Position

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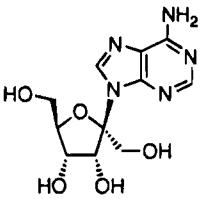
Electrophilic addition of NBS/pivalic acid (bromopivaloyloxylation) to 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (**2**), readily accessible from O^2,2′-anhydrouridine, furnished 1-[2-bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-(pivaloyloxy)-β-D-arabinofuranosyl]uracil (**7**) stereoselectively. This compound (**7**), having a leaving group at the 1′-position as well as 2′-β-Br that could exert anchimeric assistance, serves as versatile intermediate for the stereocontrolled synthesis of various types of 1′-*C*-branched derivatives through nucleophilic substitutions by the use of organosilicon and organoaluminum reagents. The whole sequence constitutes the first example of the conversion of a naturally-occurring nucleoside to the analogues branched at the anomeric position.

Introduction

Occurrence of angustmycin C (**1**)[1] as an antitumor antibiotic has stimulated the synthesis of nucleosides having a carbon substituent at the anomeric position. Although the available synthetic methods[2–6] allow the introduction of various nucleobases, there are considerable limitations in the diversity of the anomeric substituents. This can be attributed to the fact that these methods necessitate starting with sugar precursors, which have to be converted through a lengthy reaction sequences to the requisite 1-*C*-branched derivatives before being condensed with nucleobases.

We have been continuing to explore the chemistry of unsaturated-sugar nucleosides with the directed aim of developing new C–C bond-forming reactions in the sugar portion.[7] In the earlier stage of this project, uracil nucleosides containing a phenylseleno group were synthesized by nucleophilic cleavage of the anhydro derivatives with phenylselenide anions.[8a,b] This combined with the well-known selenoxide *syn*-elimination furnished a mild and regiodefined synthetic route to various types of unsaturated-sugar uracil nucleosides.[9] By applying the above reaction sequence, a mild and high-yield preparation of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (**2**), which is known to be rather unstable,[10] from readily accessible O^2,2′-anhydrouridine became possible.[9]



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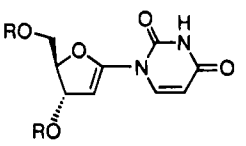
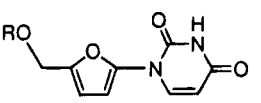


2 R= TBDMS



3 R= TBDMS

We thought **2** could serve as a substrate for the introduction of carbon substituents into the anomeric position through Lewis acid-mediated allylic rearrangement, as reported previously in the synthesis of 4′-*C*-branched 2′,3′-didehydro-2′,3′-dideoxyuridines.[7d] However, when **2** was treated with allyltrimethylsilane in the

[⊗] Abstract published in *Advance ACS Abstracts,* January 15, 1995.

(1) (a) Yüntsen, H.; Yonehara, H.; Ui, H. *J. Antibiot., Ser. A* **1954**, *7*, 113–115. (b) Yüntsen, H.; Ohkuma, K.; Ishii, Y. *Ibid.* **1956**, *9*, 195–201. (c) Schroeder, W.; Hoeksema, H *J. Am. Chem. Soc.* **1959**, *81*, 1767–1768. (d) McCarthy, J. R., Jr.; Robins, R. K.; Robins, M. J. *Ibid.* **1968**, *90*, 4993–4999.

(2) From D-fructose: (a) Farkas, J.; Sorm, F. *Tetrahedron Lett.* **1962**, 813–814; (b) *Collect. Czech. Chem. Commun.* **1963**, *28*, 882–886. (c) Hrebabecky, H.; Farkas, J.; Sorm, F. *Ibid.* **1972**, *37*, 2059–2065. (d) Prisbe, E. J.; Smejkal, J.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1976**, *41*, 1836–1846. (e) Grouiller, A.; Chattopadhyaya, J. *Acta Chem. Scand.* **1984**, *B38*, 367–373. (f) Elliott, R. D.; Niwas, S.; Riordan, J. M.; Montgomery, J. A.; Secrist, J. A., III. *Nucleosides Nucleotides* **1992**, *11*, 97–119. (g) Bouali, A.; Ewing, D. F.; Mackenzie, G. *Ibid.* **1994**, *13*, 491–499.

(3) From D-fructose *via* an aminooxazoline intermediate: (a) Holy, A. *Nucleic Acids Res.* **1974**, *1*, 289–298. (b) Tatsuoka, T.; Imao, K.; Suzuki, K. *Heterocycles* **1986**, *24*, 617–620. (c) Yoshimura, Y.; Ueda, T.; Matsuda, A. *Tetrahedron Lett.* **1991**, *32*, 4549– 4552. (d) Yoshimura, Y.; Otter, B. A.; Ueda, T.; Matsuda, A. *Chem. Pharm. Bull.* **1992**, *40*, 1761–1769.

(4) From a nitrosugar: Mahmood, K.; Vasella, A.; Bernet, B. *Helv. Chim. Acta* **1991**, *74*, 1555–1584.

(5) From D-ribonolactone: (a) Faivre-Buet, V.; Grouiller, A.; Descotes, G. *Nucleosides Nucleotides* **1992**, *11*, 1411–1424; (b) **1992**, *11*, 1651–1660. (c) Hayakawa, H.; Miyazawa, M.; Tanaka, H.; Miyasaka, T. *Ibid.* **1994**, *13*, 297–308.

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(7) (a) Haraguchi, K.; Tanaka, H.; Miyasaka, T. *Tetrahedron Lett.* **1990**, *31*, 227–230. (b) Haraguchi, K.; Tanaka, H.; Itoh, Y.; Miyasaka, T. *Ibid.* **1991**, *32*, 770–780. (c) Haraguchi, K.; Itoh, Y.; Tanaka, H.; Miyasaka, T. *Ibid.* **1991**, *32*, 3391–3394. (d) Haraguchi, K.; Tanaka, H.; Itoh, Y.; Saito, S.; Miyasaka, T. *Ibid.* **1992**, *33*, 2841– 2844. (e) Haraguchi, K.; Itoh, Y.; Tanaka, H.; Akita, M.; Miyasaka, T. *Tetrahedron* **1993**, *42*, 1371–1390. (f) Kittaka, A.; Tanaka, H.; Odanaka, Y.; Ohnuki, K.; Yamaguchi, K.; Miyasaka, T. *J. Org. Chem.* **1994**, *59*, 3636–3641.

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(9) Haraguchi, K.; Tanaka, H.; Maeda, H.; Itoh, Y.; Miyasaka, T. *J. Org. Chem.* **1991**, *56*, 5401–5408.

(10) The preparation and properties of **2** have been briefly reported: Robins, M. J.; Trip, E. M. *Tetrahedron Lett.* **1974**, 3369–3372.

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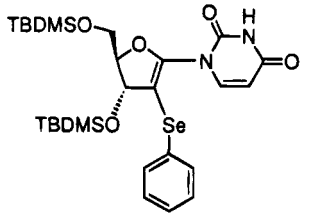
presence of $SnCl_4$ (in CH_2Cl_2, below −70 °C, for 1 h), an elimination reaction took place to give **3** in 50% yield as the sole product. This led us to investigate the present study.[11]

We describe herein the utility of **2** in a new and divergent synthesis of the title compounds, which consists of electrophilic addition (bromopivaloyloxylation) to **2** and subsequent stereocontrolled nucleophilic substitutions using either organosilicon or organoaluminum reagents.

Electrophilic Addition to 1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (2). As a promising way to construct C−C bonds at the anomeric position, nucleophilic substitution was selected. To accomplish this stereoselectively, introduction of a leaving group into the 1′-position of **2** as well as the presence of a certain 2′-β-substituent, which can exert neighboring group participation, were indispensable.

