Published in final edited form as:

Nucleosides Nucleotides Nucleic Acids. 2009 May ; 28(5): 537–549. doi:10.1080/15257770903054340.

Application of gemyldesulfonylation reactions to the synthesis of germanium-containing nucleoside analogues

Stanislaw F. Wnuk^{*}, Pablo R. Sacasa, and Jorge Restrepo

Department of Chemistry & Biochemistry, Florida International University, Miami, FL 33199, USA

Abstract

Treatment of the protected (*E*)-5'-deoxy-5'-[(*p*-toluenesulfonyl)methylene]uridine and adenosine derivatives with tributyl- or triphenylgermane hydride (AIBN/toluene/ Δ) effected radical-mediated gemyldesulfonylations to give 5'-(tributyl- or triphenylgermyl)methylene-5'-deoxyuridine and adenosine derivatives as single (*E*)-isomers. Analogous treatment of 2'-deoxy-2'-[(phenylsulfonyl)methylene]uridine with Ph_3GeH afforded the corresponding vinyl triphenylgermane product. Stereoselective halodegermylation of the (*E*)-5'-(tributylgermyl)methylene-5'-deoxy nucleosides with *N*-iodosuccinimide or *N*-bromosuccinimide provided the Wittig-type (*E*)-5'-deoxy-5'-(halomethylene) nucleosides quantitatively, while no halodegermylations was observed with the 5'-deoxy-5'-(triphenylgermyl)methylene counterparts. Treatment of the vinyl trialkylgermanes with aqueous trifluoroacetic acid effected protiodegermylation, while vinyl triarylgermanes were stable under the acidic conditions.

Keywords

Gemyldesulfonylation; germanonucleosides; vinyl germanes; vinyl sulfones

Introduction

Radical-mediated substitution of the arylsulfonyl group with tributylstannyl group at the vinylic carbon has been a critical step in the synthesis of the various nucleoside and amino acids analogues bearing a halo vinyl functionality. For example, McCarthy and coworkers employed a radical-mediated stannyldesulfonylation procedure (**1a** $\rightarrow$ **1b**) for the synthesis of (*E*)-fluorovinyl cytidine **1c** (Tezacitabine; an inhibitor of ribonucleoside reductases with potent anticancer activity), from the protected (α -fluoro)vinyl sulfone **1a** (Figure 1).^{1,2} Stannyldesulfonylation of the vinyl sulfone **2a** followed by halodestannylation of the resulting vinyl stannanes **2b** was a key step in the synthesis of 5'-deoxy-5'-(halomethylene)adenosines **2c**, which were found to be potent inhibitors of *S*-adenosyl-L-homocysteine (AdoHcy) hydrolase and valuable probes to study hydrolytic activity of the enzyme.^{3–5} Stannyldesulfonylation/protiodestannylation of the (α -fluoro)vinyl sulfones and stannyldesulfonylation/halodestannylation of the vinyl sulfones procedures allowed synthesis of the various 5'-deoxy-5'-(halomethylene)nucleoside analogues derived from uridine,⁶ L-adenosine,⁷ 3'-deoxyadenosine,⁸ and 6-*N*-cyclopropyladenosine⁹ as well as 5'-deoxy-5'-(halomethylene)ribose derivatives,¹⁰ among others.¹¹ The vinyl sulfone precursors have been conveniently prepared by treatment of the nucleoside 2'-keto or 5'-aldehyde derivatives with the sulfonyl-stabilized Wittig reagents,^{1·12·13} and chemistry of the vinyl-sulfone modified

Address correspondence to Stanislaw F. Wnuk, Department of Chemistry & Biochemistry, Florida, International University, Miami, FL 33199, E-mail: wnuk@fiu.edu.

In honor and celebration of Morris J. Robins' 70th birthday

carbohydrates and nucleosides has been reviewed.¹⁴ Sulfur extrusion from nucleosidic vinyl sulfide **3a** with tributyltin hydride has been elaborated for the synthesis of the known AdoHcy hydrolase inhibitors **3c** via halodestannylation of the intermediary vinyl stannane **3b**.¹⁵ The sequence involving introduction of the alkenes substituted with F/SO₂Ph, F/SnBu₃, F/I, F/C, or F/H into the synthesis of fluorovinyl analogues of amino acids has been developed by Berkowitz.^{16,17}

In order to eliminate toxicity factors associated with the necessity of using tributyltin hydride reagent in a stannyldesulfonylation reaction, we developed a stereoselective radical-mediated silyl- and germyldesulfonylations of vinyl and (α -fluoro)vinyl sulfones with tris(trimethylsilyl)silane (TTMSS) and germanium hydrides.¹⁸ The germyldesulfonylation protocol tolerates some functional groups vulnerable to the radical hydrogenolysis with tributyltin hydride and TTMSS. For example, a chloro substituent was not affected by the mild conditions required for germyldesulfonylation with Ph₃GeH.¹⁸

Chemistry¹⁹ and biological activity of the organogermanium compounds has been reviewed.^{20,21} Germanium containing α -aminoacids and peptides and their incorporation into biologically active decapeptides has been reported.^{22,23} The 6-trialkylgermyl-5-fluorouridine derivatives are one of the few known examples of germanium-containing nucleoside analogues²⁴ and 5-trimethylgermyl-2'-deoxyuridine was showed to inhibit HSV-1 replication *in vitro* and blocked incorporation of thymidine into DNA of cancer ovarian cells.²⁵ Herein, we report the application of germyldesulfonylation reactions to the synthesis of novel pyrimidine and purine nucleoside analogues modified in the sugar moieties with vinyl germane functionalities and their further application towards the synthesis of vinyl halides.

Results and Discussion

Moffatt oxidation of 2',3'-*O*-isopropylideneuridine **4a** or adenosine **4b** and Wittig treatment of the crude 5'-aldehydes with (*p*-toluenesulfonylmethylene)triphenylphosphorane gave (*E*)-vinyl sulfones **5**¹³ and **6**¹², respectively (Scheme 1). Treatment of the uridine-derived sulfone **5** with tributylgermane hydrides (AIBN/toluene/ Δ) effected stereoselective radical-mediated germyldesulfonylation to give the 5'-(tributylgermyl)methylene-5'-deoxyuridine **7a** as a single (*E*)-isomer ($J_{5'-6'(\text{trans})} = 18.5$ Hz) in 57% yield. Adenosine-derived sulfone **6** also underwent germyldesulfonylation reaction with Bu₃GeH to afford the vinyl germane (*E*)-**8a** (46%). The analogous stannyldesulfonylation of **5** and **6** with Bu₃SnH afforded the corresponding (*E*/*Z*)-5'-(tributylstannyl)methylene-5'-deoxyuridine⁶ and adenosine³ derivatives in 87% and 61% yields, respectively. Treatment of **5** and **6** with triphenylgermane hydride gave (*E*)-5'-deoxy-5'-(triphenylgermyl)methylene nucleosides **7b** (72%) and **8b** (42%), respectively. Thus, both purine and pyrimidine nucleosides underwent desulfonylation with either trialkyl- or triarylgermanes. The yields were higher for the uridine substrates as was also observed in the case of the stannyldesulfonylation reactions.^{3,6} It is noteworthy that contrary to the stannyldesulfonylation reactions,^{3,6} the germyldesulfonylations of the vinyl sulfones derived from the sugar modified nucleosides are stereoselective since the corresponding (*Z*)-isomers of vinyl germanes **7** or **8** were not isolated from the crude reaction mixtures. Germyldesulfonylation reactions presumably occurred via the radical addition-elimination mechanism in analogy to the silyl- and stannyldesulfonylation processes.^{1,18,26}

