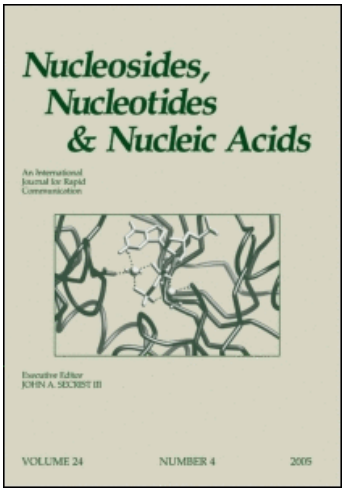

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Intramolecular Radical Reactions of 5'-*O*-Modified 2',3'-Didehydro-2',3'-Dideoxyuridine Derivatives

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INTRAMOLECULAR RADICAL REACTIONS OF 5'-*O*-MODIFIED 2',3'-DIDEHYDRO-2',3'-DIDEOXYURIDINE DERIVATIVES

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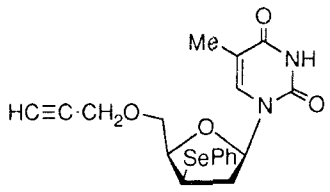
Abstract Radical reactions of 5'-*O*-(2-bromo-1-methoxy)ethyl- and 5'-*O*-(2-propynyl)-2',3'-dideoxy-2',3'-didehydrouridines were investigated. Both reactions proceeded in a 6-*exo-trig* manner to give products cyclized regio- and stereospecifically at the 3'-position. The structures of these products were analyzed by X-ray crystallography.

The use of radical reactions has become an increasingly important method for constructing C-C bonds in organic chemistry.[2)] In the case where a radical generating site and a radical acceptor are present in the same molecule, the reaction provides a highly efficient approach to the synthesis of cyclic compounds.

There has been ample precedent for radical cyclization between the base and sugar moieties of nucleosides.[3)] If one considers such intramolecular radical reactions within the sugar part of nucleosides, they may fall into two categories: either the hydroxyl protecting group is designed to react with sugar carbon radicals or the sugar backbone itself functions as a radical acceptor. Several reports have dealt with the former strategy,[4)] in which substrates such as **1** were used. In the particular case of **1**, the 3'-phenylseleno group[5)] upon reacting with tributyltin radical generates a carbon radical which undergoes 6-*exo-dig* cyclization with the 5'-*O*-propynyl group to give an *exo*-methylene product in 27% yield.[4a)] In the present work, we describe two examples of the latter approach by employing 5'-*O*-substituted 2',3'-dideoxy-2',3'-didehydrouridines (**3** and **4**) as substrates.

This paper is dedicated to Dr. Yoshihisa Mizuno, one of the founders of nucleic acids chemistry in Japan, on the occassion of his 75th birthday.



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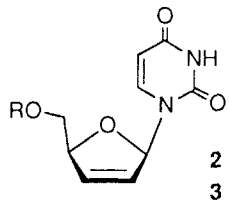
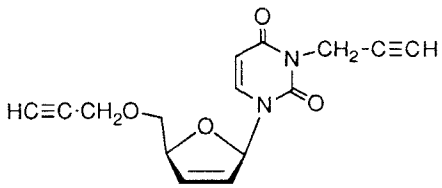


2 R= H
3 R= CH(OMe)CH_2Br
4 R= $CH_2C{\equiv}CH$

An acetal exchange reaction between **2** and bromoacetaldehyde dimethylacetal (20 equiv) in refluxing THF in the presence of pyridinium *p*-toluenesulfonate (0.1 equiv) gave **3** in 85% yield as a mixture of two diastereomers (*ca.* 1:1, estimated by ^{1}H NMR spectroscopy). Radical-mediated cyclization of **3** was carried out in refluxing benzene by adding a mixture of Bu_3SnH and 2,2'-azobisisobutyronitrile (AIBN) by a syringe pump over 6.5 h.[6] Compounds **5**, **6**, and **7** were obtained in this reaction. Structures of the 6-*exo-trig* cyclized products **5** and **6** were unambiguously determined by X-ray crystallography. The results are shown in Figures 1 and 2 by a stereoview.[7] That **7** (an inseparable mixture of two diastereomers) is the reduction product was apparent from its ^{1}H NMR spectrum which showed the presence of two quartets (δ 4.65 and 4.66 ppm) attributable to methyne resonance of the 5'-*O*-substituent.

