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Hydrogermylation of 5-Ethynyluracil Nucleosides: Formation of 5-(2-Germylvinyl)uracil and 5-(2-Germylacetyl)uracil Nucleosides

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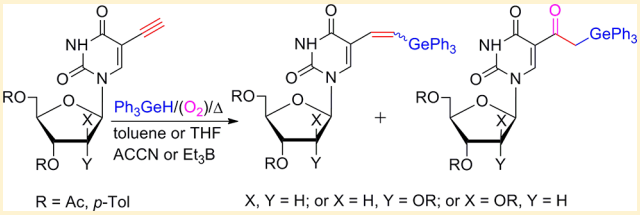
Supporting Information

ABSTRACT: A stereoselective radical-mediated hydrogermylation of the protected 5-ethynyluracil nucleosides with trialkyl-, triaryl,- or tris(trimethylsilyl)germanes gave (*Z*)-5-(2-germylvinyl)uridine, 2′-deoxyuridine, or *ara*-uridine as major products. Reaction of the *β*-triphenylgermyl vinyl radical intermediate with oxygen and fragmentation of the resulting peroxyradical provided also 5-[2-(triphenylgermyl)acetyl]-pyrimidine nucleosides in low to moderate yields. Thermal isomerization of the latter in MeOH occurred via a four-centered activated complex, and subsequent hydrolysis of the resulting *O*-germyl substituted enol yielded 5-acetyluracil nucleosides in quantitative yield.



A broad spectrum of biological activity has been described for 5-substituted pyrimidine nucleosides.[1] One especially potent and selective antiviral drug of this class is (*E*)-5-(2-bromovinyl)-2′-deoxyuridine (BVDU).[2] Pronounced cytotoxity and significant antiviral activity have been reported for 1-(*β*-D-arabinofuranosyl)-5-ethenyluracil[3] and 5-ethynyl-2′-deoxyuridine.[4] The synthesis of the numerous 5-substituted pyrimidine nucleosides via Pd-assisted routes have been reviewed.[5]

The (*E*)-5-[2-(tributylstannyl)vinyl]uracil nucleosides, prepared by coupling of (*E*)-1,2-bis(tributylstannyl)ethene with 5-iodoracil precursors[6] or via radical hydrostannylation of 5-ethynyluracil precursors,[7,8] have been developed as convenient substrates for a mild and rapid radiohalogenation via halodestannylation reactions.[6−9] However, the tendency of (*E*)-5-[2-(tributylstannyl)vinyl]arabinosyluridine[8] and 5-trimethylstannyl araU[9] to protiodestannylation was noted.

The 5-[2-(trimethylsilyl)ethynyl]uracil nucleosides, prepared by Sonogashira coupling reactions between protected 5-iodoracil nucleosides with (trimethylsilyl)acetylene,[5,10] have been hydrogenated to give (*Z*)-5-[2-(trimethylsilyl)vinyl]uracil products.[11] Solvent-dependent isomerization of the latter into the *E* isomer was observed.[10] The (*E*)-5-[2-(trimethylsilyl)-vinyl]-2′-deoxyuridine has been also prepared by direct Pd-catalyzed coupling of (*E*)-2-(tributylstannyl)-1-(trimethylsilyl)-ethene with protected 5-iodo-2′-deoxyuridine.[12] The 5-vinyl silanes were converted to 5-(2-halovinyl)uracil products upon treatment with XeF_2 and metal halides[11] and were also utilized for the radioiodination via iododesilylations reactions[10,12]

The chemistry[13] and biological activity of organogermanium compounds have been reviewed.[14,15] A few biologically active germane-modified nucleoside analogues have been developed. Among them, the 5-trimethylgermyluracil and 1-(2-tetrahydrofuranyl)-5-trimethylgermyluracil exhibit cytotoxicity to melanoma B16 cells.[16] The 1-(2-tetrahydrofuranyl)-6-trialkylgermyl-5-fluorouracil derivatives have caused inhibition of DNA and RNA biosynthesis in *Frhk* cells almost twice as efficiently as the renowned antitumor drug Ftorafur.[17] The 5-trimethylgermyl-2′-deoxyuridine, which is one of the few known examples of germanium-containing nucleoside analogues, was shown to inhibit HSV-1 replication in vitro and block incorporation of thymidine into DNA of cancer ovarian cells.[18]

Pd(0)-catalyzed,[19,20] Lewis acid-promoted,[21,22] radical-mediated,[23] and ultrasound- and microwave-accelerated[24] hydrogermylation of alkynes provide vinylgermanes with high regio and stereoselectivity. Germyldesulfonylation protocols has been also developed for the synthesis of vinyl- and (*α*-fluoro)-vinylgermanes.[25] Herein, we report that hydrogermylation of the 5-ethynyluracil nucleosides with trialkyl-, triaryl,- and tris(trimethylsilyl)germanes in addition to the expected 5-(2-germylvinyl)uracil nucleosides provides also access to 5-(2-germylacetyl)uracil nucleosides which can be converted to 5-acetyluracil products.

Several hydrogermylation approaches for the preparation of 5-(2-germylvinyl)uracil nucleosides of type **2** were initially tested. Thus, treatment of the acetyl protected 1-(*β*-D-arabinofuranosyl)-5-ethenyluracil[26] **1** with Ph_3GeH in the presence of 1,1′-azobis(cyclohexanecarbonitrile) (ACCN), as radical initiator, in toluene at 90 °C (method A) produced predominantly the *Z*-vinylgermanes **2a** (*E*/*Z*, 5:95; Scheme 1). The ^1H NMR spectra established the configuration for *E*-**2a** (*J* = 18.8 Hz) and *Z*-**2a** (*J* = 13.5 Hz) diastereomers. The formation of the *Z* isomer as the major product was in agreement with the expected[23] *anti*-addition of germyl radical to the triple bond. Careful purification of the reaction mixture on a silica gel column gave not only pure *Z*-**2a** (47%) but also led to the isolation of a new product, whose structure was assigned (vide infra) as 5-[2-(triphenylgermyl)acetyl]uracil (*β*-germyl ketone) derivative **4a** (12%; Table 1, entry 1).

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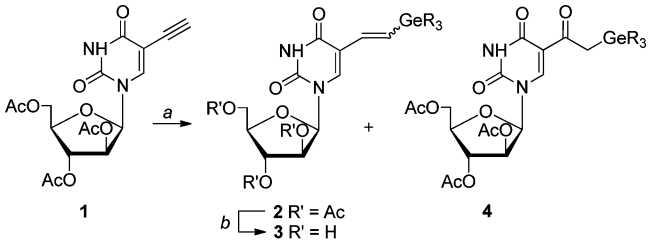
Scheme 1. Hydrogermylation of 1-(β-D-Arabinofuranosyl)-5-ethenyluracil 1 with Germane Hydrides[a]



Compounds **2-4**, Series: **a** R = Ph, **b** R = Me, **c** R = $(Me_3Si)_3$

[a]Reagents and conditions: (a) R_3GeH/(ACCN)/toluene/90 °C (method A), R_3GeH/Et_3B/THF/−78 °C (method B), or Pd-$(PPh_3)_4$/THF/rt (method C); (b) NH_3/MeOH/rt.

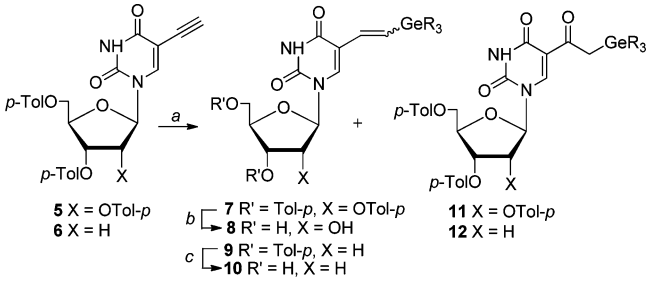
Analogous treatment of **1** with Ph_3GeH without ACCN also yielded **2a** and **4a** (entry 2).