Stereoselective iododegermylation^{27,28} of tributylgermane **7a** with *N*-iodosuccinimide (NIS) provided the Wittig-type 5'-deoxy-5'-(iodomethylene)uridine (*E*)-**12** (92%). Analogous treatment of tributylgermane **8a** with *N*-bromosuccinimide (NBS) gave 5'-deoxy-5'-(bromomethylene)adenosine (*E*)-**13** (81%) with retention of the double-bond geometry.^{27,28} It is worth mentioning that substitution of the trialkylgermyl group on a sp² carbon with a halogen proceeded more easily than the substitution of the corresponding trialkylsilyl group

with the improved stereochemical outcome.²⁷ Interestingly, treatment of the triphenylgermanes **7b** and **8b** with NBS or NIS failed to afford the corresponding halomethylene nucleosides **12** or **13** resulting instead in the recovery of the vinyl triphenylgermanes. Also treatment of **7b** with iodine ($\text{CH}_2\text{Cl}_2/-78^\circ\text{C}$ to r.t/14 h) did not effect iododegermylations, although iododestannylation of the vinyl triaryltin derivatives is known.²⁹ Apparently, the strength of the $\text{Ge-C}_{\text{sp}^2}$ bond depends on the nature of the substituents at the germanium atom^{19,30} and the stability of the $\text{C}_{\text{sp}^2}\text{-Ge(alkyl)}_3$ bonds is different than that of the $\text{C}_{\text{sp}^2}\text{-Ge(aryl)}_3$ bonds.

Different patterns of reactivity between vinyl triaryl and trialkylgermanes were also observed for the protiodegermylation reactions. Thus, treatment of the tributylgermanes **8a** with aqueous trifluoroacetic acid (TFA) effected simultaneous protiodegermylation and deacetonization to afford 5'-deoxy-5'-methyleneadenosine **14**. On the other hand, treatment of the triphenylgermanes **7b** with TFA effected only removal of the isopropylidene protection group yielding germanonucleoside **10b**. The fully deprotected trialkylgermane **11b** was, however, synthesized using base-labile protection strategy. Thus, treatment of 2',3'-*O*-diacetyl sulfone **9b** with $\text{Bu}_3\text{GeH/AIBN}$ provided **11a** (49%), while germydesulfonylation in the presence of a 2-mercaptoethanol, as a radical carrier,³¹⁻³² and 1,1'-azobis(cyclohexanecarbonitrile) (ACCN) afforded **11a** in 58% yield. Subsequent treatment of **11a** with methanolic ammonia effected deacylation yielding vinyl tributylgermane **11b** (72%). The vinyl triphenylgermane **10b** could be also prepared from the sulfone **9b** via **10a** (65% overall yield) utilizing the acetyl protection strategy.

Germydesulfonylation reaction can also be applied for the removal of the sulfonyl group from the multi-substituted alkenes at C2' position of the nucleosides. Horner-Wittig treatment of the protected 2'-ketouridine³³ **15** with sulfonyl-stabilized enolate derived from diethyl (phenylsulfonyl)methylphosphonate¹⁸ gave vinyl 2'-phenylsulfone **16** as a single (*Z*)-isomer. The *Z* stereochemistry was established using NOESY experiments and was also in agreement with McCarthy's work utilizing the fluoro(phenylsulfonyl)methylphosphonate reagent¹ (Scheme 2). It is noteworthy that reaction between ketone **15** and sulfonyl-stabilized ylide, (*p*-toluenesulfonylmethylene)triphenylphosphorane,¹² failed to give the analogous *p*-toluenesulfone. Germydesulfonylation of **16** with Ph_3GeH afforded 2'-deoxy-2'-[(triphenylgermyl)methylene]uridine **17** (51%) as a single (*Z*)-isomer. Desilylation of **17** with TBAF gave vinyl germane **18** (73%). Thus, germydesulfonylation reaction has a general character and can effect removal of the sulfonyl group from the exomethylene and the isolated double bonds at the sugar moieties of nucleosides. Treatment of **17** (or **5**) with the more reactive tris(trimethylsilyl)germane $[(\text{TMS})_3\text{GeH}]$ provided the corresponding vinyl $(\text{TMS})_3\text{Ge-}$ uridine derivatives but in less than 15% yields (^1H NMR). Therefore, no further efforts were made to optimize germydesulfonylation reactions utilizing $(\text{TMS})_3\text{GeH}$ reagent, although the vinyl tris(trimethylsilyl)germanes could serve as precursors for the further modifications via Pd-catalyzed couplings with aryl/alkenyl halides.^{18,34}

In summary, we have developed a radical-mediated germydesulfonylation procedure as a key step for the synthesis of 5'-deoxy-5'-(halomethylene) nucleosides. The method utilizes less toxic germane hydrides rather than the previously employed tin hydride reagents. The novel 5'-(tributylgermyl)methylene-5'-deoxyadenosine and uridine derivatives underwent efficient halo- and protiodegermylation reactions while the triphenyl counterparts were stable under acidic conditions and upon treatment with NBS or NIS.

Experimental Part

^1H NMR spectra at 400 MHz and ^{13}C NMR at 100.6 MHz were determined with solutions in CDCl_3 , and mass spectra (MS) were obtained by atmospheric pressure chemical ionization (APCI) technique unless noted otherwise. Reagent grade chemicals were used and solvents

were dried by reflux over and distillation from CaH_2 under an argon atmosphere. TLC was performed on Merck kieselgel 60-F₂₅₄ and products were detected with 254 nm light. Merck kieselgel 60 (230–400 mesh) was used for column chromatography. Germane hydrides were purchased from Aldrich or Gelest chemical corporations.