The reaction of **3** was examined under different conditions. The results summarized in Table 1 show that combined yield of **5** and **6** is only moderate (28-50%). Also, the yield of **5** is uniformly higher than that of **6** throughout entries 1-3. This would be explicable on the basis of steric hindrance of their transition states: carbon radical derived from (*S*)-**3** (isomer having *S*-configuration about the 5'-*O*-substituent), when undergoes 6-*exo-trig* cyclization, should suffer from a considerable steric repulsion between *endo*-OMe and the base moiety.

Tin radical-initiated cyclization of **4** which has an ene-yne structure was next examined.[8] The substrate **4** was prepared by regioselective propargylation of N^3,$O^{5'}$-dianion of **2**. Thus, when **2** was treated with NaH (2.5 equiv) in THF/DMF and reacted with propargyl bromide (1 equiv) at 7 °C, **4** was obtained in 70% yield. Compound **8** was also isolated in 10% yield.



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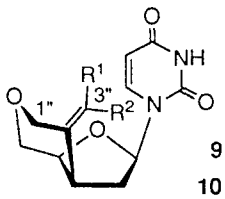

9 R^1= $SnBu_3$, R^2= H
10 R^1= H, R^2= $SnBu_3$
11 R^1= R^2= H

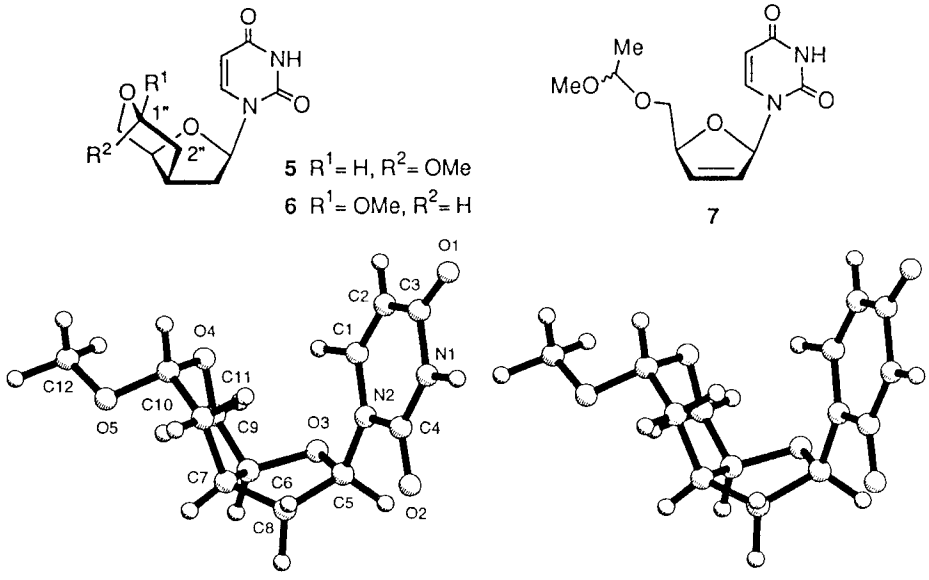

FIG. 1. Stereoview of Compound **5**.

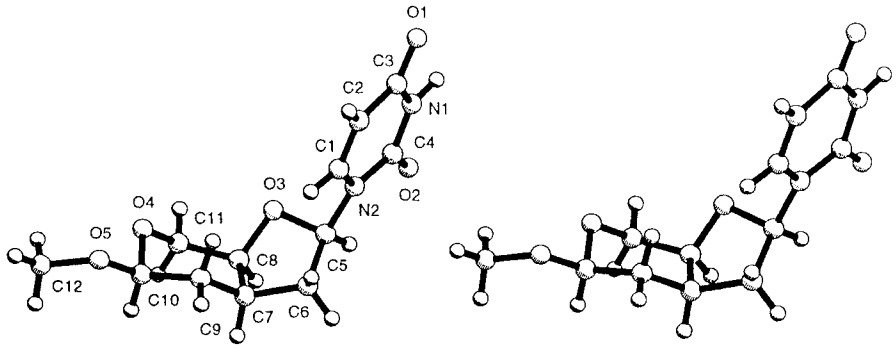

FIG. 2. Stereoview of Compound **6**.