The Et_3B-promoted addition[27] of Ph_3GeH to **1** in THF at low temperature (method B) gave *Z*-**2a** as the sole isolated product (55%, entry 3). However, analogous hydrogermylation of **1** at higher temperature (0 °C/6 h) afforded *Z*-**2a** and **4a** (~3:2, entry 4). Hydrogermylation of **1** with Ph_3GeH in the presence of $B(C_6F_5)_3$[22] in CH_2Cl_2 at ambient temperature produced **2a** in lower than 10% yields (TLC, ^1H NMR) while prolonged heating (48 h, reflux) produced a complex reaction mixture. The $Pd(PPh_3)_4$-catalyzed hydrogermylation[19] of **1** with Ph_3GeH in THF afforded a mixture of the expected *E*-isomer of **2a** and the corresponding 5-[1-(triphenylgermyl)-ethenyl] regioisomer, produced by addition of germyl radical to α-carbon,[19] in 3:2 ratio and 73% overall yield (entry 5; method C). The acyl product **4a** was not isolated from the reaction catalyzed by $Pd(PPh_3)_4$.

At low temperature (−78 °C), Et_3B-promoted hydrogermylation[27] of **1** with less reactive trimethylgermane failed to give vinylgermane **2b**. However, at ambient temperature the hydrogermylation yielded **2b** (*E*/*Z*, 15:85; entry 6) although in lower stereoselectivity. Moreover, no 5-[2-(trialkylgermyl)-acetyl] product **4b** was isolated from the reaction mixture. Hydrogermylation of **1** with reactive $(Me_3Si)_3GeH$ (ACCN/toluene/90 °C) stereoselectively produced the 5-[2-(TTMS-germyl)ethenyl]uracil analogue *Z*-**2c** (68%) in a shorter reaction time, though the acyl product **4c** was also not isolated (30 min, entry 7). Deacetylation of *Z*-**2a** with NH_3/MeOH afforded *Z*-**3a** (86%).

The Et_3B-promoted hydrogermylation of the toluoyl protected of 5-ethynyluridine **5** with Ph_3GeH/Et_3B at −78 °C showed a slow conversion to **7a** but warming of the reaction mixture to 0 °C afforded vinyl triphenylgermane *Z*-**7a** (40%) together with the 5-[2-(triphenylgermyl)acetyl] product **11a** (13%, Scheme 2; entry 8). Analogous hydrogermylation of **5**

Scheme 2. Hydrogermylation of 5-Ethenyluridine 5 and 2′-Deoxy-5-ethenyluridine 6 with Germane Hydrides[a]



Compounds **7-12**, Series: **a** R = Ph, **b** R = Me

[a]Reagents and conditions: (a) Ph_3GeH/(ACCN)/toluene/(THF or DMF)/90 °C or R_3GeH/Et_3B/THF/−78 °C; (b) MeONa/MeOH/rt; (c) NH_3/MeOH/rt.

with Me_3GeH/Et_3B at ambient temperature yielded only vinyl trimethylgermane **7b** (*E*/*Z*, 45:55; entry 9). Deprotection of *E*/*Z*-**7b** with MeONa/MeOH afforded uridine analogue *E*/*Z*-

Table 1. Hydrogermylation of 5-Ethynyluracil and Related Nucleosides with Germane Hydrides

					vinylgermanes			germyl ketones	
entry	substrate	method[a]	temp (°C)	R_3GeH	product	yield[b] (%)	ratio[b] (*E*/*Z*)	product	yield[b] (%)
1	**1**	A	90	Ph_3GeH	**2a**[c]	47	0:100	**4a**	12
2	**1**	A[d]	90	Ph_3GeH	**2a**	60	3:97	**4a**	15
3	**1**	B	−78 → −60	Ph_3GeH	**2a**	55	0:100		
4	**1**	B	0	Ph_3GeH	**2a**	28	0:100	**4a**	19
5	**1**	C	25	Ph_3GeH	**2a**[e]	45	100:0		
6	**1**	B	0 → 25	Me_3GeH	**2b**	40	15:85		
7	**1**	A	90	$(Me_3Si)_3GeH$	**2c**[f]	68	0:100		
8	**5**	B	−78 → 0	Ph_3GeH	**7a**	40	0:100	**11a**	13
9	**5**	B	0 → 25	Me_3GeH	**7b**	41	45:55		
10	**6**	B	−78 → 0	Ph_3GeH	**9a**	61	0:100	**12a**	12
11	**6**	A[g]	100[h]	Ph_3GeH	**9a**[i]	33	0:100	**12a**	17
12	**6**	B	0 → 25	Me_3GeH	**9b**	35	40:60		
13	**13**	A	90	Ph_3GeH	**14**	27	0:100	**15**	13
14	**13**	A[d]	100	Ph_3GeH	**14**	34	0:100	**15**	20
15	**13**	A[d,j]	100	Ph_3GeH	**14**	86	100:0		
16	**13**	B	0	Ph_3GeH	**14**	52	0:100		

[a]Method A: R_3GeH/ACCN/toluene/90 or 100 °C. Method B: R_3GeH/Et_3B/THF/−78 or 0 °C. Method C: $Pd(PPh_3)_4$/THF/rt. [b]For the isolated products. [c]Crude reaction mixture (*E*/*Z*-**2a**, 5:95). [d]Without ACCN. [e]In addition to *E*-**2a**, the α-addition product was formed (~3:2, 73% overall). [f]Crude reaction mixture (*E*/*Z*-**2c**, 4:96). [g]Toluene/THF (20:1, v/v) was used as solvent. [h]Oil bath. [i]With toluene/DMF/H_2O (20:1:0.1, v/v/v) as solvents *E*-**9a**, *Z*-**9a** and **12a** (~2:2:1, 40% overall) were obtained. [j]With addition of 25 μL of H_2O (14 equiv).

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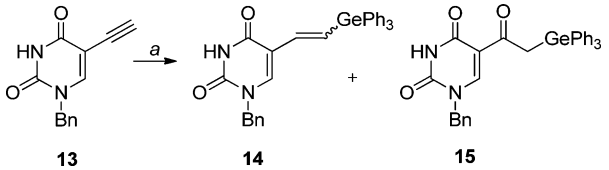
8b (71%), confirming stability[28] of the C(sp^2)-Ge(alkyl)$_3$ bond in basic conditions.

Hydrogermylation of the toluoyl protected 5-ethynyl-2′-deoxyuridine **6** with Ph_3GeH/Et_3B produced the vinyltriphenylgermane *Z*-**9a** (61%) along with the 5-[2-(triphenylgermyl)acetyl] product **12a** (12%, entry 10). Treatment of **6** with Ph_3GeH/ACCN in toluene/THF (20:1, v/v) also yielded *Z*-**9a** and **12a** (entry 11). Interestingly, analogous hydrogermylation of **6** in toluene/DMF with addition of a "measured" amount of water (14 equiv.) produced mixture of *E*/*Z* isomers of **9a** (~1:1) as well as **12a** (entry 11, footnote *i*; DMF or THF were added to increase solubility of **6** in reaction mixture). Deprotection of *Z*-**9a** with NH_3/MeOH provided 2′-deoxyuridine analogue *Z*-**10a** (65%). Treatment of **6** with Me_3GeH/Et_3B gave *E*/*Z*-**9b** (entry 12), but once again hydrogermylation with alkylgermanes did not yield the germyl ketone product.

Treatment of *E*/*Z*-**9b** (40:60) with *N*-bromosuccinimide (NBS) followed by deprotection (NH_3/MeOH) afforded a mixture of 5-(2-bromovinyl)-2′-deoxyuridines (*E*/*Z*, ~2:3; 70%) illustrating a potential application of vinyl 5-[2-(trimethylgermyl)vinyl]uracil nucleosides toward the synthesis of 5-(2-halovinyl) analogues with possible applications for radiolabeling. Stereoselective halodegermylation of vinyl trialkylgermanes with NBS or NIS with retention of the double-bond geometry is known.[22,28,29] It is also worth mentioning that substitution of the trialkylgermyl group on an sp^2 carbon[29,30] (as well as sp carbon[30,31]) with a halogen proceed not only more easily than the substitution of the corresponding trialkylsilyl group but also with improved stereochemical outcome.