1-[6-(Tributylgermyl)-5,6-dideoxy-2,3-O-isopropylidene-β-D-ribo-hex-5(E)-enofuranosyl]uracil (7a)—A suspension of 5^{13} (48 mg, 0.11 mmol) in toluene (2 mL) was deoxygenated (N_2 , 1 h), and then Bu_3GeH (49 mg, 0.052 mL, 0.20 mmol) was added. Deoxygenation was continued for 30 min, and AIBN (8.2 mg, 0.05 mmol) was added. The resulting solution was refluxed for 14 h [additional AIBN (16.4 mg, 0.1 mmol) in degassed toluene (1 mL) was added to the reaction mixture periodically]. Volatiles were evaporated (TLC analysis showed a formation of the less polar product) and the residue was partitioned ($\text{CHCl}_3/\text{H}_2\text{O}/\text{NaHCO}_3$). The organic layer was washed with brine, dried (MgSO_4) and was evaporated. The residue was column chromatographed [$\text{EtOAc}/\text{hexane}$ (7:3)] to give **7a** (33 mg, 57%) as a syrup: ^1H NMR δ 0.72–0.78 (m, 6H, Bu), 0.84–0.88 (m, 9H, Bu), 1.24–1.33 (m, 12H, Bu), 1.39 (s, 3, CH_3), 1.56 (s, 3, CH_3), 4.52 (“dd”, $J = 4.0, 6.0$ Hz, 1, H_4'), 4.69 (dd, $J = 4.3, 6.4$ Hz, 1, H_3'), 4.92 (dd, $J = 2.0, 6.4$ Hz, 1, H_2'), 5.70 (dd, $J = 1.5, 8.2$ Hz, 1, H_5), 5.72 (d, $J = 2.1$ Hz, 1, H_1'), 5.95 (dd, $J = 6.3, 18.5$ Hz, 1, H_5'), 6.14 (dd, $J = 1.1, 18.5$ Hz, 1, H_6'), 7.20 (d, $J = 8.1$ Hz, 1, H_6), 8.75 (br s, 1, NH); ^{13}C NMR δ 12.71 (Bu), 13.77 (Bu), 25.37 (CMe_2), 26.42 (Bu), 27.15 (CMe_2), 27.29 (Bu), 83.99 (C_3'), 84.83 (C_2'), 89.79 (C_4'), 93.47 (C_1'), 102.41 (C5), 114.65 (CMe_2), 134.02 (C_6'), 140.60 (C_5'), 141.64 (C6), 149.77 (C2), 162.96 (C4); MS m/z 525 (100, MH^+ , ^{74}Ge), 523 (70, MH^+ , ^{72}Ge), 521 (50, MH^+ , ^{70}Ge); HRMS calcd for $\text{C}_{25}\text{H}_{43}^{74}\text{GeN}_2\text{O}_5$ [$\text{M}+\text{H}$] $^+$ 525.2384, found 525.2385.

1-[5,6-Dideoxy-2,3-O-isopropylidene-6-(triphenylgermyl)-β-D-ribo-hex-5(E)-enofuranosyl]uracil (7b)—Treatment of 5^{13} (48 mg, 0.11 mmol) with Ph_3GeH (60 mg, 0.20 mmol) (as described for **7a**) gave **7b** (46 mg, 72%) as a foam: ^1H NMR δ 1.26 (s, 3, CH_3), 1.50 (s, 3, CH_3), 4.61 (ddd, $J = 1.2, 4.2, 5.6$ Hz, 1, H_4'), 4.71 (dd, $J = 4.1, 6.3$ Hz, 1, H_3'), 4.90 (dd, $J = 1.9, 6.4$ Hz, 1, H_2'), 5.55 (d, $J = 8.1$ Hz, 1, H_5), 5.64 (d, $J = 1.9$ Hz, 1, H_1'), 6.12 (dd, $J = 5.7, 18.3$ Hz, 1, H_5'), 6.52 (dd, $J = 1.3, 18.3$ Hz, 1, H_6'), 7.10 (d, $J = 8.1$ Hz, 1, H_6), 7.26–7.33 (m, 9H, Ph), 7.36–7.42 (m, 6H, Ph), 8.65 (br s, 1, NH); ^{13}C NMR δ 25.34 & 27.11 (CMe_2), 84.14 (C_3'), 84.69 (C_2'), 89.48 (C_4'), 93.92 (C_1'), 102.61 (C5), 114.63 (CMe_2), 128.35, 128.53, 129.26, 135.03 (Ph), 135.64 (C_6'), 141.80 (C_5'), 145.00 (C6), 149.75 (C2), 162.99 (C4); MS m/z 585 (100, MH^+ , ^{74}Ge), 583 (70, MH^+ , ^{72}Ge), 581 (50, MH^+ , ^{70}Ge); HRMS calcd for $\text{C}_{31}\text{H}_{31}^{74}\text{GeN}_2\text{O}_5$ [$\text{M}+\text{H}$] $^+$ 585.1485, found 585.1447.

9-[6-(Tributylgermyl)-5,6-dideoxy-2,3-O-isopropylidene-β-D-ribo-hex-5(E)-enofuranosyl]adenine (8a)—Treatment of 6^{12} (50 mg, 0.11 mmol) with Bu_3GeH (47 mg, 0.050 mL, 0.19 mmol) (as described for **7a**) gave **8a** (27 mg, 46%) as a syrup: ^1H NMR δ 0.66–0.71 (m, 6H, Bu), 0.85–0.89 (m, 9H, Bu), 1.26–1.34 (m, 12H, Bu), 1.42 (s, 3, CH_3), 1.62 (s, 3, CH_3), 4.71 (dd, $J = 3.1, 5.0$ Hz, 1, H_4'), 5.02 (dd, $J = 3.1, 6.2$ Hz, 1, H_3'), 5.57 (dd, $J = 1.8, 6.3$ Hz, 1, H_2'), 5.64 (br s, 2, NH_2), 5.95 (dd, $J = 5.1, 18.6$ Hz, 1, H_5'), 6.01 (d, $J = 18.5$ Hz, 1, H_6'), 6.12 (d, $J = 1.8$ Hz, 1, H_1'), 7.88 (s, 1, H_2), 8.35 (s, 1, H_8); ^{13}C NMR δ 12.69 (Bu), 13.85 (Bu), 26.54 (Bu), 26.63 & 27.26 (CMe_2), 27.38 (Bu), 84.70 (C_3'), 85.39 (C_2'), 90.63 (C_4'), 91.27 (C_1'), 114.97 (CMe_2), 120.99 (C5), 133.70 (C_6'), 140.89 (C_5'), 142.02 (C8), 150.44 (C4), 154.05 (C2), 156.36 (C6); MS m/z 548 (100, MH^+ , ^{74}Ge), 546 (70, MH^+ , ^{72}Ge), 544 (50, MH^+ , ^{70}Ge); HRMS calcd for $\text{C}_{26}\text{H}_{44}^{74}\text{GeN}_5\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 548.2656, found 548.2650.