On the basis of these considerations, acetoxyphenylselenation of **2** was first examined.[12,13] When **2** was reacted with PhSeOAc in toluene at room temperature, TLC analysis of the reaction mixture (hexane/EtOAc = 3/1) showed complete conversion of **2** (R_f 0.27) to a product (R_f 0.15) which was assumed to be a mixture of the adducts. However, this product appeared to be rather unstable, giving a complex mixture upon attempted purification by silica gel column chromatography, from which only **4**[14] and **5**[15] were isolated. The formation of **4** can be explained, at least in part, by assuming an α-anion-stabilizing effect of the selenium atom[16] which facilitates elimination of AcOH from the initially formed adduct.



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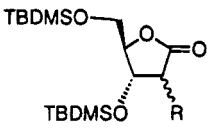


5 R= SePh

6 R= Br

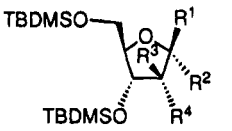
Acetoxybromination of **2**, by using NBS and AcOH in CH_2Cl_2, again formed a mixture of unstable adducts which decomposed to **6**[17] during column chromatography. The observed formation of the lactone derivatives **5** and **6** indicated that the carbonyl carbon of the introduced C-1′ acetoxy group was highly susceptible to nucleophilic attack, and consequently the uracil moiety had served as a leaving group.

Table 1. Bromopivaloyloxylation of 2[a]

entry	solvent	PivOH (equiv)	NBS (equiv)	yield[b] (%)	ratio of **7**−**10** (**7**:**8**:**9**:**10**)	ratio of *anti*/*syn*	face selectivity (β/α)
1	CH_2Cl_2	5	2	66	62:6:26:6	7.3/1	2.1/1
2	CCl_4	5	2	68	46:32:12:10	1.4/1	3.5/1
3	benzene	5.4	2	67	45:35:12:8	1.3/1	4/1
4	THF	5	2.1	*c*			
5	CH_2Cl_2	22	1.3	80	54:18:19:9	2.7/1	2.6/1
6	EtOAc	25	1.2	77	37:38:7:18	1/1.3	3/1
7	ether	24	1.2	82	33:50:4:13	1/1.7	4.9/1
8	dioxane	25	1.2	80	33:48:7:12	1/1.5	4.3/1
9	$(i\text{-Pr})_2O$	25	1.2	68	41:44:6:9	1/1.1	5.6/1
10	ether[d]	5	1,2	91	82:1:17:0	99/1	4.9/1

[a] All reactions were carried out at room temperature for 0.5 h. [b] Combined yield of the adducts (**7**−**10**). [c] The isolated adducts were contaminated with unknown impurities. [d] Triethylamine (5 equiv) was added.

We found that the pivaloyloxy group, when introduced into the anomeric position in place of the acetoxy group, offered enough stability to the adduct. Thus, when bromopivaloyloxylation of **2** was conducted in CH_2Cl_2 by using pivalic acid (PivOH, 5 equiv) and NBS (2 equiv), a mixture of four adducts (**7**−**10**) was obtained in 66% yield after silica gel column chromatography, as shown in entry 1 in Table 1 (the ratios of **7**−**10** listed in Table 1 were calculated from the 400 MHz ^1H NMR spectrum of the mixture by integrating H-6).



7 R^1= uracil-1-yl, R^2= OPiv, R^3= Br, R^4= H

8 R^1= OPiv, R^2= uracil-1-yl, R^3= Br, R^4= H

9 R^1= OPiv, R^2= uracil-1-yl, R^3= H, R^4= Br

10 R^1= uracil-1-yl, R^2= OPiv, R^3= H, R^4= Br

Each adduct was isolated from the mixture by HPLC separation, and their stereochemistry was determined as described below. Among the four adducts, the main product **7** was obtained as crystals from EtOAc−hexane (mp 157−159 °C). Its X-ray crystallographic analysis[18] showed that **7** was an *anti*-adduct with required 2′-β-Br and 1′-α-OPiv configurations. In the ^1H NMR spectrum of **7**, H-2′ appeared as a singlet ($J_{2',3'}$ values of other adducts: **8**, 1.1 Hz; **9**, 4.4 Hz; **10**, 5.1 Hz), which is consistent with the trans-disposition of H-2′ and H-3′. Compound **8**, which gave the second smallest $J_{2',3'}$ value, was therefore assumed to be the *syn*-adduct having the same 2′-configuration as **7**. When **8** was treated with

(11) Part of this study has been published as a communication: Haraguchi, K.; Itoh, Y.; Tanaka, H.; Miyasaka, T. *Tetrahedron Lett.* **1993**, *34*, 6913−6916.

(12) For examples of acetoxyphenylselenation: (a) Reich, H. J. *J. Org. Chem.* **1974**, *39*, 428−429. (b) Sharpless, K. B.; Lauer, R. F. *Ibid.* **1974**, *39*, 429−430. (c) Clive, D. L. J.; Beaulieu, P. L. *J. Chem. Soc., Chem. Commun.* **1983**, 307−309.

(13) Electrophilic addition of PhSeCl to furanoid glycals has recently been used for the synthesis of 2′-deoxynucleosides: El-Laghdach, A.; Díaz, Y.; Castillón, S. *Tetrahedron Lett.* **1993**, *34*, 2821−2822.

(14) Physical data of **4** are as follows: ^1H NMR ($CDCl_3$) δ 0.02, 0.06, and 0.07 (12H, each as s), 0.86 and 0.89 (18H, each as s), 3.74 (1H, dd, J_{gem} = 10.6, $J_{4',5'a}$ = 6.2 Hz), 3.85 (1H, dd, $J_{4',5'b}$ = 5.1 Hz), 4.53 (1H, m), 4.90 (1H, d, $J_{3',4'}$ = 2.9 Hz), 5.68 (1H, d, $J_{5,6}$ = 8.1 Hz), 7.10 (1H, d), 7.20−7.25 (3H, m), 7.38−7.41 (2H, m), 8.71 (1H, br); FAB-MS (fragment ion peaks corresponding to ^{80}Se and ^{78}Se are shown) *m*/*z* 553 and 551 (M^+ − Bu-*t*).

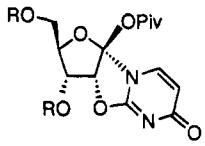
(15) Physical data of **5** (a mixture of two diastereomers) are as follows: ^1H NMR ($CDCl_3$) δ 0.02, 0.04, 0.06, 0.07, 0.14, and 0.21 (12H, each as s), 0.85, 0.88, 0.81, and 0.96 (18H, each as s), 3.72−3.81 (2H, m), 3.86 and 4.08 (1H, each as d, $J_{2,3}$ = 2.9 and 6.2 Hz), 4.25 and 4.30 (1H, each as m), 4.46 and 4.63 (1H, each as dd, *J* = 2.9 and 4.4, *J* = 3.7 and 6.2 Hz), 7.25−7.37 and 7.68−7.71 (5H, each as m); FAB-MS (ion peaks corresponding ^{80}Se and ^{78}Se are shown) *m*/*z* 517 and 515 (M^+ + H).

(16) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986.

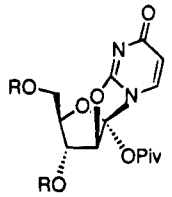
(17) Physical data of **6** (a mixture of two diastereomers) are as follows: ^1H NMR ($CDCl_3$) δ 0.08, 0.13, 0.14, and 0.19 (12H, each as s), 0.88, 0.90, and 0.93 (18H, each as s), 3.71−4.04 (2H, m), 4.17−4.76 (3H, m); FAB-MS *m*/*z* 441 and 439 (M^+ + H), 383 and 381 (M^+ − Bu-*t*).

(18) Although the X-ray analysis of **7** gave confirmation of its stereochemistry, the coordinates of substituents on the 3′- and 5′-*O*-silicon atoms were not obtained due to instability of the crystal during the measurement. Partial X-ray data as well as an ORTEP drawing of **7** can be obtained from the authors on request.

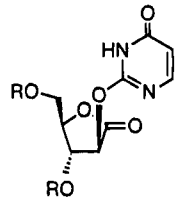
DBU in CH_2Cl_2 (at room temperature, 1.5 h) the O^2,2′-anhydronucleoside **11** was formed, while similar treatment of **7** resulted in the recovery of the starting material. The stereochemistry of **9** and **10** was determined again by applying the above anhydronucleoside chemistry. In the case of **10**, partial decomposition of the initially formed **12** occurred to give **13** as an additional product.