It is noteworthy that hydrogermylation of the alkyl- or arylalkynes usually provides vinylgermanes in high yields, while the formation of the corresponding β-germyl ketones have not been observed.[23,24,27,32] We reexamined the hydrogermylation of phenylacetylene with Ph_3GeH under conditions described in methods A and B and found no formation of the β-germyl ketones. We also found that hydrostannylation and hydrosilylation of alkyne **5** with Ph_3SnH and Ph_3SiH under analogous conditions failed to yield 5-[2-(triphenylstannyl- or -silyl)acyl] products of type **11a** suggesting that the formation of 5-acyluracil products is selective for germane hydrides. Intrigued by this interesting finding, we have examined the chemistry involving the formation of 5-ketopyrimidine nucleosides (e.g., **4a**, **11a**, or **12a**) employing 1-*N*-benzyl-5-ethynyluracil **13** as a model substrate. Thus, hydrogermylation of the readily available[33,34] **13** with Ph_3GeH/ACCN in toluene (90 °C/2 h) produced the *Z*-vinylgermane **14** and germyl ketone **15** (~2:1, entry 13; Scheme 3). Analogous treatment of **13** with Ph_3GeH in toluene without ACCN yielded *Z*-**14** and **15** in 34% and 20% yields (entry 14), whereas similar reaction of **13** with Ph_3GeH in "moist" toluene interestingly yielded only the *syn*-addition product *E*-**14** (86%, entry 15; see also entry 11, footnote i). Hydrogermylation of **13** with Ph_3GeH in the presence of Et_3B/THF at 0 °C produced *Z*-**14** as a sole product (entry 16).

Scheme 3. Hydrogermylation of the 5-Ethenyluracil 13[a]



[a]Reagents and conditions: (a) Ph_3GeH/(ACCN)/toluene/(H_2O)/100 or 90 °C or Ph_3GeH/Et_3B/THF/0 °C.

The structures of the (triphenylgermyl)methyl ketone (β-germyl ketone) products were established by spectroscopic analysis. Thus, the ^1H NMR spectrum of **11a** confirmed the absence of the vinyl unit, whereas two upfield shifted doublets at 3.76 and 3.87 ppm (J = 9.0 Hz) supported the presence of the C(O)CH_2Ge moiety. The peak at 193.3 ppm in the ^{13}C NMR spectrum of **11a** confirmed the presence of the ketone. The HMBC and NOE correlations also supported the proposed structures (Figure S1, Supporting Information). The (+)ESI-MS analyses of **15** produced the $[M + Na]^+$ ion as the predominant peak. The (−)ESI-MS/MS product ion spectrum of $[M - H]^-$ (m/z 547 [^{74}Ge]) showed a loss of 43u (CONH) as the most abundant product ion (m/z 504[^{74}Ge]).

Formation of the β-germyl ketones (e.g., **15**) probably involves an initial attack of the triphenylgermyl radical at the triple bond of **13** to give a vinylic radical **16** (Figure 1).

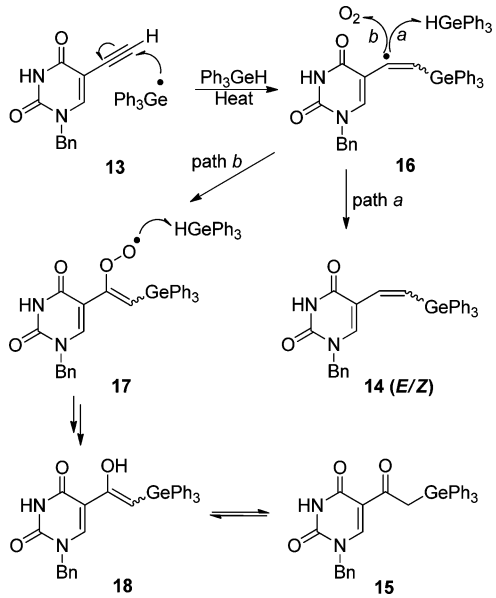


Figure 1. Plausible pathway for the formation of β-germyl ketone **15** during radical hydrogermylation of alkyne **13** with Ph_3GeH.

Abstraction of hydrogen from triphenylgermane in an *anti* fashion would produce *Z*-vinylgermane **14** as a major product while the *syn* addition could produce the *E* isomer (path *a*). Reaction of radical **16** with residual oxygen present in the reaction mixture might lead to peroxyl radical **17** which should abstract hydrogen from germane hydride[35] to produce hydroperoxide. The latter can be converted to enol **18**, probably by radical mechanism, and undergo tautomerization to yield the conjugated β-germyl ketone **15** (path *b*).

Efforts have been made to further optimize conditions for the preparation of **15** (and **14**) from the reaction of **13** with Ph_3GeH. Thus, experiments under Ar vs N_2 vs atmospheric conditions as well as using dry vs reagent-grade toluene vs "moist" toluene (with the added measured amount of H_2O or D_2O) did not improve the yield of **15**. In fact, they led mainly to the formation of *Z*-**14** or *E*/*Z*-**14** and **15** albeit in different yields and ratios. It is noteworthy that treatment of **13** with

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Ph_3GeH in oxygenated toluene resulted in the recovery of unchanged **13**. Optimal conditions for the formation of *β*-germyl ketones would require very low rate of initiation and very low and nearly constant concentration of Ph_3GeH and oxygen, which would allow the germyl radical to react with the vinyl group rather than oxygen and the vinylic radical **16** to react with oxygen rather than germane. Still our experiments employing slow addition of Ph_3GeH via syringe-pump over 24 h did not improve the yield of **15**.

During recrystallization of the crude **15** from MeOH, we noticed the formation of a new byproduct whose structure was established as 5-acetyl-1-*N*-benzyluracil **20** both spectroscopically and by comparison with a sample of **20** that was independently synthesized by acid-catalyzed hydration[36] of **13.** We found that heating of **15** in MeOH gave the 5-acetyl product **20** quantitatively. Conversion of (triphenylgermyl)-methyl ketone **15** to methyl ketone **20** most probably involves intramolecular thermal isomerization which proceedes via a four-centered activated complex. Hydrolysis of the resulting *O*-germyl substituted enol **19** led to ketone **20** (Figure 2).

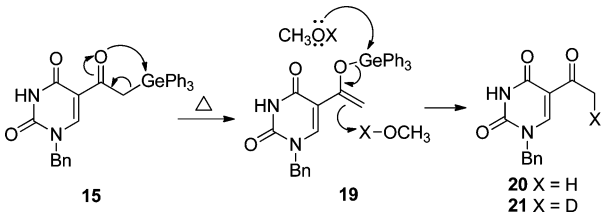

Figure 2. Plausible pathway for the thermal degradation of *β*-germyl ketone **15**.

Analogous thermal rearrangements of the *β*-silylketones into *O*-silyl substituted enols have been reported.[37] Heating **15** in MeOD or MeOH-d_4 provided quantitatively 1-deuteriomethyl ketone **21**, which supports the proposed degradation pathway.

In summary, we have demonstrated that radical hydrogermylation of the 5-acetylenic derivatives of protected uracil, uridine, 2′-deoxyuridine, and 1-(*β*-D-arabinofuranosyl)uracil analogues with triphenylgermane in toluene at elevated temperature provided vinylgermanes in good yields and high *Z*-stereoselectivity. The *E* isomers can be formed in the presence of an added "measured" amount of water. Hydrogermylation of 5-ethynyluracil nucleosides with triphenylgermane in addition to vinylgermanes produced also 5-[2-(triphenylgermyl)acetyl]uracil nucleosides in yields up to 20%. Thermolysis of the latter in MeOH afforded quantitatively 5-acetyluracil nucleosides via hydrolysis of the *O*-germyl substituted enols. The Et_3B-promoted hydrogermylation of 5-ethynyluracil nucleosides with trimethylgermane in THF at low temperature gave *E*/*Z* mixture of vinylgermanes. Bromodegermylation of vinyl trimethylgermanes with NBS provides access to 5-(2-bromovinyl) analogues.