9-[5,6-Dideoxy-2,3-O-isopropylidene-6-(triphenylgermyl)-β-D-ribo-hex-5(E)-enofuranosyl]adenine (8b)—Treatment of 6^{12} (50 mg, 0.11 mmol) with Ph_3GeH (57 mg, 0.19 mmol) (as described for **7a**) gave **8b** (28 mg, 42%) as a foam: ^1H NMR δ 1.39 (s, 3, CH_3), 1.62 (s, 3, CH_3), 4.83 (ddd, $J = 1.3, 3.2, 5.8$ Hz, 1, H_4'), 5.09 (dd, $J = 3.2, 6.3$ Hz, 1,

H3'), 5.55 (dd, $J = 1.9, 6.3$ Hz, 1, H2'), 5.61 (br s, 2, NH₂), 6.11 (d, $J = 1.9$ Hz, 1, H1'), 6.20 (dd, $J = 5.9, 18.3$ Hz, 1, H5'), 6.46 (dd, $J = 1.4, 18.3$ Hz, 1, H6'), 7.31–7.40 (m, 15H, Ph), 7.85 (s, 1, H2), 8.11 (s, 1, H8); ¹³C NMR δ 25.44 & 27.11 (CMe₂), 84.13 (C3'), 84.81 (C2'), 89.75 (C4'), 90.74 (C1'), 114.38 (CMe₂), 120.13 (C5), 127.96, 128.26, 129.13, 134.95 (Ph), 135.67 (C6'), 140.03 (C5'), 145.44 (C8), 149.44 (C4), 153.04 (C2), 155.31 (C6) MS m/z 608 (100, MH⁺, ⁷⁴Ge), 606 (68, MH⁺, ⁷²Ge), 604 (50, MH⁺, ⁷⁰Ge); HRMS calcd for C₃₂H₃₂⁷⁴GeN₅O₃ [M+H]⁺ 608.1717, found 608.1722.

1-[2,3-Di-O-acetyl-5,6-dideoxy-6-(*p*-toluenesulfonyl)- β -D-ribo-hex-5(*E*)-enofuranosyl]uracil (9b)—DMAP (5 mg, 0.04 mmol) was added to a stirred solution of 9a¹³ (80 mg, 0.18 mmol) in Ac₂O (4 mL) at ambient temperature. After 14 h, MeOH (10 mL) was added and stirring was continued for 1 h. Volatiles were evaporated and the residue was co-evaporated with MeOH (2 $\times$ 5 mL). The crude product was partitioned (CHCl₃/H₂O/HCl) and the organic layer was washed with NaHCO₃/H₂O, brine, dried (MgSO₄) and was evaporated to give **9b** (83 mg, 96%) of sufficient purity to be used in next step: ¹H NMR δ 2.05 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.38 (s, 3, CH₃), 4.64 (ddd, $J = 1.6, 4.6, 6.0$ Hz, 1, H4'), 5.24 (t, $J = 6.1$ Hz, 1, H3'), 5.36 (t, $J = 5.5$ Hz, 1, H2'), 5.70 (d, $J = 8.1$ Hz, 1, H5), 5.86 (d, $J = 4.8$ Hz, 1, H1'), 6.62 (dd, $J = 1.6, 15.1$ Hz, 1, H6'), 6.98 (dd, $J = 4.4, 15.1$ Hz, 1, H5'), 7.18 (d, $J = 8.1$ Hz, 1, H6), 7.28 (d, $J = 8.2$ Hz, 2H, Ar), 7.71 (d, $J = 8.3$ Hz, 2H, Ar), 9.45 (br s, 1, NH); ¹³C NMR δ 20.39 (2 $\times$) & 21.65 (CH₃ & 2 $\times$ Ac), 72.16 (C3'), 72.39 (C2'), 79.17 (C4'), 89.35 (C1'), 103.68 (C5), 127.94 (Ar), 129.78 (Ar), 133.33 (C6'), 136.47 (Ar), 138.66 (C5'), 140.21 (C6), 145.01 (Ar), 149.98 (C2), 162.67 (C4), 169.44 & 169.58 (2 $\times$ Ac); MS m/z 479 (100, MH⁺).

1-[2,3-Di-O-acetyl-5,6-dideoxy-6-(triphenylgermyl)- β -D-ribo-hex-5(*E*)-enofuranosyl]uracil (10a)—Treatment of **9b** (90 mg, 0.19 mmol) with Ph₃GeH (104 mg, 0.34 mmol) (as described for **7a**) gave **10a** (81 mg, 68%) as an amorphous solid: ¹H NMR δ 2.09 (s, 3H, Ac), 2.11 (s, 3H, Ac), 4.66 (ddd, $J = 1.5, 5.2, 5.4$ Hz, 1, H4'), 5.27 (t, $J = 5.2$ Hz, 1, H3'), 5.32 (t, $J = 5.4$ Hz, 1, H2'), 5.65 (d, $J = 8.1$ Hz, 1, H5), 6.10 (d, $J = 5.1$ Hz, 1, H1'), 6.17 (dd, $J = 5.4, 18.3$ Hz, 1, H5'), 6.73 (dd, $J = 1.4, 18.3$ Hz, 1, H6'), 7.18 (d, $J = 8.2$ Hz, 1, H6), 7.37–7.43 (m, 9H, Ph), 7.45–7.50 (m, 6H, Ph), 8.98 (br s, 1, NH); ¹³C NMR δ 20.43 & 20.54 (2 $\times$ Ac), 72.55 (C2'), 72.96 (C3'), 83.18 (C4'), 87.43 (C1'), 103.47 (C5), 128.48, 129.44, 134.96, 135.21 (Ph), 131.02 (C6'), 139.34 (C6), 142.87 (C5'), 150.22 (C2), 162.63 (C4), 169.61 (2 $\times$ Ac); MS m/z 629 (100, MH⁺, ⁷⁴Ge), 627 (70, MH⁺, ⁷²Ge), 625 (50, MH⁺, ⁷⁰Ge); HRMS calcd for C₃₂H₃₁⁷⁴GeN₂O₇ [M+H]⁺ 629.1343, found 629.1335.