11 R= TBDMS



12 R= TBDMS



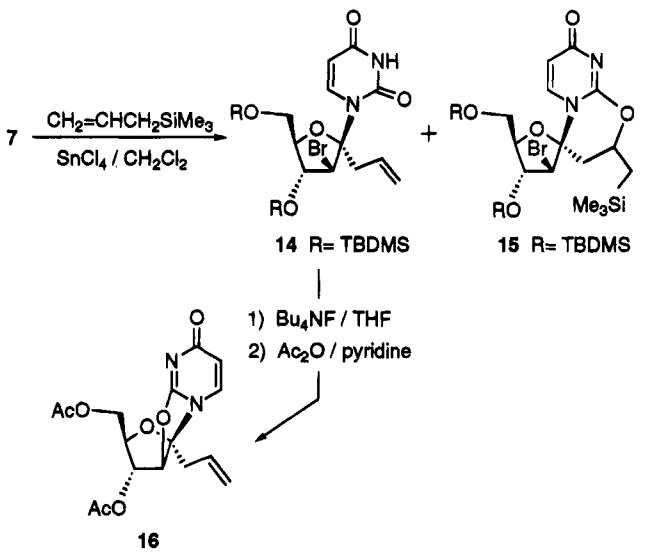
13 R= TBDMS

Several attempts to optimize the reaction conditions in favor of the formation of **7** were carried out, the results of which are summarized in Table 1. As can be seen in entries 1–3, the use of 2 equiv of NBS tends to decrease the yields of adducts, due to the formation of a considerable amount of polar byproducts which were assumed to have resulted from nucleophilic attack by succinimide [FAB-MS *m*/*z* 656 and 654 (M^+ + Na); ^{1}H NMR ($CDCl_3$) δ 2.75 (methylene protons of succinimido moiety)]. When the amount of NBS was reduced to 1.2–1.3 equiv and a large excess of PivOH (22–25 equiv) was used (entries 5–9), higher yields of adducts were obtained, except entry 9 where significant amounts of polar unknown products were formed. Preferential β-face selectivity is always the case irrespective of the solvent used, presumably due to the presence of the bulky 3′-α-*O*-TBDMS group, while the ratio of *anti*/*syn*-addition varies from solvent to solvent.

When the bromopivaloyloxylation of **2** was carried out in ether with the addition of Et_3N, which apparently increases the nucleophilicity of PivOH, almost exclusive *anti*-addition was observed (entry 10). It is worth noting, from a practical viewpoint, that the desired adduct **7** can be readily separated from other diastereomers simply by short-column chromatography followed by crystallization (isolated yield of **7**, *ca.* 55%).

Nucleophilic Substitution between 7 and Organosilicon Reagents. It is known that allylsilanes react efficiently with a wide range of electrophilic substrates, including acetals and ethyl orthoformate.[19] We first examined the reaction of **7** with allyltrimethylsilane in the presence of $SnCl_4$. When a CH_2Cl_2 solution of **7** and the allylsilane was treated with $SnCl_4$ at −40 °C and the mixture was allowed to warm to −20 °C, two products **14** and **15** were formed as shown in Scheme 1. The ^{1}H NMR and FAB-MS spectra of the less polar product **14**, isolated in 65% yield, were in full agreement with the depicted structure. The stereochemistry of **14** was confirmed by converting it to the O^2,2′-anhydro derivative **16**, which was analyzed by X-ray crystallography.[20] The UV spectrum of the highly polar product **15** (isolated in 25% yield) in MeOH showed a typical absorption pattern (λ_{max} 229 nm, $\lambda_{shoulder}$ 250 nm) of anhydrouridines. This

Scheme 1



together with its ^{1}H NMR and FAB-MS [*m*/*z* 649 and 647 (M^+ + H)] spectra suggested the cyclized structure **15**, which had apparently been formed by intramolecular trapping of the incipient silicon-stabilized β-carbocation with the base moiety.[21,22] Under similar reaction conditions, the use of cinnamyltrimethylsilane gave **17** (52%, a mixture of two diastereomers, *ca.* 10:1.3) as the sole product.

Recently, ribofuranosylthymine having a cyano group at the anomeric position has been synthesized from a ribofuranosyl cyanide *via* its photobromination and subsequent condensation with the nucleobase.[6] In our case, the use of cyanotrimethylsilane enabled us to introduce a cyano group at the anomeric position of **7** to furnish **18** in 80% yield.

In terms of the scope of the present method, it may offer considerable merit that applicable organosilicon reagents can be extended to silyl enol ethers, since various types of this class of reagents are readily prepared either by enolate trapping or by hydrosilylation.[23] The enol ethers derived from acetophenone and acetone, upon reacting with **7** in CH_2Cl_2 in the presence of $SnCl_4$, gave the 1′-*C*-phenacyl (**19**, 69%) and acetonyl (**20**, 30%) derivatives, respectively. In the case of the latter, the elimination product **3** (11%) was also formed. Compound **21** was prepared in 32% yield (a single isomer, configuration of the newly constructed chiral center is not known) by the use of the enol ether prepared from cyclopentanone.

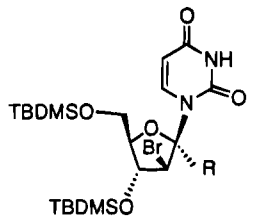
(19) For a review: Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1–22.

(20) The coordinates of **16** can be obtained, on request, from the Cambridge Crystallographic Data Centre, University of Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

(21) Compound **15** was obtained as a single isomer, although configuration of the β- carbon to $SiMe_3$ is not clear at the present time. A similar cyclization has been observed in the reaction between allyltrimethylsilane and perfluoroacetone: Abel, E. W.; Rowley, R. J. *J. Organomet. Chem.* **1975**, *84*, 199–229.

(22) When **15** was treated with Bu_4NF (4 equiv) in THF for 2 h and then reacted with benzoic anhydride (5 equiv) in a one-pot manner, 1-(1-*C*-allyl-3,5-di-*O*-benzoyl-2-bromo-2-deoxy-β-D-arabinofuranosyl)-uracil was obtained in 61% yield. Physical data of this compound are as follows: mp 212–214 °C (EtOH–Et_2O); UV (MeOH) λ_{max} 231 nm (ϵ 31 300) and 261 nm (ϵ 13 800), λ_{min} 250 nm (ϵ 12 200); ^{1}H NMR ($CDCl_3$) δ 2.99 and 3.40 (2H, each as dd, J_{gem} = 14.7, J = 5.5 and 8.8 Hz), 4.58 (1H, m), 4.80 and 4.95 (2H, each as dd, J_{gem} = 12.1, $J_{4',5'}$ = 5.9 and 4.0 Hz), 5.10–5.17 (3H, m), 5.67 (1H, d, $J_{5,6}$ = 8.1 Hz), 5.68 (1H, m), 5.82 (1H, d, $J_{2',3'}$ = 2.9 Hz), 7.44–7.71 (6H, m), 8.03–8.12 (5H, m), 8.67 (1H, br); FAB-MS *m*/*z* 557 and 555 (M^+ + H), 515 and 513 (M^+ − $CH_2CH{=}CH_2$). Anal. Calcd for $C_{26}H_{23}BrN_2O_7{\cdot}H_2O$: C, 54.46; H, 4.39; N, 4.89. Found: C, 54.81; H, 4.17; N, 4.81.

(23) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988.