TABLE 1. Radical-mediated cyclization of **3**.[a)]

Entry	Bu_3SnH (equiv)	Concentration (M) of **3**	Products (% yield)
1	2	0.02	**5** (21), **6** (7), and **7** (17)[b)]
2	3	0.02	**5** (32), **6** (16), and **7** (31)
3	3	0.01	**5** (32), **6** (18), and **7** (23)

[a)] All reactions were carried out in refluxing benzene by adding a mixture of AIBN (0.1 equiv) and Bu_3SnH in benzene by a syringe pump over 6.5 h.

[b)] The starting material (**3**) was also isolated in 6% recovery.

The cyclization of **4** was carried out under similar conditions to those used for **3**, except that THF was used as a co-solvent due to poor solubility of **4** in benzene. As compared to the result of **3**, a significant increase in combined yield (81%) of the cyclized products (**9**: 64%, **10**: 17%) was attained in this reaction, suggesting highly reactive nature of the β-stannylvinyl radical intermediate. Mass spectrometric analyses of these products, which showed a characteristic cluster of tin-isotopes, clearly indicated the presence of tributylstannyl group. The olefinic stereochemistry of **9** and **10** was assumed based on their NOESY spectra: NOE correlation was observed between H-3" and H-3' plus H-2'α in the former, while it was observed between H-3" and H-1" in the case of the latter. The stannyl group in these products can readily be removed by acidic treatment,[9)] as verified by the conversion of **9** to **11** in 80% yield. The structure of **11** was confirmed again by X-ray analysis[7)] and its stereoview is given in Figure 3.

In conclusion, the present study shows that radical-mediated cyclizations of **3** and **4** take place exclusively in a 6-*exo-trig* manner to form C-C bonds at the β-face of the 3'-position. The products involved in this study can be further transformed to 3'-*C*-branched derivatives. Also, our preliminary experiments using **3** (or **4**) and Bu_3SnD indicated that the deuterium is incorporated solely into the α-face of 2'-position of the products. This fact may add an appeal to the present method in that simultaneous C-C bond formation at both the β-face of 3'- and the α-face of 2'-positions would become possible. Further studies are now in progress in our laboratory.

EXPERIMENTAL

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 a JEOL JNM-GX 400 spectrometer. Mass spectra (MS) were taken on either a JEOL SX-

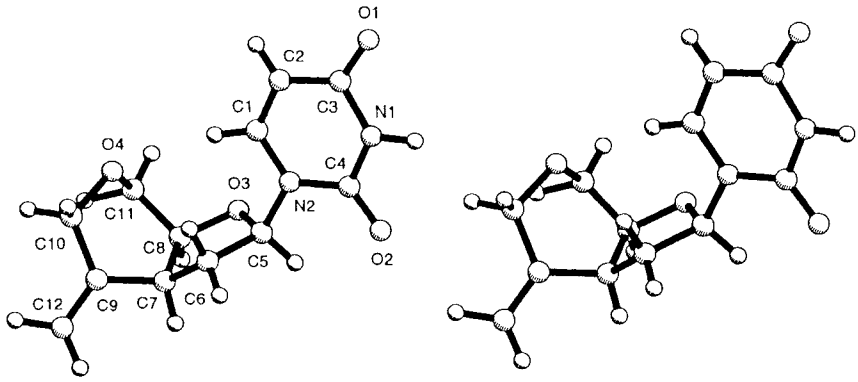

FIG. 3. Stereoview of Compound **11**.

102A (in FAB mode, *m*-nitrobenzyl alcohol as a matrix) or a JEOL JMS-D 300 (in EI mode) spectrometer. Ultraviolet spectra (UV) were recorded on a JASCO Ubest-55 spectrophotometer. Column chromatography was carried out on either Florisil® or silica gel (Silica Gel 60, Merck). Thin layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck).