1-[5,6-Dideoxy-6-(triphenylgermyl)- β -D-ribo-hex-5(*E*)-enofuranosyl]uracil (10b)

Method A: A solution of **10a** (32 mg, 0.05 mmol) in NH₃/MeOH (2 mL) was stirred at $\sim 0^\circ$ C for 2 h, and was evaporated and co-evaporated (MeOH). The residue was column chromatographed (EtOAc/hexane, 4:1) to give **10b** (26 mg, 96%) as a white powder: ¹H NMR δ 4.01 (t, $J = 5.5$ Hz, 1, H3'), 4.19 (dd, $J = 3.5, 5.0$ Hz, 1, H2'), 4.62 ("t", $J = 5.5$ Hz, 1, H4'), 5.20 (br s, 2, 2 $\times$ OH), 5.58 (d, $J = 8.1$ Hz, 1, H5), 5.82 (d, $J = 3.2$ Hz, 1, H1'), 6.20 (dd, $J = 5.3, 18.4$ Hz, 1, H5'), 6.71 (dd, $J = 1.4, 18.3$ Hz, 1, H6'), 7.32–7.46 (m, 16H, Ph & H6), 8.92 (br s, 1, NH); ¹³C NMR δ 73.82 (C3'), 75.10 (C2'), 85.81 (C4'), 91.11 (C1'), 102.52 (C5), 128.43, 128.87, 130.98, 134.85 (Ph), 136.36 (C6'), 139.54 (C6), 144.29 (C5'), 151.21 (C2), 163.69 (C4); MS m/z 545 (100, MH⁺, ⁷⁴Ge), 543 (75, MH⁺, ⁷²Ge), 541 (45, MH⁺, ⁷⁰Ge); HRMS calcd for C₂₈H₂₇⁷⁴GeN₂O₅ [M+H]⁺ 545.1132, found 545.1132.

Method B: A solution of **7b** (29 mg, 0.05 mmol) in TFA/H₂O (9:1, 1.5 mL) was stirred at $\sim 0^\circ$ C for 1 hr. The volatiles were evaporated, co-evaporated (3 $\times$) with toluene and the residue was column chromatographed (EtOAc) to give **10b** (18 mg, 66%) with data identical as above.

1-[2,3-Di-O-acetyl-6-(tributylgermyl)-5,6-dideoxy- β -D-ribo-hex-5-(*E*)-enofuranosyl]uracil (**11a**)

Method A: Treatment of **9b** (39 mg, 0.08 mmol) with Bu₃GeH (39 mg, 0.041 mL, 0.16 mmol) (as described for **7a**) gave **11a** (22 mg, 49%) as a foam: ¹H NMR δ 0.78–0.92 (m, 15H, Bu), 1.26–1.38 (m, 12H, Bu), 2.08 (s, 3H, Ac), 2.10 (s, 3H, Ac), 4.52 (“t”, J = 5.5 Hz, 1, H4’), 5.22 (t, J = 5.3 Hz, 1, H3’), 5.30 (t, J = 5.4 Hz, 1, H2’), 5.75 (d, J = 8.1 Hz, 1, H5), 5.95 (dd, J = 5.7, 18.5 Hz, 1, H5’), 6.02 (d, J = 5.2 Hz, 1, H1’), 6.26 (dd, J = 1.2, 18.5 Hz, 1, H6’), 7.26 (d, J = 8.1 Hz, 1, H6), 8.27 (s, 1, NH); ¹³C NMR δ 12.71 (Bu), 13.73 (Bu), 26.35 (Bu), 27.32 (Bu), 20.42 & 20.49 (2 $\times$ Ac), 72.78 (C3’), 72.91 (C2’), 83.57 (C4’), 87.73 (C1’), 103.24 (C5), 135.65 (C6’), 138.84 (C5’), 139.50 (C6), 149.89 (C2), 162.27 (C4); 169.56 & 169.57 (2 $\times$ Ac); MS m/z 569 (100, MH⁺, ⁷⁴Ge), 567 (72, MH⁺, ⁷²Ge), 565 (51, MH⁺, ⁷⁰Ge); HRMS calcd for C₂₆H₄₃⁷⁴GeN₂O₇ [M+H]⁺ 569.2282, found 569.2289.

Method B: A suspension of **9b** (29 mg, 0.06 mmol) in toluene (4 mL) was degassed (N₂, 1 h), and then Bu₃GeH (29 mg, 0.031 mL, 0.12 mmol) was added and deoxygenation was continued for an additional 1 h. The 2-mercaptoethanol (2 mg, 2 μ L, 0.02 mmol) and ACCN (14.5 mg, 0.06 mmol) were added and the resulting solution was refluxed for 20 h. The aqueous work-up and column chromatography (as described for **7a**) gave **11a** (20 mg, 58%) with data as reported above.

1-[6-(Tributylgermyl)-5,6-dideoxy- β -D-ribo-hex-5-(*E*)-enofuranosyl]uracil (**11b**)

—Treatment of **11a** (23 mg, 0.04 mmol) with NH₃/MeOH (2 mL) (as described for **10a**) gave **11b** (14 mg, 72%) as a white powder: ¹H NMR (MeOH-*d*₄) δ 0.83–0.97 (m, 15H, Bu), 1.30–1.46 (m, 12H, Bu), 3.96 (“t”, J = 5.7 Hz, 1, H3’), 4.18 (dd, J = 3.8, 5.3 Hz, 1, H2’), 4.35 (t, J = 5.8 Hz, 1, H4’), 5.69 (d, J = 8.1 Hz, 1, H5), 5.83 (d, J = 3.8 Hz, 1, H1’), 6.11 (dd, J = 5.3, 18.5 Hz, 1, H5’), 6.20 (d, J = 18.6 Hz, 1, H6’), 7.55 (d, J = 8.1 Hz, 1, H6); ¹³C NMR (MeOH-*d*₄) δ 13.71 (Bu), 14.09 (Bu), 27.46 (Bu), 28.56 (Bu), 75.12 & 75.13 (C2’/3’), 87.08 (C4’), 92.09 (C1’), 102.78 (C5), 133.15 (C6’), 142.39 (C5’), 143.20 (C6), 152.22 (C2), 166.08 (C4); MS m/z 485 (100, MH⁺, ⁷⁴Ge), 483 (77, MH⁺, ⁷²Ge), 481 (52, MH⁺, ⁷⁰Ge); HRMS calcd for C₂₂H₃₉⁷⁴GeN₂O₅ [M+H]⁺ 485.2071, found 485.2065.