17 R= CH(Ph)CH=CH_2

18 R= CN

19 R= CH_2COPh

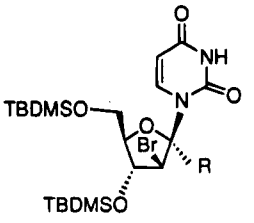
20 R= CH_2COMe

21 R= cyclopentanon-2-yl

Synthesis of 1′-*C*-Alkyl and Alkynyl Derivatives Based on the Reactions between 7 and Organoaluminum Reagents. To compensate limitations associated with organosilicon reagents, other organometallics which allow the introduction of simple alkyl and alkynyl groups were neccessary. Several organometallic reagents have been used for the cleavage of acetals.[24] In the present study, the application of organoaluminum reagents[25] were investigated, since their inherent Lewis acid character would certainly simplify the reaction conditions.

When **7** was reacted with Me_3Al in CH_2Cl_2 at 0 °C for 3.5 h, the 1′-*C*-methyl derivative **22** was obtained in 73% yield. Similarly, **23** was prepared in 59% yield by the use of Et_3Al. The reaction of **7** with $(i\text{-}Bu)_3Al$ gave a mixture of three products, from which **24** was isolated in only 10% yield. As can be anticipated, the main pathway was due to nucleophilic attack of hydride which resulted in the formation of **25** (36%). An additional product in this reaction appeared to be the elimination product **26** (10%). Despite the fact that alkyl halides react with trialkylaluminum,[26] no evidence was obtained for replacement or reduction of the 2′-Br throughout the above experiments.

It is known that an alkynyl group in dialkylalkynylaluminum can be selectively tranferred to electrophilic substrates.[27,28] When $Et_2AlC{\equiv}CPh$, prepared from Et_2AlCl and $LiC{\equiv}CPh$, was reacted with **7** in CH_2Cl_2 at 0 °C, the reaction proceeded very sluggishly. Even after 5.5 h, a large amount of **7** (54%) remained intact and an inseparable mixture of **23** (9%) and **27** (15%) was obtained (the yields were calculated based on ^1H NMR spectroscopy). The use of $PhC{\equiv}CAlCl_2$ was an improvement both in terms of reaction time (3.5 h) and yield of **27** (50%) but again a considerable amount of **7** (33%) was recovered. We found $PhC{\equiv}CAlEtCl$ to be the most suitable reagent for the present purpose: after reaction for 1 h, **27** was isolated in 69% yield without forming **23**. Compounds **28** (86%) and **29** (76%) were prepared in a similar manner by using $C_4H_9C{\equiv}CAlEtCl$ and $Me_3SiC{\equiv}CAlEtCl$, respectively.



22 R= Me

23 R= Et

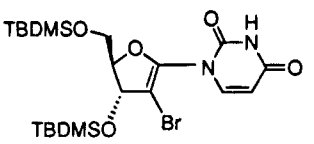
24 R= CH_2CHMe_2

25 R= H

27 R= $C{\equiv}CPh$

28 R= $C{\equiv}CC_4H_9$

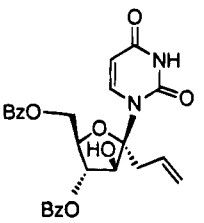
29 R= $C{\equiv}CSiMe_3$



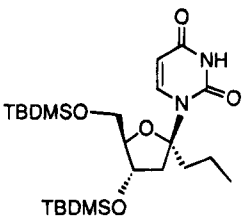
26

Conclusion

The present study shows that **7** is a highly versatile intermediate for the stereospecific synthesis of a range of 1′-*C*-branched derivatives. This combined with our previous study[9] for the preparation of **2** from uridine has disclosed the first report on the transformation of a naturally-occurring nucleoside to the analogues branched at the anomeric position. The 2′-bromine atom in these compounds, which had been introduced to control the stereochemistry of C−C bond formation, can be used for further modification of the sugar portion, as exemplified here by the preparation of the arabino (**30**) and 2′-deoxy (**31**) analogues from **14** (see the Experimental Section). Further experiments are in progress to extend this methodology to purine nucleosides.



30



31

Experimental Section

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. ^1H NMR spectra were measured at 23 °C (internal standard, Me_4Si) with either a JEOL JNM-GX 400 or a JEOL JNM-FX 100 spectrometer. Mass spectra (MS) were taken on a JEOL SX-102A spectrometer in FAB mode (*m*-nitrobenzyl alcohol as a matrix). Ultraviolet spectra (UV) were recorded on a JASCO Ubest-55 spectrophotometer. Column chromatography was carried out on silica gel (silica gel 60, Merck). Thin layer chromatography (TLC), including preparative TLC, was performed on silica gel (precoated silica gel plate F_{254}, Merck). HPLC was carried out on a Shimadzu LC-6AD with a Shim-pack PREP-SIL (H)-KIT column (2 × 25 cm).

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-(pivaloyloxy)-β-D-arabinofuranosyl]uracil (7) and Other Adducts (8−10). To a mixture of **2** (2.38 g, 5.23 mmol), pivalic acid (2.67 g, 26.2 mmol), and Et_3N (3.66 mL, 26.2 mmol) in ether (40 mL) was added finely powdered NBS (1.13 g, 6.33 mmol). After being stirred for 0.5 h at room temperature, the reaction mixture was treated with aqueous $NaHCO_3$ and then extracted with $CHCl_3$. Silica gel column chromatography (hexane/EtOAc = 9/1) gave a mixture of adducts (3.03 g, 91%). Crystallization of the mixture from EtOAc−hexane gave analytically pure crystals of **7** (1.83 g, 55%, mp 157−159 °C).

(24) Lindell, S. D.; Elliott, J. D.; Johnson, W. S. *Tetrahedron Lett.* **1984**, *25*, 3947−3950 and references cited therein.

(25) Mori, A.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *J. Organomet. Chem.* **1985**, *285*, 83−94.

(26) Miller, D. B. *J. Org. Chem.* **1966**, *31*, 908−912.

(27) For an example: Hooz, J.; Layton, R. B. *J. Am. Chem. Soc.* **1971**, *93*, 7320−7322.

(28) An exception has been reported in the reaction between 1-bromoadamantane and 1-hexynyldiethylaluminum: Negishi, E.; Baba, S. *J. Am. Chem. Soc.* **1975**, *97*, 7385−7387.

Physical data of **7** are as follows: UV (MeOH) λ_{max} 254 nm (ϵ 10 700), λ_{min} 227 nm (ϵ 3500); ^{1}H NMR ($CDCl_3$) δ 0.09, 0.12, 0.17 (12H, each as s), 0.91 and 0.92 (18H, each as s), 1.20 (9H, s), 3.87−3.89 (2H, m), 4.12 (1H, m), 4.73 (1H, d, $J_{3',4'}$ = 3.3 Hz), 4.89 (1H, s), 5.68 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.6 Hz), 7.82 (1H, d), 8.05 (1H, br); FAB-MS *m/z* 659 and 657 (M^+ + Na), 579 and 577 (M^+ − Bu-*t*), 535 and 533 (M^+ − OPiv). Anal. Calcd for $C_{26}H_{47}BrN_2O_7Si_2$: C, 49.12; H, 7.45; N, 4.41. Found: C, 49.13; H, 7.72; N, 4.42.

Compounds **8**−**10** were isolated by HPLC (hexane/EtOAc = 7/1) separation of the reaction mixture obtained as shown in entry 1 of Table 1.

Physical data of **8** are as follows: ^{1}H NMR ($CDCl_3$) δ 0.06 and 0.09 (12H, each as s), 0.79 and 0.91 (18H, each as s), 1.22 (9H, s), 3.96−3.98 (2H, m), 4.09 (1H, m), 4.55 (1H, d, $J_{2',3'}$ = 1.1 Hz), 5.01 (1H, d), 5.70 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.2 Hz), 7.79 (1H, d), 8.19 (1H, br); FAB-MS *m/z* 637 and 635 (M^+ + H), 579 and 577 (M^+ − Bu-*t*), 535 and 533 (M^+ − OPiv). Physical data of **9** are as follows: ^{1}H NMR ($CDCl_3$) δ 0.08, 0.14, and 0.16 (12H, each as s), 0.91 and 0.93 (18H, each as s), 1.17 (9H, s), 3.69 (1H, dd, J_{gem} = 12.1, $J_{4',5'a}$ = 4.8 Hz), 3.96 (1H, dd, $J_{4',5'b}$ = 1.8 Hz), 4.27 (1H, m), 4.41 (1H, dd, $J_{2',3'}$ = 4.4, $J_{3',4'}$ = 8.8 Hz), 5.17 (1H, d), 5.70 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.2 Hz), 7.91 (1H, d), 8.75 (1H, br); FAB-MS *m/z* 659 and 657 (M^+ + Na), 579 and 577 (M^+ − Bu-*t*), 535 and 533 (M^+ − OPiv).