EXPERIMENTAL SECTION

^1H (Me_4Si) NMR spectra at 400 MHz and ^{13}C (Me_4Si) at 100.6 MHz were determined in $CDCl_3$ unless otherwise noted. Mass spectra (MS) were obtained with atmospheric pressure chemical ionization (APCI) technique and HRMS in ESI TOF mode unless otherwise noted.

1-(2,3,5-Tri-*O*-acetyl-*β*-D-arabinofuranosyl)-5-(*E*/*Z*)-[2-(triphenylgermyl)ethenyl]uracil (2a) and 1-(2,3,5-Tri-*O*-acetyl-*β*-D-arabinofuranosyl)-5-[2-(triphenylgermyl)acetyl]uracil (4a). *Method A.* Nucleoside **1**[26] (50 mg, 0.13 mmol) was added to freshly distilled toluene (6 mL) and the suspension was stirred and degassed with N_2 for 30 min. The mixture was then preheated at 80 °C, and Ph_3GeH (50 mg, 0.16 mmol) and ACCN (4 mg, 0.02 mmol) were added. The temperature was increased to 90 °C, and the solution was stirred until **1** was completely consumed (TLC; 14 h). The volatiles were removed in vacuo, and the residue was chromatographed (hexane/EtOAc, 2:3) to give a separable mixture of *Z*-**2a** (43 mg, 47%) and **4a** (11 mg, 12%). *Z*-**2a**: ^1H NMR *δ* 1.99 (s, 3H), 2.09 (s, 3H), 2.11 (s, 3H), 3.70 (dd, *J* = 13.7, 7.7 Hz, 1H), 3.91−3.98 (m, 2H), 4.97 (dd, *J* = 3.2, 2.0 Hz, 1H), 5.27 (dd, *J* = 4.1, 1.9 Hz, 1H), 5.71 (d, *J* = 4.1 Hz, 1H), 6.56 (d, *J* = 13.5 Hz, 1H), 7.08 (d, *J* = 1.0 Hz, 1H), 7.36−7.52 (m, 16H), 8.30 (br s, 1H); ^{13}C NMR *δ* 20.4, 20.6, 20.7, 62.3, 74.6, 76.1, 79.8, 84.4, 113.4, 128.4, 129.1, 131.7, 134.8, 136.38, 136.41, 138.2, 148.6, 161.3, 168.5, 169.4, 170.2; MS *m*/*z* 701 (100, MH^+, ^{74}Ge), 699 (71, MH^+, ^{72}Ge) 698 (51, MH^+, ^{70}Ge). Anal. Calcd for $C_{35}H_{34}GeN_2O_9 \cdot 0.25EtOH$ (710.81): C, 59.99; H, 5.03; N, 3.94. Found: C, 59.63; H, 4.92; N, 4.00. ^1H NMR of the crude reaction mixture also showed presence (∼5%) of the *E*-**2a** with the characteristic peaks at *δ* 6.31 (d, *J* = 4.0 Hz, H1′), 6.69 (d, *J* = 18.8 Hz, CH).

Compound **4a**: ^1H NMR *δ* 1.90 (s, 3H), 2.14 (s, 3H), 2.15 (s, 3H), 3.48 (d, *J* = 9.3 Hz, 1H), 4.16−4.19 (m, 1H), 4.17 (d, *J* = 9.3 Hz, 1H), 4.33 (dd, *J* = 12.1, 4.5 Hz, 1H), 4.44 (dd, *J* = 12.1, 4.9 Hz, 1H), 5.12 (dd, *J* = 3.3, 1.6 Hz, 1H), 5.33 (dd, *J* = 4.1, 1.6 Hz, 1H), 6.23 (d, *J* = 4.1 Hz, 1H), 7.21−7.55 (m, 15H), 8.08 (s, 1H), 8.49 (br s, 1H); ^{13}C NMR *δ* 20.4, 20.7, 20.8, 33.0, 62.4, 74.6, 76.6, 80.8, 83.9, 113.3, 128.4, 129.5, 135.1, 135.3, 146.6, 148.8, 160.4, 168.8, 169.6, 170.8, 194.2; HRMS calcd for $C_{35}H_{34}{}^{74}GeN_2NaO_{10}$ $[M + Na]^+$ 739.1323, found 739.1311.

Method B. Et_3B (1M/THF; 140 *μ*L, 0.14 mmol) was added to a stirred solution of **1** (50 mg, 0.127 mmol) and Ph_3GeH (43 mg, 0.14 mmol) in anhydrous THF (5 mL) placed in screw-capped glass tube at −78 °C. After 3 h, when TLC showed appearance of less polar spot, and the reaction mixture was warmed up to −60 °C and was stirred for 1.5 h. The volatiles were evaporated, and the residue was chromatographed (hexane/EtOAc, 2:3) to give *Z*-**2a** (49 mg, 55%) as a white powder after crystallization from hexane/Et_2O.

Method C. Ph_3GeH (59 mg, 0.2 mmol) and $Pd(PPh_3)_4$ (8 mg, 0.08) were added to a stirred suspension of **1** (70 mg, 0.18 mmol) in THF (3 mL) in a flamed-dried round bottle flask at rt under N_2. After 5 h, the volatiles were evaporated in vacuo, and the residue was chromatographed (hexane/EtOAc, 1:1) to give inseparable mixture of the *E*-isomer of **2a** and the *α*-addition product (90 mg, 73%; *E*-**2a**/*α*-addition product, 3:2): MS (ESI) *m*/*z* 701 (100, MH^+, ^{74}Ge), 699 (70, MH^+, ^{72}Ge), 697 (50, MH^+, ^{70}Ge). *E*-**2a**: ^1H NMR *δ* 1.88 (s, 3H), 1.98 (s, 3H), 2.14 (s, 3H), 4.23 (m, 2H), 4.35−4.39 (m, 1H), 5.09 (dd, *J* = 3.4, 1.5 Hz, 1H), 5.43 (dd, *J* = 3.9, 1.5 Hz, 1H), 6.31 (d, *J* = 4.0 Hz, 1H), 6.69 (d, *J* = 18.8 Hz, 1H), 7.33−7.55 (m, 16H), 7.60 (s, 1H), 9.29 (br s, 1H). The *α*-addition product 1-(2,3,5-tri-*O*-acetyl-*β*-D-arabinofuranosyl)-5-[1-(triphenylgermyl)ethenyl]uracil: ^1H NMR *δ* 1.80 (s, 3H), 2.07 (s, 3H), 2.11 (s, 3H), 4.00−4.23 (m, 2H), 4.45−4.49 (m, 1H), 4.98 (dd, *J* = 3.5, 1.9 Hz, 1H), 5.35 (dd, *J* = 4.1, 1.5 Hz, 1H), 5.72 (d, *J* = 2.0 Hz, 1H), 6.17 (d, *J* = 4.1 Hz, 1H), 6.41 (d, *J* = 2.0 Hz, 1H), 7.33−7.55 (m, 16H), 8.98 (br s, 1H).