1-[5,6-Dideoxy-6-iodo-2,3-O-isopropylidene- β -D-ribo-hex-5(*E*)-enofuranosyl]uracil (**12**)

—A solution of NIS (22 mg, 0.10 mmol) in CHCl₃/CH₂Cl₂ (1:1, 5 mL) was added dropwise to a stirred solution of **7a** (48 mg, 0.09 mmol) in CHCl₃/CH₂Cl₂ (1:1, 5 mL) at 0 °C. After 1 h (TLC showed exclusive formation of a more polar product), the pink reaction mixture was treated with NaHSO₃/H₂O and the separated organic layer was washed with brine, dried (MgSO₄) and was evaporated. Purification on a short silica gel column (CHCl₃/MeOH, 30:1) gave **12** (34 mg, 92%) with data as reported.⁶

9-[6-Bromo-5,6-dideoxy-2,3-O-isopropylidene- β -D-ribo-hex-5(*E*)-enofuranosyl]adenine (**13**)

—A solution of NBS (18 mg, 0.10 mmol) in CHCl₃/CH₂Cl₂ (1:1, 5 mL) was added dropwise to a stirred solution of **8a** (50 mg, 0.09 mmol) in CHCl₃/CH₂Cl₂ (1:1, 5 mL) at 0 °C. After 6 h, the reaction mixture was washed with NaHCO₃/H₂O and brine and the separated organic layer was dried (Na₂SO₄) and was evaporated. Purification on a short silica gel column (CHCl₃/MeOH, 20:1) gave **13** (28 mg, 81%) with data as reported.

9-(5,6-Dideoxy- β -D-ribo-hex-5-enofuranosyl)adenine [5’-deoxy-5’-methyleneadenosine] (**14**)

—A solution of **8a** (22 mg, 0.04 mmol) in CF₃CO₂H/H₂O (9:1, 1 mL) was stirred at 0 °C for 1 h. The volatiles were evaporated and the residue was co-evaporated (2 $\times$) with toluene. The residue was column chromatographed (1 $\rightarrow$ 5% MeOH/EtOAc) to give **14** (8 mg, 76%): ¹H NMR (MeOH-*d*₄) δ 4.25 (t, J = 5.1 Hz, 1, H3’), 4.48 (dd, J = 5.3, 6.5 Hz, 1, H4’), 4.74 (t, J = 4.9 Hz, 1, H2’), 5.26 (“dt”, J = 1.4, 10.5 Hz, 1, H6”),

5.41 (“dt”, $J = 1.5, 17.1$ Hz, 1, H6’), 6.04 (d, $J = 5.0$ Hz, 1, H1’), 6.11 (“ddd”, $J = 6.6, 10.5, 17.1$ Hz, 1, H5’), 8.23 (s, 1, H2), 8.26 (s, 1, H8).

2'-Deoxy-3',5'-O-(1,1,3,3-tetraisopropyl-1,3-disiloxanyl)-2'-[(phenylsulfonyl)methylene]uridine [16(Z)]—Lithium bis(trimethylsilyl)amide (1 M/THF; 0.18 mL, 0.18 mmol) was added dropwise to a stirred solution of diethyl (phenylsulfonyl)methylphosphonate¹⁸ (53 mg, 0.18 mmol) in THF (2 mL) at -78 °C under nitrogen. After 30 min, ketone **15**³³ (78 mg, 0.16 mmol) was added and the resulting solution was allowed to warm up to -30 °C over 2 h and then to ~ 0 °C over 15 min. $\text{NH}_4\text{Cl}/\text{H}_2\text{O}$ (0.5 mL) was added and the volatiles were evaporated. The residue was partitioned ($\text{CHCl}_3/\text{H}_2\text{O}/\text{NaHCO}_3$) and the organic layer was washed with brine, dried (MgSO_4) and was evaporated. Column chromatography (30 $\rightarrow$ 40% EtOAc/hexane) gave **16** (62 mg, 62%) as a pale-yellow powder: ^1H NMR δ 0.97–1.05 (m, 28H, $4 \times i\text{-Pr}$), 3.62 (ddd, $J = 3.0, 4.2, 8.7$ Hz, 1, H4’), 3.99 (dd, $J = 3.0, 12.8$ Hz, 1, H5’), 4.06 (dd, $J = 4.2, 12.8$ Hz, 1, H5’’), 5.35 (dt, $J = 2.1, 8.5$ Hz, 1, H3’), 5.70 (d, $J = 8.0$ Hz, 1, H5), 6.43 (“t”, $J = 1.8$ Hz, 1, H1’), 6.48 (“t”, $J = 2.3$ Hz, 1, H2’’), 7.27 (d, $J = 8.1$ Hz, 1, H6), 7.51 (“t”, $J = 7.4$ Hz, 2H, Ph), 7.60 (“tt”, $J = 1.3, 7.4$ Hz, 1H, Ph), 7.68 (“dd”, $J = 1.4, 7.1$ Hz, 2H, Ph), 8.30 (s, 1, NH); ^{13}C NMR δ 12.58 (CH), 16.86, 16.94, 17.05, 17.13, 17.20, 17.21, 17.23, 17.35 (CH_3), 61.21 (C5'), 73.02 (C3'), 81.38 (C4'), 85.83 (C1'), 102.06 (C5), 124.17 (C2''), 126.57, 129.56, 134.02, 140.57 (Ph), 145.08 (C6), 148.65 (C2), 156.65 (C2'), 162.91 (C4); MS m/z 623 (100, MH^+).

2'-Deoxy-3',5'-O-(1,1,3,3-tetraisopropyl-1,3-disiloxanyl)-2'-[(triphenylgermyl)methylene]uridine [17(Z)]—Treatment of **16** (43 mg, 0.07 mmol) with Ph_3GeH (40 mg, 0.13 mmol) (as described for **7a**) gave **17** (28 mg, 51%) as a white powder: ^1H NMR δ 0.91–0.97 (m, 24H, $8 \times \text{CH}_3$), 1.03 (s, 4H, $4 \times \text{CH}$), 3.50 (dt, $J = 3.2, 8.7$ Hz, 1, H4’), 3.86 (dd, $J = 3.2, 12.1$ Hz, 1, H5’), 3.91 (dd, $J = 3.6, 12.1$ Hz, 1, H5’’), 4.88 (“dt”, $J = 2.2, 8.4$ Hz, 1, H3’), 5.15 (d, $J = 8.1$ Hz, 1, H5), 5.83 (t, $J = 1.7$ Hz, 1, H1’), 6.29 (d, $J = 8.1$ Hz, 1, H6), 6.77 (t, $J = 2.1$ Hz, 1, H2’’), 7.20–7.26 (m, 9H, Ph), 7.30–7.36 (m, 6H, Ph), 8.28 (s, 1, NH); ^{13}C NMR δ 12.60, 12.66, 13.05, 13.65 (CH), 16.92, 17.02, 17.22, 17.24, 17.27, 17.31, 17.36 (CH_3), 61.31 (C5'), 73.50 (C3'), 82.12 (C4'), 85.37 (C1'), 102.24 (C5), 122.63 (C2''), 128.62, 129.53, 134.63, 135.29 (Ph), 141.17 (C6), 149.03 (C2), 155.27 (C2'), 162.21 (C4); MS m/z 787 (50, MH^+ , ^{74}Ge), 785 (35, MH^+ , ^{72}Ge), 783 (25, MH^+ , ^{70}Ge); HRMS calcd for $\text{C}_{40}\text{H}_{53}^{74}\text{GeN}_2\text{O}_6\text{Si}_2$ [$\text{M}+\text{H}$] $^+$ 787.2654, found 787.2663.