Physical data of **10** are as follows: ^{1}H NMR ($CDCl_3$) δ 0.07, 0.08, 0.09, and 0.14 (12H, each as s), 0.90 and 0.91 (18H, each as s), 1.22 (9H, s), 3.74 and 4.07 (2H, each as dd, J_{gem} = 12.5, $J_{4',5'}$ = 1.5 Hz), 4.22 (1H, dd, $J_{2',3'}$ = 5.1, $J_{3',4'}$ = 8.8 Hz), 4.32 (1H, m), 5.35 (1H, d), 5.65 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 1.8 Hz), 8.08 (1H, d), 8.58 (1H, br); FAB-MS *m/z* 637 and 635 (M^+ + H), 579 and 577 (M^+ − Bu-*t*), 535 and 533 (M^+ − OPiv).

Anhydronucleosides 11 and 12. Formation from 8 and 10. Compound **8** (10 mg) was treated with DBU (3 μL) in CH_2Cl_2 (3 mL) at room temperature for 1.5 h. Silica gel column chromatography ($CHCl_3$/EtOH = 20/1) of the reaction mixture followed by purification by preparative TLC ($CHCl_3$/EtOH = 50/1) gave **11** (4.4 mg, 50%). Similar DBU treatment of **10** (11.4 mg) gave **12** (2.0 mg, 20%) and **13** (6.3 mg, 75%).

Physical data of **11** are as follows: UV (MeOH) λ_{max} 252 nm, λ_{min} 218 nm; ^{1}H NMR ($CDCl_3$) δ 0.04, 0.05, 0.14, and 0.17 (12H, each as s), 0.89 and 0.91 (18H, each as s), 1.24 (9H, s), 3.74 (1H, m), 3.78 (1H, dd, J_{gem} = 12.1, $J_{4',5'a}$ = 3.7 Hz), 3.91 (1H, dd, $J_{4',5'b}$ = 1.5 Hz), 4.82 (1H, dd, $J_{2',3'}$ = 6.2, $J_{3',4'}$ = 8.1 Hz), 5.23 (1H, d), 6.14 (1H, d, $J_{5,6}$ = 7.7 Hz), 7.34 (1H, d); FAB-MS *m/z* 555 (M^+ + H), 497 (M^+ − Bu-*t*).

Physical data of **12** are as follows: UV (MeOH) λ_{max} 224 nm, $\lambda_{shoulder}$ 245 nm, λ_{min} 214 nm; ^{1}H NMR ($CDCl_3$) δ −0.03, 0.01, 0.12, and 0.17 (12H, each as s), 0.79 and 0.91 (18H, each as s), 1.24 (9H, s), 3.64 and 3.83 (2H, each as dd, J_{gem} = 12.2, $J_{4',5'}$ = 2.2 Hz), 4.45 (1H, m), 4.63 (1H, dd, $J_{2',3'}$ = 4.8, $J_{3',4'}$ = 8.1 Hz), 5.33 (1H, d), 6.10 (1H, d, $J_{5,6}$ = 7.7 Hz), 7.31 (1H, d); FAB-MS *m/z* 555 (M^+ + H).

Physical data of **13** are as follows: UV (MeOH) λ_{max} 267 nm, λ_{min} 234 nm; ^{1}H NMR ($CDCl_3$) δ 0.01, 0.09, and 0.10 (12H, each as s), 0.85 and 0.91 (18H, each as s), 3.82 (1H, dd, J_{gem} = 12.5, $J_{4',5'a}$ = 2.6 Hz), 4.00 (1H, dd, $J_{4',5'b}$ = 1.8 Hz), 4.22 (1H, m), 4.85 (1H, t, $J_{2',3'}$ = $J_{3',4'}$ = 8.8 Hz), 5.94 (1H, d), 6.16 (1H, d, $J_{5,6}$ = 6.6 Hz), 7.71 (1H, d), 10.73 (1H, br); FAB-MS *m/z* 471 (M^+ + H), 413 (M^+ − Bu-*t*).

1-[1-*C*-Allyl-2-bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-arabinofuranosyl]uracil (14). A mixture of **7** (500 mg, 0.79 mmol) and allyltrimethylsilane (628 μL, 3.95 mmol) in CH_2Cl_2 (30 mL) was cooled to −40 °C. To this was added, a CH_2Cl_2 solution of $SnCl_4$ (1.0 M solution, 1.03 mL, 1.03 mmol), and the reaction mixture was allowed to warm to −20 °C over 2 h. The mixture was partitioned between $CHCl_3$ and aqueous $NaHCO_3$. Silica gel column chromatography (hexane/EtOAc = 8/1) of the $CHCl_3$ layer gave **14** (295 mg, 65%). Further elution with hexane/EtOAc = 1/1 gave **15** (126 mg, 25%).

Physical data of **14** are as follows: mp 133−134 °C (EtOAc−hexane); UV (MeOH) λ_{max} 262 nm (ϵ 12 200), λ_{min} 230 nm (ϵ 1800); ^{1}H NMR ($CDCl_3$) δ 0.10, 0.12, and 0.15 (12H, each as s), 0.91 and 0.92 (18H, each as s), 3.10 (1H, dd, J = 15.0 and 6.2 Hz), 3.21 (1H, dd, J = 15.0 and 8.6 Hz), 3.82 (1H, dd, J_{gem} = 10.3, $J_{4',5'a}$ = 7.3 Hz), 3.92 (1H, dd, $J_{4',5'b}$ = 5.5 Hz), 4.07 (1H, m), 4.64 (1H, d, $J_{3',4'}$ = 2.2 Hz), 4.66 (1H, s), 5.08 (2H, m), 5.61 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 5.65 (1H, m), 7.65 (1H, d), 8.37 (1H, br); FAB-MS *m/z* 577 and 575 (M^+ + H), 535 and 533 (M^+ − allyl), 519 and 517 (M^+ − Bu-*t*). Anal. Calcd for $C_{24}H_{43}BrN_2O_5Si_2$: C, 50.07; H, 7.53; N, 4.87. Found: C, 49.74; H, 7.63; N, 4.78.

Physical data of **15** are as follows: mp 154−156 °C (EtOH−hexane); UV (MeOH) λ_{max} 229 nm (ϵ 11 900), $\lambda_{shoulder}$ 250 nm (ϵ 7800); ^{1}H NMR ($CDCl_3$) δ 0.12, 0.14, and 0.20 (21H, each as s), 0.90 and 0.94 (18H, each as s), 1.00 (1H, dd, J = 14.5 and 6.1 Hz), 1.23 (1H, dd, J = 14.5 and 8.3 Hz), 2.38−2.40 (2H, m), 3.78−3.85 (2H, m), 4.03 (1H, dd, J_{gem} = 12.1, $J_{4',5'b}$ = 1.8 Hz), 4.19 (1H, d, $J_{2',3'}$ = 8.8 Hz), 4.59 (1H, t, $J_{3',4'}$ = 8.4 Hz), 4.85 (1H, m), 6.07 (1H, d, $J_{5,6}$ = 7.7 Hz), 7.89 (1H, d); FAB-MS *m/z* 649 and 647 (M^+ + H). Anal. Calcd for $C_{27}H_{51}BrN_2O_5Si_3$: C, 50.05; H, 7.93; N, 4.32. Found: C, 49.92; H, 8.20; N, 4.16.