1-(2,3,5-Tri-*O*-acetyl-*β*-D-arabinofuranosyl)-5-(*E*/*Z*)-[2-(trimethylgermyl)ethenyl]uracil (2b). Nucleoside **1** (50 mg, 0.13 mmol) was treated with Me_3GeH (30 mg, 29.6 *μ*L, 0.25 mmol) in dry THF (5 mL) as described in method B (with injection of Me_3GeH into the reaction mixture via syringe and progressive warming from 0 °C to rt) for 14 h. The volatiles were removed under reduced pressure, and the residue was chromatographed (hexane/EtOAc, 2:3) to give *E*/*Z*-**2b** (27 mg, 40%; *E*/*Z*, 15:85): ^1H NMR *δ* 0.26 (s, 7.65H), 0.28 (s, 1.35H), 2.02 (s, 3H), 2.12 (s, 2.55H), 2.15 (s, 0.45H), 2.16 (s, 2.55H), 2.17 (s, 0.45H), 4.19−4.25 (m, 1H), 4.34 (dd, *J* = 11.9, 6.2 Hz, 0.85H), 4.37−4.45 (m, 0.15H), 4.44 (dd, *J* = 11.9, 4.2 Hz, 0.85H), 4.52 (dd, *J* = 11.9, 6.2 Hz, 0.15H), 5.11 (dd, *J* = 3.8, 1.4 Hz, 0.85H), 5.15 (dd, *J* = 3.4, 1.6 Hz, 0.15H), 5.44−5.48 (m, 1H), 6.10 (d, *J* = 13.8 Hz, 0.85H), 6.24 (d, *J* = 3.8 Hz, 0.85H), 6.33 (d, *J* = 4.0 Hz, 0.15H), 6.60 (d, *J* = 18.9 Hz, 0.15H), 6.80 (d, *J* = 19.0 Hz, 0.15H), 6.98 (dd, *J* = 13.8, 1.0 Hz, 0.85H), 7.45 (d, *J* = 1.0 Hz, 0.85H), 7.59 (s, 0.15H), 8.97 (br s, 0.15H), 9.09 (br s, 0.85H); ^{13}C NMR *δ* −1.7, −0.2, 20.5,

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20.6, 20.8, 20.87, 20.92, 62.7, 63.2, 74.7, 74.8, 76.4, 76.5, 80.4, 80.8, 84.6, 112.9, 114.2, 132.1, 133.6, 134.3, 136.1, 136.4, 137.6, 149.2, 149.6, 161.8, 162.2, 168.6, 168.7, 169.7, 169.8, 170.5; HRMS calcd for $C_{20}H_{28}{}^{74}GeNaN_2O_9$ $[M + Na]^+$ 537.0899, found 537.0888.

1-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)-5-(*Z*)-[2-(tris-(trimethylsilyl)germyl)ethenyl]uracil (2c). Nitrogen gas was bubbled through a heterogeneous mixture of **1** (127 mg, 0.32 mmol) in dry toluene (10 mL) for 30 min. The suspension was preheated to 90 °C (~5 min), and $(Me_3Si)_3GeH$ (115 mg, 123 μL, 0.39 mmol) was added via syringe followed by ACCN (8 mg, 0.04 mmol) dissolved in degassed toluene (1 mL). The reaction mixture was heated at 90 °C for 30 min. Volatiles were evaporated, and the residue was chromatographed (hexane/EtOAc, 3:2) to give *Z*-**2c** (152 mg, 68%): ^{1}H NMR δ 0.20 (s, 27H), 2.01 (s, 3H), 2.10 (s, 3H), 2.14 (s, 3H), 4.17−4.24 (m, 1H), 4.34 (dd, *J* = 12.0, 5.5 Hz, 1H), 4.38 (dd, *J* = 12.0, 5.2 Hz, 1H), 5.14 (dd, *J* = 3.8, 1.6 Hz, 1H), 5.47 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.16 (d, *J* = 3.9 Hz, 1H), 6.28 (d, *J* = 13.5 Hz, 1H), 6.90 (dd, *J* = 13.5, 1.4 Hz, 1H), 7.29 (d, *J* = 1.4 Hz,1H), 8.27 (br s, 1H); ^{13}C NMR δ 1.95, 20.7, 20.9, 21.0, 63.1, 75.0, 76.5, 80.7, 85.4, 116.1, 133.9, 134.1, 136.2, 149.6, 162.0, 168.9, 169.7, 170.6; HRMS calcd for $C_{26}H_{47}{}^{74}GeN_2O_9Si_3$ $[M + H]^+$ 689.1801, found 689.1798. ^{1}H NMR of the crude reaction mixture showed 4:96 mixture of *E*/*Z* isomers of **2c**. The *E*-**2c** had the characteristic peaks on the ^{1}H NMR spectrum at: δ 6.36 (d, *J* = 3.5 Hz, H1′), 6.63 (d, *J* = 18.7 Hz, CH), 6.86 (d, *J* = 18.5 Hz, CH).

1-(β-D-Arabinofuranosyl)-5-(*Z*)-[2-(triphenylgermyl)ethenyl]-uracil (3a). A saturated solution of NH_3/MeOH (3 mL) was added to a suspension of *Z*-**2a** (40.0 mg, 0.057 mmol) in MeOH (2 mL) and the reaction mixture stirred for 6 h at 0 °C and then for 2 h at rt. Volatiles were evaporated and the residue was chromatographed (EtOAc/MeOH, 98:2) to give *Z*-**3a** (28.2 mg, 86%): ^{1}H NMR (MeOH-d_4) δ 3.28 (dd, *J* = 11.3, 4.0 Hz, 1H), 3.37 (dd, *J* = 11.3, 5.6 Hz, 1H), 3.76 (ddd, *J* = 5.8, 4.1, 2.1 Hz, 1H), 3.98−4.02 (m, 2H), 5.59 (d, *J* = 3.3 Hz, 1H), 6.50 (d, *J* = 13.2 Hz, 1H), 7.30 (d, *J* = 13.3 Hz, 1H), 7.35−7.51 (m, 16H); ^{13}C NMR (MeOH-d_4) δ 62.6, 76.6, 78.4, 87.0, 88.3, 113.8, 129.3, 130.0, 131.5, 136.0, 138.2, 139.9, 140.7, 151.3, 165.0; HRMS calcd for $C_{29}H_{28}{}^{74}GeNaN_2O_6$ $[M + Na]^+$ 597.1051, found 597.1076. Anal. Calcd for $C_{29}H_{28}GeN_2O_6{\cdot}CH_3OH{\cdot}H_2O$ (623.24): C, 57.81; H, 5.50; N, 4.49. Found: C, 57.84; H, 5.41; N, 4.69.

5-Ethynyl-2′,3′,5′-tri-*O*-*p*-toluoyluridine (5). The *p*-toluoyl chloride (86 μL, 101 mg, 0.65 mmol) was added to a stirred solution of 5-ethynyluridine[38] (50 mg, 0.19 mmol) in pyridine (5 mL). After 24 h, volatiles were evaporated and the residue was partitioned ($NaHCO_3/H_2O$//$CHCl_3$). The organic layer was washed with HCl/H_2O, $NaHCO_3/H_2O$ and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed (hexane/EtOAc, 7:3 → 6:4) to give **5** (85 mg, 73%): ^{1}H NMR δ 2.40 (s, 3H), 2.44 (s, 6H, 2 x Me), 2.94 (s, 1H), 4.69−4.76 (m, 2H), 4.78−4.84 (m, 1H), 5.70 ("t", *J* = 6.0 Hz, 1H), 5.84 (dd, *J* = 5.9, 3.6 Hz, 1H, H3), 6.37 (d, *J* = 6.1 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.81 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 8.02 (d, *J* = 8.2 Hz, 2H), 8.18 (s, 1H); ^{13}C NMR δ 21.8, 21.9, 63.8, 71.5, 73.76, 73.77, 81.4, 82.5, 87.9, 100.6, 125.7, 126.1, 126.5, 129.4, 129.5, 129.7, 129.9, 130.1, 130.2, 143.2, 144.6, 144.8, 144.9, 148.8, 160.6, 165.4, 165.5, 166.3; HRMS calcd for $C_{35}H_{31}N_2O_9$ $[M + H]^+$ 623.2024, found 623.2033.