2'-Deoxy-2'-[(triphenylgermyl)methylene]uridine [18(Z)]— Bu_4NF (1 M/THF, 0.12 mL, 0.12 mmol) was added to a solution of **17** (31 mg, 0.04 mmol) in THF (2 mL) and the resulting mixture was stirred at ~ 0 °C for 3 h. Volatiles were evaporated and the residue was partitioned between diethyl ether and water. The aqueous layer was evaporated and the oily residue was column chromatographed (EtOAc) to give **18** (16 mg, 73%) as an amorphous solid: ^1H NMR ($\text{MeOH}-d_4$) δ 3.66–3.73 (m, 2, H4’,5’), 3.83–3.89 (m, 1, H5’’), 4.77 (dt, $J = 2.2, 8.0$ Hz, 1, H3’), 5.32 (d, $J = 8.0$ Hz, H5), 6.14 (t, $J = 1.7$ Hz, 1, H1’), 6.86 (t, $J = 2.2$ Hz, 1, H2’’), 7.04 (d, $J = 8.0$ Hz, 1, H6), 7.37–7.43 (m, 9H, Ph), 7.49–7.52 (m, 6H, Ph); ^{13}C NMR ($\text{MeOH}-d_4$) δ 62.33 (C5'), 73.43 (C3'), 85.44 (C4'), 86.93 (C1'), 102.93 (C5), 124.67 (C2''), 129.65, 130.54, 135.76, 136.76 (Ph), 143.85 (C6), 151.61 (C2), 159.02 (C2'), 166.01 (C4); MS m/z 545 (50, MH^+ , ^{74}Ge), 543 (35, MH^+ , ^{72}Ge), 541 (25, MH^+ , ^{70}Ge); HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{26}^{74}\text{GeN}_2\text{NaO}_5$ [$\text{M}+\text{Na}$] $^+$ 567.0951, found 567.0960.

Acknowledgments

This investigation was supported by NIGMS and NCI SC1CA138176 award. P.R.S and J.R were sponsored by MBRS RISE program (NIGMS; R25GM61347).

References

- McCarthy JR, Matthews DP, Stermerick DM, Huber EW, Bey P, Lippert BJ, Snyder RD, Sunkara PS. Stereospecific method to (*E*) and (*Z*) terminal fluoroolefins and its application to the synthesis of 2'-deoxy-2'-fluoromethylenenucleosides as potential inhibitors of ribonucleoside diphosphate reductase. *J Am Chem Soc* 1991;113:7439–7440.
- Shao J, Zhou B, Chu B, Yen Y. Ribonucleotide reductase inhibitors and future drug design. *Curr Cancer Drug Targets* 2006;6:409–431. [PubMed: 16918309]
- Wnuk SF, Yuan CS, Borchardt RT, Balzarini J, De Clercq E, Robins MJ. Nucleic Acid-Related Compounds. 84. Synthesis of 6'-(*E* and *Z*)-Halohomovinyl Derivatives of Adenosine, Inactivation of S-Adenosyl-L-homocysteine Hydrolase, and Correlation of Anticancer and Antiviral Potencies with Enzyme Inhibition. *J Med Chem* 1994;37:3579–3587. [PubMed: 7932585]
- Yuan CS, Wnuk SF, Liu S, Robins MJ, Borchardt RT. (*E*)-5' and 6'-Didehydro-6'-deoxy-6'-fluorohomoadenosine: A Substrate That Measures the Hydrolytic Activity of S-Adenosylhomocysteine Hydrolase. *Biochemistry* 1994;33:12305–12311. [PubMed: 7918452]
- Yuan CS, Liu S, Wnuk SF, Robins MJ, Borchardt RT. Mechanism of Inactivation of S-Adenosylhomocysteine Hydrolase by (*E*)-5',6'-Didehydro-6'-deoxy-6'-halohomoadenosines. *Biochemistry* 1994;33:3758–3765. [PubMed: 8142376]
- Wnuk SF, Robins MJ. Nucleic acid related compounds. 78. Stereocontrolled syntheses of 6'(*E* and *Z*)-halovinyl analogs from uridine-derived vinylsulfones via vinyltin intermediates. *Can J Chem* 1993;71:192–198.
- Wang JF, Yang XD, Zhang LR, Yang ZJ, Zhang LH. Synthesis and biological activities of 5'-ethylenic and acetylenic modified L-nucleosides and isonucleosides. *Tetrahedron* 2004;60:8535–8546.
- Robins MJ, Neschadimenko V, Ro BO, Yuan CS, Borchardt RT, Wnuk SF. Nucleic Acid Related Compounds. 101. S-Adenosyl-L-homocysteine Hydrolase Does Not Hydrate (5'-Fluoro)vinyl or (6'-Halo)homovinyl Analogs Derived from 3'-Deoxyadenosine or 3'-(Chloro or Fluoro)-3'-deoxyadenosine. *J Org Chem* 1998;63:1205–1211.
- Rapp M, Haubrich TA, Perrault J, Mackey ZB, McKerrow JH, Chiang PK, Wnuk SF. Antitrypanosomal Activity of 5'-Deoxy-5'-(iodo-methylene)adenosine and Related 6-N-Cyclopropyl-adenosine Analogs. *J Med Chem* 2006;49:2096–2102. [PubMed: 16539398]
- Wnuk SF, Lalama J, Garmendia CA, Robert J, Zhu J, Pei D. S-Ribosylhomocysteine analogues with the carbon-5 and sulfur atoms replaced by a vinyl or (fluoro)vinyl unit. *Bioorg Med Chem* 2008;16:5090–5102. [PubMed: 18375129]
- Shen Y. Recent advances in fluorinated vinylstannanes and their synthetic utility. *J Organomet Chem* 2006;691:1452–1461.
- Wnuk SF, Robins MJ. Nucleic acid related compounds. 63. Synthesis of 5'-deoxy-5'-methyleneadenosine and related Wittig-extended nucleosides. *Can J Chem* 1991;69:334–338.
- Wnuk SF, Dalley NK, Robins MJ. Nucleic acid related compounds. 67. Synthesis of 5'-amino and 5'-methylthio chain-extended nucleosides from uridine. *Can J Chem* 1991;69:2104–2111.
- Pathak T. Vinyl sulfone-modified carbohydrates: an inconspicuous group of chiral building blocks. *Tetrahedron* 2008;64:3605–3628.
- Kumamoto H, Onuma S, Tanaka H. Sulfur Extrusion with Tin Radical: Synthesis of 4',5'-Didehydro-5'-deoxy-5'-(tributylstannyl)adenosine, an Intermediate for Potential Inhibitors against S-Adenosyl Homocysteine Hydrolase. *J Org Chem* 2004;69:72–78. [PubMed: 14703380]
- Berkowitz DB, delaSalud-Bea R, Jahng WJ. Synthesis of Quaternary Amino Acids Bearing a (2'*Z*)-Fluorovinyl α -Branch: Potential PLP Enzyme Inactivators. *Org Lett* 2004;6:1821–1824. [PubMed: 15151423]
- Karukurichi KR, delaSalud-Bea R, Jahng WJ, Berkowitz DB. Examination of the New α -(2'*Z*-Fluoro)vinyl Trigger with Lysine Decarboxylase: The Absolute Stereochemistry Dictates the Reaction Course. *J Am Chem Soc* 2007;129:258–259. [PubMed: 17212389]
- Wnuk SF, Garcia PI Jr, Wang Z. Radical-Mediated Silyl- and Germlydesulfonylation of Vinyl and (α -Fluoro)vinyl Sulfones: Application of Tris(trimethylsilyl)silanes and Tris(trimethylsilyl)germanes in Pd-Catalyzed Couplings. *Org Lett* 2004;6:2047–2049. [PubMed: 15176815]