3′,5′-Di-*O*-acetyl-1′-*C*-allyl-O^2,2′-anhydrouridine (16). A mixture of **14** (54 mg, 0.09 mmol) and Bu_4NF (THF solution, 0.40 mmol) in THF (5 mL) was stirred at room temperature for 14 h. The resulting desilylated product was purified by short column chromatography on silica gel ($CHCl_3$/EtOH = 10/1) and then treated with Ac_2O (57 μL, 0.60 mmol) in pyridine (3 mL) for 12 h. After evaporation of the solvent, the reaction mixture was chromatographed on a silica gel column ($CHCl_3$/EtOH = 50/1). This gave **16** (17.7 mg, 54%), which was crystallized from EtOH: mp 216−218 °C; UV (MeOH) λ_{max} 224 nm (ϵ 10 800) and 251 nm (ϵ 9400), $\lambda_{shoulder}$ 240 nm (ϵ 4000), λ_{min} 237 nm (ϵ 8300); ^{1}H NMR ($CDCl_3$) δ 1.99 and 2.15 (6H, each as s), 2.89 (2H, m), 4.00 and 4.27 (2H, each as dd, J_{gem} = 12.5, $J_{4',5'}$ = 3.7 Hz), 4.50 (1H, m), 5.08 (1H, s), 5.29−5.36 (3H, m), 5.65 (1H, m), 6.10 (1H, d, $J_{5,6}$ = 7.3 Hz), 7.32 (1H, d); FAB-MS *m/z* 351 (M^+ + H). Anal. Calcd for $C_{16}H_{18}N_2O_7$: C, 54.86; H, 5.18; N, 8.00. Found: C, 54.76; H, 5.13; N, 7.87.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-(1-phenylallyl)-β-D-arabinofuranosyl]uracil (17). This compound was obtained as a syrup (diastereomeric mixture, *ca.* 10:1.3) in 52% yield from **7** (100 mg, 0.16 mmol) and (α-phenylallyl)trimethylsilane (152 μL, 0.80 mmol) by the same procedure as described for the preparation of **14**.

^{1}H NMR data shown below are those of the major diastereomer: UV (MeOH) λ_{max} 260 nm (ϵ 12 300), λ_{min} 232 nm (ϵ 4100); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.10, and 0.13 (12H, each as s), 0.85 and 0.92 (18H, each as s), 3.60 (1H, m), 3.73 (1H, dd, J_{gem} = 11.4, $J_{4',5'a}$ = 4.0 Hz), 3.90 (1H, dd, $J_{4',5'b}$ = 4.4 Hz), 4.53 (1H, dd, $J_{2',3'}$ = 4.0, $J_{3',4'}$ = 5.1 Hz), 4.80 (1H, d), 4.89 (1H, d, J = 9.2 Hz), 5.15 (1H, dd, J = 10.3 and 1.5 Hz), 5.20 (1H, d, J = 17.2 Hz), 5.46 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.6 Hz), 6.38 (1H, m), 7.23−7.32 (5H, m), 7.58 (1H, d), 8.32 (1H, br); FAB-MS *m/z* 675 and 673 (M^++Na), 595 and 593 (M^+ − Bu-*t*). Anal. Calcd for $C_{30}H_{47}BrN_2O_5Si_2$: C, 55.28; H, 7.27; N, 4.30. Found: C, 55.22; H, 7.38; N, 4.14.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-1-*C*-cyano-2-deoxy-β-D-arabinofuranosyl]uracil (18). This compound was obtained as a powder in 80% yield from **7** (100 mg, 0.16 mmol) and trimethylsilyl cyanide (107 μL, 0.80 mmol) by the same procedure as described for the preparation of **14**: UV (MeOH) λ_{max} 253 nm (ϵ 10 300), λ_{min} 227 nm (ϵ 3400); IR (KBr) 2200 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$) δ 0.11, 0.14, and 0.18 (12H, each as s), 0.92 and 0.94 (18H, each as s), 3.88−3.96 (2H, m), 4.39 (1H, m), 4.70 (1H, m), 5.00 (1H, d, $J_{2',3'}$ = 0.7 Hz), 5.78 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.58 (1H, d), 8.62 (1H, br); FAB-MS *m/z* 562 and 560 (M^+ + H), 504 and 502 (M^+ − Bu-*t*). Anal. Calcd for $C_{22}H_{38}BrN_3O_5Si_2 \cdot 1/2H_2O$: C, 46.39; H, 6.90; N, 7.38. Found: C, 46.22; H, 6.92; N, 7.40.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-phenacyl-β-D-arabinofuranosyl]uracil (19). This compound was obtained as a syrup in 69% yield from **7** (100 mg, 0.16 mmol) and 1-phenyl-1-((trimethylsilyl)oxy)ethylene (164 μL, 0.80 mmol) by the same procedure as for the preparation of **14**, except that the reaction mixture was allowed to warm to −10 °C over 4 h. The eluent used for column chromatographic purification was hexane/EtOAc = 4/1: UV (MeOH) λ_{max} 250 nm (ϵ 20 300), λ_{min} 223 nm (ϵ 7400); ^{1}H NMR ($CDCl_3$)

δ 0.06, 0.17, and 0.22 (12H, each as s), 0.88 and 0.97 (18H, each as s), 3.80 (1H, dd, J_{gem} = 10.3, $J_{4',5'a}$ = 8.4 Hz), 3.88 (1H, dd, $J_{4',5'b}$ = 5.1 Hz), 4.10 and 4.31 (2H, each as d, J = 16.5 Hz), 4.14 (1H, m), 4.74 (1H, d, $J_{3',4'}$ = 1.8 Hz), 4.80 (1H, s), 5.65 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.2 Hz), 7.41–7.45 and 7.54–7.58 (3H, m), 7.73 (1H, d), 7.86–7.88 (2H, m), 7.80 (1H, br); FAB-MS m/z 677 and 675 (M^+ + Na), 543 and 541 (M^+ − Bu-t). Anal. Calcd for $C_{29}H_{45}BrN_2O_6Si_2$: C, 53.28; H, 6.94; N, 4.28. Found: C, 53.12; H, 7.01; N, 4.08.