5-(*Z*)-[2-(Triphenylgermyl)ethenyl]-2′,3′,5′-tri-*O*-*p*-toluoyluridine (7a) and 5-[2-(Triphenylgermyl)acetyl]-2′,3′,5′-tri-*O*-*p*-toluoyluridine (11a). Nucleoside **5** (49 mg, 0.08 mmol) was treated with Ph_3GeH (26 mg, 0.085 mmol) in dry THF (5 mL) as described in method B. After 6 h at −78 °C, the reaction mixture was slowly warmed to 0 °C (~24 h). The volatiles were evaporated, and the residue was chromatographed (hexane/EtOAc, 1:1) to give a separable mixture of *Z*-**7a** (29 mg, 40%) and **11a** (10 mg, 13%). *Z*-**7a**: ^{1}H NMR δ 2.40 (s, 6H), 2.42 (s, 3H), 4.34 (dd, *J* = 12.2, 5.4 Hz, 1H), 4.40 (dd, *J* = 12.2, 3.4 Hz, 1H), 4.47 (ddd, *J* = 5.8, 5.4, 3.5 Hz, 1H), 5.38 (dd, *J* = 6.2, 4.5 Hz, 1H), 5.51 ("t", *J* = 6.0 Hz, 1H), 5.52 (d, *J* = 4.4 Hz, 1H), 6.50 (d, *J* = 13.6 Hz, 1H), 7.11 (d, *J* = 0.9 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.22 (dd, *J* = 13.5, 0.9 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.31−7.55 (m, 15H), 7.80 (d, *J* = 8.2 Hz, 4H), 7.96 (d, *J* = 8.2 Hz, 2H), 8.09 (br s, 1H); ^{13}C NMR δ 21.67, 21.69, 21.72, 63.5, 70.5, 73.6, 79.9, 89.8, 115.0, 125.9, 126.0, 126.7, 128.5, 129.1, 129.2, 129.3, 129.7, 129.8, 129.9, 131.4, 134.7, 136.6, 137.0, 138.2, 144.2, 144.4, 144.5, 148.8, 161.4, 165.0, 165.1, 166.1; HRMS calcd for $C_{53}H_{46}{}^{74}GeN_2NaO_9$ $[M + Na]^+$ 951.2307, found 951.2315.

Compound **11a** had: UV (MeOH) λ_{max} = 282 nm; ^{1}H NMR δ 2.35 (s, 3H), 2.40 (s, 3H), 2.42 (s, 3H), 3.76 (d, *J* = 9.0 Hz, 1H), 3.87 (d, *J* = 9.0 Hz, 1H), 4.67−4.75 (m, 3H), 5.66 (dd, *J* = 5.9, 5.1 Hz, 1H), 5.83 ("t", *J* = 5.7 Hz, 1H), 6.01 (d, *J* = 5.0 Hz, 1H), 7.16−7.55 (m, 21H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 2H), 8.02 (d, *J* = 8.2 Hz, 2H), 8.05 (s, 1H); ^{13}C NMR δ 21.7, 33.0, 63.5, 71.0, 73.9, 80.9, 90.4, 113.7, 125.7, 126.0, 126.6, 128.2, 129.21, 129.24, 129.3, 129.4, 129.8, 129.9, 135.0, 135.1, 144.1, 144.5, 144.7, 146.6, 148.5, 160.2, 165.19, 165.21, 166.3, 193.3; HRMS calcd for $C_{53}H_{47}{}^{74}GeN_2O_{10}$ $[M + H]^+$ 945.2437, found 945.2456.

5-(*E*/*Z*)-[2-(Trimethylgermyl)ethenyl]-2′,3′,5′-tri-*O*-*p*-toluoyluridine (7b). Nucleoside **5** (50.0 mg, 0.08 mmol) was treated with Me_3GeH (19.0 mg, 18.8 μL 0.16 mmol) in dry THF (5 mL) as described in method B (with injection of Me_3GeH into the reaction mixture via syringe and progressive warming from 0 °C to rt) for 10 h. The volatiles were evaporated and the residue was chromatographed (hexane/EtOAc, 3:2) to give *E*/*Z*-**7b** (24.5 mg, 41%; *E*/*Z*, 45:55): ^{1}H NMR δ 0.12 (s, 4.05H), 0.20 (s, 4.95H), 2.40, 2.43, 2.44 (singlets, 9H), 4.68−4.82 (m, 3H), 5.72 ("t", *J* = 6.0 Hz, 0.55H), 5.78 ("t", *J* = 6.3 Hz, 0.45H), 5.82 (dd, *J* = 6.1, 3.9 Hz, 0.55H), 5.88 (dd, *J* = 5.8, 2.8 Hz, 0.45H), 5.98 (d, *J* = 13.7 Hz, 0.55H), 6.34 (d, *J* = 5.9 Hz, 0.55H), 6.37 (d, *J* = 19.0 Hz, 0.45H), 6.50 (d, *J* = 6.8 Hz, 0.45H), 6.69 (d, *J* = 19.0 Hz, 0.45H), 6.72 (dd, *J* = 13.7, 1.0 Hz, 0.55H), 7.16−7.32 (m, 6H), 7.34 (d, *J* = 1.0 Hz, 0.55H), 7.54 (s, 0.45H), 7.83−8.04 (m, 6H), 8.24 (br s, 0.45H), 8.27 (br s, 0.55H); ^{13}C NMR δ −2.0, −0.2, 21.7, 63.7, 64.2, 71.1, 71.5, 73.45, 73.53, 80.7, 81.0, 86.9, 88.0, 114.4, 116.0, 125.65, 125.70, 125.96, 125.97, 126.3, 126.5, 129.24, 129.25, 129.29, 129.4, 129.6, 129.71, 129.73, 129.88, 129.9, 129.95, 130.0, 131.8, 134.1, 134.4, 135.1, 135.8, 138.7, 144.3, 144.5, 144.57, 144.63, 144.64, 144.7, 149.3, 149.7, 161.3, 161.7, 165.3, 165.35, 165.38, 165.5, 166.1; MS (ESI$^+$) *m*/*z* 765 (100, MNa^+, ^{74}Ge), 763 (71, MNa^+, ^{72}Ge), 762 (52 MNa^+, ^{70}Ge). Anal. Calcd for $C_{38}H_{40}GeN_2O_9{\cdot}H_2O$ (759.39): C, 60.10; H, 5.57; N, 3.69. Found: C, 60.39; H, 5.38; N, 3.87.

5-(*E*/*Z*)-[2-(Trimethylgermyl)ethenyl]uridine (8b). A 0.1 N solution of MeONa in MeOH (2.5 mL) was added to **7b** (18.8 mg, 0.025 mmol; *E*/*Z*, ~45:55) and the resulting mixture was stirred at rt for 12 h. The reaction mixture was neutralized to pH ~6.2 by addition of Dowex 50WX2-200(H^+). Dowex resin was filtered off and the filtrate was evaporated and residue partitioned between Et_2O/H_2O. The organic layer was extensively washed with water and the combined aqueous layer was evaporated to yield *E*/*Z*-**8b** (7 mg, 71%; *E*/*Z*, ~40:60): ^{1}H NMR (D_2O) δ 0.27 (s, 5.4H), 0.32 (s, 3.6H), 3.84−3.91 (m, 1H), 3.95 (dd, *J* = 12.7, 2.7 Hz, 0.6H), 4.05 (dd, *J* = 12.9, 2.4 Hz, 0.4H), 4.18−4.24 (m, 1H), 4.29 ("t", *J* = 5.0 Hz, 0.6H), 4.34 ("t", *J* = 5.7 Hz, 0.4H), 4.39−4.44 (m, 1H), 6.00 (d, *J* = 3.8 Hz, 0.4H), 6.05 (d, *J* = 5.3 Hz, 0.6H), 6.36 (d, *J* = 13.6 Hz, 0.6H), 6.70 (d, *J* = 19.0 Hz, 0.4H), 6.83 (d, *J* = 19.0 Hz, 0.4H), 6.93 (d, *J* = 13.6 Hz, 0.6H), 7.77 (s, 0.6H), 8.20 (s, 0.4H); ^{13}C NMR (MeOH-d_4) δ −2.9, −1.2, 60.1, 61.0, 68.9, 69.8, 73.7, 74.1, 84.0, 84.7, 88.8, 89.7, 113.8, 115.7, 132.1, 134.1, 134.7, 137.6, 137.8, 140.8, 151.1, 151.6, 164.6, 165.3; HRMS calcd for $C_{14}H_{23}{}^{74}GeN_2O_6$ $[M + H]^+$ 389.0762, found 389.0775.