19. Patai, S.; Rappoport, Z. The Chemistry of Organic Germanium, Tin and Lead Compounds. Vol. 1. John Wiley & Sons; Chichester, UK: 1995. & 2002; Vol 2
20. Lukevics, E.; Ignatovich, L. ^{32}Ge Biological Activity of Organogermanium Compounds. In: Gielen, M.; Tiekink, ERT., editors. Metallotherapeutic Drugs and Metal-Based Diagnostic Agents. 2005. p. 279-295.
21. Lukevics, E.; Ignatovich, L. Biological Activity of Organogermanium Compounds. In: Rappoport, Z., editor. The Chemistry of Organic Germanium, Tin and Lead Compounds. 2002. p. 1653-1683.
22. Tacke R, Merget M, Bertermann R, Bernd M, Beckers T, Reissmann T. Syntheses and Properties of Silicon- and Germanium-Containing α -Amino Acids and Peptides: A Study on C/Si/Ge Bioisosterism. *Organometallics* 2000;19:3486–3497.
23. Merget M, Gunther K, Bernd M, Gunther E, Tacke R. Syntheses of racemic and non-racemic silicon- and germanium-containing $[\alpha]$ -amino acids of the formula type $\text{H}_2\text{NCH}(\text{CH}_2\text{ElR}_3)\text{COOH}$ (El=Si, Ge; R=organyl) and incorporation of $-\text{H}_2\text{NCH}(\text{CH}_2\text{SiMe}_3)\text{COOH}$ and $-\text{H}_2\text{NCH}(\text{CH}_2\text{GeMe}_3)\text{COOH}$ into biologically active decapeptides: a study on C/Si/Ge bioisosterism. *J Organomet Chem* 2001;628:183–194.
24. Lukevics E, Ignatovich L, Shilina N, Kemme A, Sjakste N. Synthesis, structure and biological activity of 6- $\text{R}_3\text{Si}(\text{Ge}, \text{Sn})$ -substituted 5-fluorouracils. *Metal-Based Drugs* 1994;1:65–72. [PubMed: 18476217]
25. Mel'nik, SI; Bakhmedova, AA.; Nedorezova, TP.; Iartseva, IV.; Zhukova, OS.; Dobrynin, YV.; Preobrazhenskaya, MN.; Kolesnikov, SP.; Li, VY. Synthesis of anomeric 5-trimethylgermyl-2'-deoxyuridines and study of their antiviral and cytotoxic properties. *Bioorg Khim* 1985;11:1248–1252. [PubMed: 2998405]
26. Chatgililoglu C. $(\text{Me}_3\text{Si})_3\text{SiH}$: Twenty Years After Its Discovery as a Radical-Based Reducing Agent. *Chem Eur J* 2008;14:2310–2320.
27. Oda H, Morizawa Y, Oshima K, Nozaki H. Stereoselective synthesis of vinylgermanes and their facile transformation into vinyl halides. *Tetrahedron Lett* 1984;25:3221–3224.
28. Schwier T, Gevorgyan V. Trans- and Cis-Selective Lewis Acid Catalyzed Hydrogermylation of Alkynes. *Org Lett* 2005;7:5191–5194. [PubMed: 16268535]
29. Dimopoulos P, Athlan A, Manaviazar S, Hale KJ. On the Stereospecific Conversion of Proximally-Oxygenated Trisubstituted Vinyltriphenylstannanes into Stereodefined Trisubstituted Alkenes. *Org Lett* 2005;7:5373–5376. [PubMed: 16288509]
30. Basch H. Bond dissociation energies in organometallic compounds. *Inorg Chim Acta* 1996;252:265–279.
31. Roberts BP. Polarity-reversal catalysis of hydrogen-atom abstraction reactions: concepts and applications in organic chemistry. *Chem Soc Rev* 1999;28:25–35.
32. Postigo A, Kopsov S, Ferreri C, Chatgililoglu C. Radical Reactions in Aqueous Medium Using $(\text{Me}_3\text{Si})_3\text{SiH}$. *Org Lett* 2007;9:5159–5162. [PubMed: 17997562]
33. Hansske F, Madej D, Robins MJ. 2' and 3'-ketonucleosides and their arabino and xylo reduction products: Convenient access via selective protection and oxidation of ribonucleosides. *Tetrahedron* 1984;40:125–135.
34. Wang Z, Wnuk SF. Application of Vinyl Tris(trimethylsilyl)germanes in Pd-Catalyzed Couplings. *J Org Chem* 2005;70:3281–3284. [PubMed: 15822995]

Figure 1.

Nucleoside analogues whose synthesis were accomplished by tin radical-mediated extrusion of sulfur atoms

Scheme 1.

Reagents and conditions: (a) (i) DCC/DMSO/Cl₂CHCO₂H, (ii) Ph₃P=CHTs; (b) Bu₃GeH or Ph₃GeH/AIBN/PhCH₃/heat; (c) NIS or NBS; (d) TFA/H₂O; (e) Bu₃GeH/ACCN/HOCH₂CH₂SH/PhCH₃/heat; (f) DMAP/Ac₂O; (g) NH₃/MeOH.

Scheme 2.

Reagents and conditions: (a) PhSO₂CH₂PO(OEt)₂/LHMDS/THF; (b) Ph₃GeH/AIBN/PhCH₃/heat; (c) TBAF/THF