1-[1-*C*-Acetonyl-2-bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-arabinofuranosyl]uracil (20). This compound was obtained as a powder in 30% yield from **7** (100 mg, 0.16 mmol) and (isopropenyloxy)trimethylsilane (134 μL, 0.80 mmol) by the same procedure for the preparation of **14**, except that the reaction mixture was allowed to warm to 0 °C over 3 h and then stirred for 18 h at room temperature. The reaction mixture was purified by preparative TLC (hexane/EtOAc = 4/1). Compound **3** was also obtained in 11% yield: UV (MeOH) λ_{max} 261 nm (ϵ 11 500), λ_{min} 230 nm (ϵ 2400); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.13, and 0.16 (12H, each as s), 0.90 and 0.93 (18H, each as s), 2.10 (3H, s), 3.68 (2H, s), 3.81 (1H, dd, J_{gem} = 10.3, $J_{4',5'a}$ = 8.1 Hz), 3.91 (1H, dd, $J_{4',5'b}$ = 5.5 Hz), 4.11 (1H, m), 4.63 (1H, s), 4.66 (1H, d, $J_{3',4'}$ = 1.8 Hz), 5.69 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 7.77 (1H, d), 8.87 (1H, br); FAB-MS m/z 615 and 613 (M^+ + Na), 593 and 591 (M^+ + H), 535 and 533 (M^+ − Bu-t). Anal. Calcd for $C_{24}H_{43}BrN_2O_6Si_2$: C, 48.72; H, 7.32; N, 4.73. Found: C, 48.97; H, 7.41; N, 4.52.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-1-*C*-(cyclopentanon-2-yl)-2-deoxy-β-D-arabinofuranosyl]uracil (21). This compound was obtained as crystals (mp 183–186 °C, EtOAc–hexane) in 32% yield from **7** (100 mg, 0.16 mmol) and 1-(trimethylsilyloxy)cyclopentene (142 μL, 0.80 mmol) by the same procedure for the preparation of **14**, except that the reaction mixture was allowed to warm to −10 °C over 4 h. The eluent used for column chromatographic purification was hexane/EtOAc = 4/1. The starting material **7** was also isolated in 31% recovery: UV (MeOH) λ_{max} 261 nm (ϵ 12 700), λ_{min} 230 nm (ϵ 2700); ^{1}H NMR ($CDCl_3$) δ 0.09, 0.14, and 0.19 (12H, each as s), 0.89 and 0.91 (18H, each as s), 1.66–1.85 and 2.16–2.26 (6H, each as m), 3.22 (1H, t, J = 8.4 Hz), 3.85–3.86 (2H, m), 4.01 (1H, m), 4.65 (1H, dd, $J_{2',3'}$ = 2.2, $J_{3',4'}$ = 3.3 Hz), 5.35 (1H, d), 5.68 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.2 Hz), 7.92 (1H, d), 8.80 (1H, br); FAB-MS m/z 619 and 617 (M^+ + H), 561 and 559 (M^+ − Bu-t). Anal. Calcd for $C_{26}H_{45}BrN_2O_6Si_2 \cdot 1/2H_2O$: C, 49.83; H, 7.40; N, 4.47. Found: C, 49.51; H, 7.34; N, 4.34.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-methyl-β-D-arabinofuranosyl]uracil (22). To a solution of **7** (100 mg, 0.16 mmol) in CH_2Cl_2 (8 mL) was added Me_3Al (hexane solution, 1.3 mmol) at 0 °C. After being stirred for 3.5 h at 0 °C, the reaction mixture was partitioned between $CHCl_3$ and aqueous $NaHCO_3$. Preparative TLC (hexane/EtOAc = 4/1) of the $CHCl_3$ layer gave **22** (63 mg, 73%) as a syrup: UV (MeOH) λ_{max} 261 nm (ϵ 12 300), λ_{min} 230 nm (ϵ 2400); ^{1}H NMR ($CDCl_3$) δ 0.09, 0.11, and 0.14 (12H, each as s), 0.90 and 0.91 (18H, each as s), 1.96 (3H, s), 3.80 and 3.90 (2H, each as dd, J_{gem} = 10.3, $J_{4',5'}$ = 7.3, 5.9 Hz), 4.08 (1H, m), 4.59 (1H, d, $J_{3',4'}$ = 2.2 Hz), 4.68 (1H, s), 5.66 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 7.78 (1H, d), 8.82 (1H, br); FAB-MS m/z 573 and 571 (M^+ + Na). Anal. Calcd for $C_{22}H_{41}BrN_2O_5Si_2 \cdot 1/2H_2O$: C, 47.30; H, 7.58; N, 5.01. Found: C, 47.69; H, 7.53; N, 4.88.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-ethyl-β-D-arabinofuranosyl]uracil (23). This compound was obtained as a powder in 59% yield from **7** (100 mg, 0.16 mmol) and Et_3Al (hexane solution, 1.3 mmol) by the same procedure as for the preparation of **22**: UV (MeOH) λ_{max} 262 nm (ϵ 12 100), λ_{min} 230 nm (ϵ 2500); ^{1}H NMR ($CDCl_3$) δ 0.09, 0.10, and 0.14 (12H, each as s), 0.81 (3H, t, J = 7.3 Hz), 0.89 and 0.91 (18H, each as s), 2.30 and 2.51 (2H, each as m), 3.81 and 3.90 (2H, each as dd, J_{gem} = 10.3, $J_{4',5'}$ = 7.0, 5.5 Hz), 3.96 (1H, m), 4.61 (1H, d, $J_{3',4'}$ = 2.2 Hz), 4.64 (1H, s), 5.64 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 7.73 (1H, d), 8.77 (1H, br); FAB-MS m/z 587 and 585 (M^+ + Na). Anal. Calcd for $C_{23}H_{43}BrN_2O_5Si_2$: C, 49.01; H, 7.69; N, 4.97. Found: C, 49.13; H, 7.89; N, 4.97.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-isobutyl-β-D-arabinofuranosyl]uracil (24). This compound was obtained as a syrup in 10% yield from **7** (50 mg, 0.08 mmol) and $(Me_2CHCH_2)_3Al$ (hexane solution, 0.64 mmol) by the same procedure for the preparation of **22**. Compounds **25** (36%) and **26** (10%) were also isolated.

Physical data of **24** are as follows: UV (MeOH) λ_{max} 262 nm (ϵ 10 800), λ_{min} 231 nm (ϵ 2000); ^{1}H NMR ($CDCl_3$) δ 0.10, 0.11, and 0.14 (12H, each as s), 0.79 and 0.96 (6H, each as d, J = 6.6 Hz), 0.90 and 0.92 (18H, each as s), 1.66 (1H, m), 2.26 and 2.43 (2H, each as dd, J_{gem} = 15.4, J = 6.2 Hz), 3.81 and 3.90 (2H, each as dd, J_{gem} = 10.3, $J_{4',5'}$ = 7.3, 5.5 Hz), 4.00 (1H, m), 4.60 (1H, d, $J_{3',4'}$ = 2.2 Hz), 4.61 (1H, s), 5.66 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.6 Hz), 7.78 (1H, d), 8.23 (1H, br); FAB-MS m/z 615 and 613 (M^+ + Na), 593 and 591 (M^+ + H), 535 and 533 (M^+ − Bu-t). Anal. Calcd for $C_{25}H_{47}BrN_2O_5Si_2$: C, 50.74; H, 8.01; N, 4.73. Found: C, 51.12; H, 8.25; N, 4.54.

Physical data of **25** obtained as a syrup are as follows: UV (MeOH) λ_{max} 261 nm (ϵ 10 400), λ_{min} 229 nm (ϵ 2300); ^{1}H NMR ($CDCl_3$) δ 0.11, 0.13, and 0.18 (12H, each as s), 0.90 and 0.94 (18H, each as s), 3.82–3.87 (2H, m), 3.96 (1H, dd, J_{gem} = 12.1, $J_{4',5'}$ = 4.8 Hz), 4.48 and 4.55 (2H, each as t, $J_{1',2'} = J_{2',3'} = J_{3',4'}$ = 5.5 Hz), 5.71 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 6.20 (1H, d), 7.69 (1H, d), 8.22 (1H, br); FAB-MS m/z 537 and 535 (M^+ + H), 479 and 477 (M^+ − Bu-t). Anal. Calcd for $C_{21}H_{39}BrN_2O_5Si_2 \cdot 1/4H_2O$: C, 46.70; H, 7.37; N, 5.19. Found: C, 46.76; H, 7.44; N, 5.10.