1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-5-(*Z*)-[2-(triphenylgermyl)ethenyl]uracil (9a) and 1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-5-[2-(triphenylgermyl)acetyl]uracil (12a). Nucleoside **6**[10] (44 mg, 0.09 mmol) was treated with Ph_3GeH (30 mg, 0.1 mmol) in dry THF (5 mL) as described in method B. After 6 h at −78 °C, the reaction mixture was slowly warmed to 0 °C and stirred for 3 h. The volatiles were evaporated, and the residue was chromatographed (hexane/EtOAc, 3:2) to give a separable mixture of *Z*-**9a** (43 mg, 61%) and **12a** (9 mg, 12%). *Z*-**9a**: ^{1}H NMR δ 1.68 (ddd, *J* = 14.9, 8.1, 7.0 Hz, 1H), 2.31 (ddd, *J* = 14.5, 5.7, 1.8 Hz, 1H), 2.41 (s, 3H), 2.45 (s, 3H), 4.16 (dd, *J* = 11.1, 3.5 Hz, 1H), 4.26−4.30 (m, 1H), 4.32 (dd, *J* = 11.1, 5.0

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Hz, 1H), 5.15 ("dt", J = 6.8, 1.8 Hz, 1H), 5.84 (dd, J = 8.1, 5.7 Hz, 1H), 6.51 (d, J = 13.5 Hz, 1H), 7.11 (d, J = 1.0 Hz, 1H), 7.21−7.56 (m, 20H), 7.88 (d, J = 8.2 Hz, 2H), 7.91 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 21.68, 21.72, 37.3, 63.9, 74.5, 82.3, 85.5, 114.8, 126.4, 126.7, 128.5, 129.2, 129.25, 129.28, 129.6, 129.8, 131.0, 134.8, 135.6, 136.6, 138.8, 144.2, 144.5, 149.3, 161.7, 165.8, 166.0; HRMS calcd for $C_{45}H_{41}{}^{74}GeN_2O_7$ $[M + H]^+$ 795.2120, found 795.2131.

Compound **12a** had: ^{1}H NMR δ 2.18−2.27 (m, 1H), 2.36 (s, 3H), 2.45 (s, 3H), 2.64 (ddd, J = 14.3, 5.7, 1.8 Hz, 1H), 3.81 (d, J = 9.1 Hz, 1H), 3.85 (d, J = 9.1 Hz, 1H), 4.53−4.60 (m, 2H), 4.74−4.80 (m, 1H), 5.54 ("d", J = 6.6 Hz, 1H), 6.16 (dd, J = 8.3, 5.7 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.32−7.57 (m, 15H), 7.94 (d, J = 8.2 Hz, 2H), 7.95 (d, J = 8.2 Hz, 2H), 8.15 (s, 1H); ^{13}C NMR δ 21.70, 21.73, 32.8, 38.4, 63.8, 74.5, 83.2, 86.2, 113.6, 126.3, 126.6, 128.2, 129.25, 129.28, 129.3, 129.8, 135.1, 135.2, 144.1, 144.5, 145.2, 148.8, 160.3, 165.8, 166.2, 193.5; HRMS calcd for $C_{45}H_{41}{}^{74}GeN_2O_8$ $[M + H]^+$ 811.2075, found 811.2063.

Treatment of **6** (50 mg, 0.10 mmol) with Ph_3GeH (36 mg, 0.12 mmol) in toluene (4 mL) as described in Method A [DMF (0.2 mL) and water (25 μL, 25 mg, 1.4 mmol) were added to the preheated reaction mixture] gave partially separated *E*-**9a** (13 mg, 16%), **12a** (6.5 mg, 8%), and *Z*-**9a** (13 mg, 16%). Compound *E*-**9a** had characteristic peaks for vinylic protons at δ 6.63 (d, J = 18.8 Hz, 1H) and within the envelope of aromatic protons at δ 7.20−7.50 (Cosy).

1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-β-D-*erythro*-pentofuranosyl)-5-(*E*/*Z*)-[2-(trimethylgermyl)ethenyl]uracil (9b). Nucleoside **6**[10] (45.0 mg, 0.092 mmol) was treated with Me_3GeH (21.8 mg, 21.6 μL, 0.18 mmol) in dry THF (5 mL) as described in method B (with injection of Me_3GeH into the reaction mixture via syringe and progressive warming from 0 °C to rt) for 10 h. The volatiles were evaporated, and the residue was chromatographed (hexane/EtOAc, 1:1) to give *E*/*Z*-**9b** (16.5 mg, 35%; *E*/*Z*, 40:60): ^{1}H NMR δ 0.14 (s, 3.6H), 0.21 (s, 5.4H), 2.25−2.34 (m, 1H), 2.42, 2.43, 2.45 (singlets, 6H), 2.78 (ddd, J = 14.2, 5.5, 1.6 Hz, 0.6H), 2.80 (ddd, J = 14.3, 5.1, 1.2 Hz, 0.4H), 4.56−4.61 (m, 1H), 4.65 (dd, J = 12.2, 3.2 Hz, 0.6H), 4.73−4.77 (m, 0.8H), 4.75 (dd, J = 12.2, 3.8 Hz, 0.6H), 4.59 ("dt", J = 4.9, 1.9 Hz, 0.6H), 4.63 ("d", J = 6.4 Hz, 0.4H), 6.00 (d, J = 13.7 Hz, 0.6H), 6.40 (dd, J = 8.7, 5.4 Hz, 0.6H), 6.41 (d, J = 19.2 Hz, 0.4H), 6.46 (d, J = 8.9, 5.2 Hz, 0.4H), 6.72 (d, J = 19.0 Hz, 0.4H), 6.78 (dd, J = 13.7, 1.0 Hz, 0.6H), 7.22−7.32 (m, 4H), 7.48 (d, J = 1.0 Hz, 0.6H), 7.67 (s, 0.4H), 7.85−7.99 (m, 4H), 8.51 (br s, 0.4H), 8.57 (br s, 0.6H); ^{13}C NMR δ −2.0, −0.2, 21.70, 21.73, 38.5, 64.1, 64.4, 74.7, 75.0, 82.9, 83.1, 85.6, 113.9, 115.4, 126.3, 126.4, 126.5, 129.30, 129.34, 129.50, 129.54 129.6, 129.8, 131.9, 133.9, 134.2, 134.9, 135.1, 138.3, 144.4, 144.5, 144.6, 149.2, 149.7, 161.5, 161.9, 166.0, 166.1; HRMS calcd for $C_{30}H_{34}{}^{74}GeN_2NaO_7$ $[M + Na]^+$ 631.1470, found 631.1482.

Note: Treatment of **9b** (*E*/*Z*, 40:60; 12 mg; 0.02 mmol) with NBS (5 mg, 0.028 mmol) in $CHCl_3/CH_2Cl_2$ (1:1.5, v/v; 2.5 mL) for 6 h at 0 °C followed by deprotections with NH_3/MeOH (0 °C to rt, 12 h) gave 5-(2-bromovinyl)-2′-deoxyuridine[39,40] (*E*/*Z*, 2:3; 70% from **9b**).