Physical data of **26** are as follows: mp 151–152 °C (EtOAc–hexane); UV (MeOH) λ_{max} 253 nm (ϵ 9900), λ_{min} 235 nm (ϵ 8500); ^{1}H NMR ($CDCl_3$) δ 0.09, 0.15, and 0.18 (12H, each as s), 0.90 and 0.92 (18H, each as s), 3.74 and 3.82 (2H, each as dd, J_{gem} = 11.0, $J_{4',5'}$ = 5.9, 4.8 Hz), 4.45 (1H, m), 4.94 (1H, d, $J_{3',4'}$ = 2.9 Hz), 5.79 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 1.5 Hz), 7.20 (1H, d), 8.60 (1H, br); FAB-MS m/z 535 and 533 (M^+ + H), 477 and 475 (M^+ − Bu-t). Anal. Calcd for $C_{21}H_{37}BrN_2O_5Si_2$: C, 47.27; H, 6.99; N, 5.25. Found: C, 47.18; H, 7.15; N, 5.21.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-(phenylethynyl)-β-D-arabinofuranosyl]uracil (27). To a solution of phenylacetylene (70 μL, 0.64 mmol) in toluene (1 mL) was added BuLi (hexane solution, 0.64 mmol) at 0 °C. The mixture was stirred for 0.5 h and then treated with $EtAlCl_2$ (hexane solution, 0.64 mmol) for further 0.5 h at 0 °C. The reagent (PhC≡CAlEtCl) thus prepared was added to a solution of **7** (50 mg, 0.08 mmol) in CH_2Cl_2 (3 mL), and the reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was partitioned beween $CHCl_3$ and aqueous $NaHCO_3$. Silica gel column chromatography (hexane/EtOAc = 6/1) of the $CHCl_3$ layer gave **27** (35 mg, 69%) as a syrup: UV (MeOH) λ_{max} 244 (ϵ 28 100) and 255 nm (ϵ 28 800), λ_{min} 218 (ϵ 9600) and 249 nm (ϵ 26 100), $\lambda_{shoulder}$ 233 nm (ϵ 16 500); ^{1}H NMR ($CDCl_3$) δ 0.10, 0.11, and 0.15 (12H, each as s), 0.85 and 0.93 (18H, each as s), 3.92–3.93 (2H, m), 4.31 (1H, m), 4.70 (1H, d, $J_{3',4'}$ = 3.7 Hz), 5.02 (1H, s), 5.70 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 7.27–7.36 (3H, m), 7.43–7.46 (2H, m), 7.78 (1H, d), 8.56 (1H, br); FAB-MS m/z 659 and 657 (M^+ + Na), 579 and 577 (M^+ − Bu-t). Anal. Calcd for $C_{29}H_{43}BrN_2O_5Si_2 \cdot 1/2H_2O$: C, 54.02; H, 6.88; N, 4.34. Found: C, 53.87; H, 6.94; N, 4.13.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-(hexyn-1-yl)-β-D-arabinofuranosyl]uracil (28). This compound was obtained as a syrup in 86% yield from **7** (50 mg, 0.08 mmol) by the same procedure as for the preparation of **27**, except that the reagent (C_4H_9C≡CAlEtCl) was added at −40 °C and the reaction mixture was allowed to warm to −10 °C over 2 h. The eluent used for silica gel column chromatography is hexane/EtOAc = 10/1: UV (MeOH) λ_{max} 259 nm (ϵ 11 500), λ_{min} 228 nm (ϵ 2600); ^{1}H NMR ($CDCl_3$) δ 0.09, 0.10, and 0.14 (12H, each as s), 0.90 (3H, m), 0.91 (18H, s), 1.38 and 1.49 (4H, each as m), 2.23 (2H, t, J = 7.0 Hz), 3.88–3.89 (2H, m), 4.18 (1H, m), 4.63 (1H, dd, $J_{2',3'}$ = 0.7, $J_{3',4'}$ = 4.0 Hz), 4.86 (1H, d), 5.66 (1H, dd, $J_{5,6}$ = 8.4, $J_{5,NH}$ = 2.2 Hz), 7.72 (1H, d), 8.93 (1H, br); FAB-MS m/z 559 and 557 (M^+ − Bu-t). Anal. Calcd for $C_{27}H_{47}BrN_2O_5Si_2$: C, 52.67; H, 7.69; N, 4.55. Found: C, 52.67; H, 7.83; N, 4.68.

1-[2-Bromo-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-1-*C*-(trimethylsilyl)ethynyl-β-D-arabinofuranosyl]uracil (29). This compound was obtained as a syrup in 76% yield from **7** (50 mg, 0.08 mmol) by the same procedure as for

the preparation of **27**. The eluent used for silica gel column chromatography is hexane/EtOAc = 10/1: UV (MeOH) λ_{max} 260 nm (ϵ 12 900), λ_{min} 229 nm (ϵ 3200); ^{1}H NMR ($CDCl_3$) δ 0.10, 0.15, and 0.17 (21H, each as s), 0.91 and 0.92 (18H, each as s), 3.87 and 3.92 (2H, each as dd, J_{gem} = 11.4, $J_{4',5'}$ = 4.4 Hz), 4.20 (1H, m), 4.66 (1H, d, $J_{3',4'}$ = 4.8 Hz), 4.87 (1H, s), 5.67 (1H, d, $J_{5,6}$ = 8.4 Hz), 7.70 (1H, d), 8.41 (1H, br); FAB-MS m/z 633 and 631 ($M^+ + H$), 575 and 573 ($M^+ - Bu$-*t*). Anal. Calcd for $C_{26}H_{47}BrN_2O_5Si_3$: C, 49.43; H, 7.50; N, 4.43. Found: C, 49.58; H, 7.65; N, 4.26.

1-[1-*C*-Allyl-3,5-di-*O*-benzoyl-β-D-arabinofuranosyl]-uracil (30). A mixture of **14** (58 mg, 0.10 mmol) and Bu_4NF (THF solution, 0.40 mmol) in THF (5 mL) was stirred at room temperature for 24 h and then treated with benzoic anhydride (113 mg, 0.50 mmol) for a further 6 h. The reaction mixture was partitioned between $CHCl_3$ and aqueous $NaHCO_3$, and the $CHCl_3$ layer was chromatographed on a silica gel column (CH_2Cl_2/EtOH = 100/1). This gave 1′-*C*-allyl-3′,5′-di-*O*-benzoyl-O^2,2′-anhydrouridine (52.7 mg), which was dissolved in DMF (2 mL) containing 2 N HCl (2 mL). After being heated for 12 h at 60 °C, the reaction mixture was partitioned between EtOAc and H_2O. Silica gel column chromatography (hexane/EtOAc = 1/1) of the organic layer gave **30** (38.4 mg, 78%), which was crystallized from DMF–H_2O (mp 206–208 °C): UV (MeOH) λ_{max} 230 nm (ϵ 29 600) and 265 nm (ϵ 14 400), λ_{min} 249 nm (ϵ 10 600); ^{1}H NMR ($CDCl_3$) δ 2.79 and 3.17 (2H, each as dd, J_{gem} = 14.3, J = 5.9 and 8.8 Hz), 3.49 (1H, d, J = 5.9 Hz, D_2O exchangeable), 4.62–4.70 (3H, m), 4.87 (1H, d), 5.12 (2H, m), 5.46 (1H, d, $J_{3',4'}$ = 1.8 Hz), 5.63 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 5.75 (1H, m), 7.27–7.51 and 7.57–7.63 (6H, m), 7.78 (1H, d), 8.03–8.08 (4H, m), 8.46 (1H, br, D_2O exchangeable); FAB-MS m/z 493 ($M^+ + H$), 475 ($M^+ - OH$). Anal. Calcd for $C_{26}H_{24}N_2O_8$: C, 63.41; H, 4.91; N, 5.69. Found: C, 63.44; H, 4.86; N, 5.70.

3′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-1′-*C*-propyluridine (31). A mixture of **14** (60 mg, 0.10 mmol) and Et_3N (28 μL, 0.20 mmol) in EtOH (5 mL) was hydrogenated in the presence of 10% Pd–C (10 mg) for 18 h. The catalyst was removed by filtration, and the filtrate was purified by silica gel column chromatography (hexane/EtOAc = 8/1). This gave **31** (32.8 mg, 74%) as a syrup: UV (MeOH) λ_{max} 264 nm (ϵ 10 800), λ_{min} 232 nm (ϵ 1800); ^{1}H NMR ($CDCl_3$) δ 0.03, 0.04, and 0.06 (12H, each as s), 0.85–0.87 (21H, m), 1.06 and 1.44 (2H, each as m), 1.92 and 2.28 (2H, each as m), 2.42 and 2.77 (2H, each as dd, J_{gem} = 14.3, $J_{2',3'}$ = 4.4 and 6.2 Hz), 3.61 and 3.68 (2H, each as dd, J_{gem} = 11.4, $J_{4',5'}$ = 3.3 and 4.0 Hz), 4.00 (1H, m), 4.24 (1H, m), 5.59 (1H, dd, $J_{5,6}$ = 8.1, $J_{5,NH}$ = 2.2 Hz), 7.95 (1H, d), 9.14 (1H, br); FAB-MS m/z 521 ($M^+ + Na$). Anal. Calcd for $C_{24}H_{46}N_2O_5Si_2 \cdot 1/2H_2O$: C, 56.76; H, 9.33; N, 5.52. Found: C, 57.10; H, 9.26; N, 5.14.

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