1-(β-D-*Erythro*-pentofuranosyl)-5-(*Z*)-[2-(triphenylgermyl)-ethenyl]uracil (10a). A saturated solution of NH_3/MeOH (2 mL) was added to a suspension of *Z*-**9a** (33 mg, 0.042 mmol) in MeOH (2 mL), and the resulting mixture was stirred for 24 h at rt. The volatiles were evaporated, and the residue was chromatographed (EtOAc) to give *Z*-**10a** (15 mg, 65%): ^{1}H NMR (MeOH-d_4) δ 1.44 (ddd, J = 14.2, 7.9, 6.6 Hz, 1H), 1.87 (ddd, J = 13.6, 5.9, 2.7 Hz, 1H), 3.38 ("d", J = 4.4 Hz, 2H), 3.70 ("q", J = 3.8 Hz, 1H), 3.97 (ddd, J = 6.0, 3.3, 2.8 Hz, 1H), 5.81 (dd, J = 8.0, 6.0 Hz, 1H), 6.52 (d, J = 13.3 Hz, 1H), 7.28 (d, J = 1.1 Hz, 1H), 7.31 (dd, J = 13.3, 1.1 Hz, 1H), 7.36−7.54 (m, 15H); ^{13}C NMR (MeOH-d_4) δ 40.3, 63.0, 72.3, 86.3, 88.6, 115.8, 129.5, 130.2, 131.8, 135.9, 138.1, 138.2, 140.8, 151.6, 164.7; MS (ESI$^+$) m/z 581 (100, MNa$^+$, ^{74}Ge), 579 (70, MNa$^+$, ^{72}Ge), 577 (49, MNa$^+$, ^{70}Ge). Anal. Calcd for $C_{29}H_{28}GeN_2O_5$ (557.18): C, 62.51; H, 5.07; N, 5.03. Found: C, 62.14; H, 5.28; N, 4.86.

1-*N*-Benzyl-5-(*Z*)-[2-(triphenylgermyl)ethenyl]uracil (14). Alkyne **13**[33,34] (50 mg, 0.22 mmol) was dissolved in anhydrous THF (5 mL), and the resulting solution was stirred for 20 min under N_2 at 0 °C. Ph_3GeH (73 mg, 0.24 mmol) and Et_3B (1M/THF 265 μL, 0.265 mmol) were added, and the resulting solution was stirred at 0 °C for 7 h. The volatiles were evaporated, and the residue was chromatographed (hexane/EtOAc, 1:1) to give *Z*-**14** (61 mg, 52%) as a white powder: mp 202−204 °C (MeOH); UV (MeOH) max 296 nm (ε 11 000), min 255 (ε 3500); ^{1}H NMR δ 4.03 (s, 2H), 6.30 (d, J = 13.5 Hz, 1H), 6.69 ("d", J = 7.0 Hz, 2H), 6.84 (s, 1H), 7.09 ("t", J = 7.5 Hz, 2H), 7.16 ("t", J = 7.1 Hz, 1H), 7.23−7.35 (m, 10H), 7.37−7.46 (m, 6H), 8.51 (br s, 1H); ^{13}C NMR δ 51.2, 113.7, 128.3, 128.3, 128.4, 128.8, 129.1, 129.5, 134.8, 135.0, 136.7, 138.7, 141.0, 150.1, 162.4; HRMS calcd for $C_{31}H_{26}{}^{74}GeN_2NaO_2$ $[M + Na]^+$ 555.1105, found 555.1113.

1-*N*-Benzyl-5-(*E*)-[2-(triphenylgermyl)ethenyl]uracil (14). Ph_3GeH (118.6 mg, 0.38 mmol) and H_2O (25 μL, 25 mg, 1.4 mmol) were added to a stirred solution of **13** (80 mg, 0.35 mmol) in toluene (5 mL) at rt. The resulting mixture was heated at 100 °C for 12 h. The volatiles were evaporated, and the residue was chromatographed (CH_2Cl_2/EtOAc, 10:1) to give *E*-**14** (126 mg, 86%) as a white solid. Recrystallization (MeOH) gave white crystals: mp 185−186 °C; UV (MeOH) max 300 nm (ε 13900), 251 nm (ε 15500), min 272 (ε 7100); ^{1}H NMR δ 4.92 (s, 2H), 6.56 (d, J = 18.7 Hz, 1H), 7.21 (s, 1H), 7.28−7.30 (m, 2H), 7.33 (d, J = 18.7 Hz, 1H), 7.35−7.51 (m, 18H), 8.78 (br s, 1H); ^{13}C NMR δ 51.5, 113.8, 127.2, 127.9, 128.3, 128.6, 129.1, 129.2, 135.1, 135.2, 136.1, 136.9, 141.7, 150.1, 161.8; HRMS calcd for $C_{31}H_{26}{}^{74}GeN_2NaO_2$ $[M + Na]^+$ 555.1105, found 555.1111. Anal. Calcd for $C_{31}H_{26}GeN_2O_2$ (531.19): C, 70.09; H, 4.93; N, 5.27. Found: C, 69.82; H, 4.64; N, 5.35.

1-*N*-Benzyl-5-[2-(triphenylgermyl)acetyl]uracil (15). Alkyne **13** (50 mg, 0.22 mmol) was suspended in dry toluene (5 mL), and the suspension was degassed with N_2 for 45 min at ambient temperature. Ph_3GeH (73 mg, 0.24 mmol) and ACCN (10 mg, 0.041 mmol) were added, and the suspension was heated at 90 °C for 2 h. The volatiles were evaporated, and residue was chromatographed (hexane/EtOAc, 3:2) to give **15** (15 mg, 13%) followed by *Z*-**14** (31 mg, 27%). Compound **15** was recrystallized (MeOH) to give colorless crystals: mp 205−207 °C; UV (MeOH) max 294 nm (ε 10 600), min 255 (ε 3800); ^{1}H NMR δ 3.81 (s, 2H), 4.77 (s, 2H), 7.24−7.54 (m, 20H), 7.79 (br s, 1H), 7.85 (s, 1H); ^{13}C NMR δ 33.1, 52.4, 113.3, 128.3, 128.5, 129.1, 129.3, 129.5, 134.5, 135.2, 135.3, 149.7, 149.9, 160.7, 194.3; HRMS calcd for $C_{31}H_{26}{}^{74}GeN_2NaO_3$ $[M + Na]^+$ 571.1054, found 571.1068. Anal. Calcd for $C_{31}H_{26}GeN_2O_3$ (547.2): C, 68.04; H, 4.79; N, 5.12. Found: C, 68.26; H, 4.60; N, 4.81.

1-*N*-Benzyl-5-acetyluracil (20). A solution of **15** (15 mg, 0.03 mmol) in CH_3OH (3 mL) was heated for 12 h at 65 °C. Volatiles were evaporated, and the residue was chromatographed (CH_2Cl_2/EtOAc, 2:1) to give **20**[41] (6.5 mg, 95%) as a white powder: UV (MeOH) max 290 nm (ε 12200), 226 nm (ε 8100), min 249 (ε 1400); ^{1}H NMR δ 2.61 (s, 3H), 5.01 (s, 2H), 7.33−7.41 (m, 5H), 8.28 (s, 1H), 8.59 (br s, 1H); ^{13}C NMR δ 30.6, 52.5, 112.8, 128.3, 129.0, 129.3, 134.3, 150.2, 150.6, 161.2, 193.9; GC−MS (t_R 26.87 min) m/z 244 (20, M$^+$), 91 (100; HRMS calcd for $C_{13}H_{12}N_2NaO_3$ $[M + Na]^+$ 267.0740, found 267.0739.

Analogous treatment of **15** (10 mg, 0.02 mmol) using MeOD or MeOH-d_4 instead of MeOH gave 1-*N*-benzyl-5-(2-deuterioacetyl)-uracil (**21**; 4.2 mg, 94%): GC−MS (t_R 26.87 min) m/z 245 (20, M$^+$), 91 (100). ^{1}H NMR spectrum of **21** corresponded to this of the above **20** with 1/3 reduction of the integrated intensity for the signal from methyl group at 2.61 ppm.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NOE and HMBC interactions observed for **11a**, and ^{1}H and ^{13}C NMR spectra for all compounds. 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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