5'-*O*-[2-Bromo-(*RS*)-1-methoxy]ethyl-2',3'-didehydro-2',3'-dideoxyuridine (3). In a 200 mL round-bottomed flask equipped with a Dean-Stark trap, a mixture of **2** (403 mg, 1.92 mmol), bromoacetaldehyde dimethylacetal (4.65 mL, 34.8 mmol), pyridinium *p*-toluenesulfonate (48 mg, 0.19 mmol) and THF (50 mL) was placed. The mixture was refluxed with stirring under Ar. MeOH formed was separated as the THF azeotrope, while THF (20 mL) was added every 2 h. After 15 h, the reaction mixture was allowed to cool to room temperature and quenched by adding Et_3N (27 μL, 1.92 mmol). Florisil column chromatography (50% EtOAc in hexane) of the reaction mixture gave **3** (565 mg, 85%) as a solid. Compound **3** consisted of two diastereomers (*ca.* 1:1). UV (MeOH) λ_{max} 260 nm (ε 9000), λ_{min} 230 nm (ε 2100); FAB-MS *m/z* 349 and 347 (M^++H), 317 and 315 (M^+–OMe). Anal. Calcd for $C_{12}H_{15}BrN_2O_5$: C, 41.52; H, 4.36; N, 8.07. Found: C, 41.19; H, 4.76; N, 7.73.

^{1}H NMR data of one diastereomer are as follows: ^{1}H NMR ($CDCl_3$) δ 3.36 (2H, d, J= 5.1 Hz, CH_2Br), 3.38 (3H, s, OMe), 3.78 (1H, dd, $J_{4',5'}$= 2.9, J_{gem}= 11.0 Hz, H-5'), 3.85 (1H, dd, $J_{4',5'}$= 2.9 Hz, H-5'), 4.62 (1H, t, J= 5.1 Hz, C*H*OMe), 5.02 (1H, m, H-4'), 5.72 (1H, dd, $J_{5,NH}$= 2.6, $J_{5,6}$= 8.1 Hz, H-5), 5.85 (1H, m, H-3'), 6.36 (1H, dt,

$J_{1',2'}$= $J_{2',4'}$= 1.8, $J_{2',3'}$= 6.2 Hz, H-2'), 7.02 (1H, t, $J_{1',2'}$= $J_{1',3'}$= 1.8 Hz, H-1'), 7.69 (1H, d, H-6), 7.97 (1H, br, NH).

^{1}H NMR data of the other diastereomer are as follows: ^{1}H NMR ($CDCl_3$) δ 3.31-3.44 (2H, m, CH_2Br), 3.35 (3H, s, OMe), 3.72 (1H, dd, $J_{4',5'}$= 2.9, J_{gem}= 10.6 Hz, H-5'), 3.94 (1H, dd, $J_{4',5'}$= 2.9 Hz, H-5'), 4.65 (1H, dd, J= 4.8 and 6.2 Hz, C*H*OMe), 5.01 (1H, m, H-4'), 5.70 (1H, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.1 Hz, H-5), 5.85 (1H, m, H-3'), 6.34 (1H, dt, $J_{1',2'}$= $J_{2',4'}$= 1.8, $J_{2',3'}$= 5.5 Hz, H-2'), 7.03 (1H, t, $J_{1',2'}$= $J_{1',3'}$= 1.8 Hz, H-1'), 7.74 (1H, d, H-6), 8.40 (1H, br, NH).

Radical-mediated cyclization of 3. Formation of 5 and 6. To a refluxing benzene (31 mL) solution of **3** (109 mg, 0.31 mmol), a mixture of Bu_3SnH (0.26 mL, 0.93 mmol) and AIBN (5.1 mg, 0.03 mmol) in benzene (7.4 mL) was added over 6.5 h by a syringe pump. Florisil column chromatography (hexane and then EtOAc) followed by preparative TLC (hexane/EtOAc= 1/1) gave **5** (27 mg, 32%), **6** (15 mg, 18%), and **7** (19 mg, 23%).

Compound **5** was crystallized from $CHCl_3$: mp 172-173 °C; UV (MeOH) λ_{max} 263 nm (ε 9700), λ_{min} 230 nm (ε 1700); ^{1}H NMR ($CDCl_3$) δ 1.55 (1H, ddd, $J_{2'',3''}$= 8.8, $J_{1'',2''}$= 4.4, J_{gem}= 14.7 Hz, H-2''), 1.71 (1H, ddd, $J_{2'',3''}$= 6.2, $J_{1'',2''}$= 3.7, H-2''), 1.88 (1H, dt, $J_{1',2'}$= $J_{2',3'}$= 4.0, J_{gem}= 12.8 Hz, H-2'), 2.53-2.63 (1H, m, H-2' and H-3'), 3.39 (3H, s, OMe), 3.92 (2H, d, $J_{4',5'}$= 1.8, H-5'), 4.10 (1H, dt, $J_{3',4'}$= 6.2 Hz, H-4'), 4.74 (1H, dd, J= 3.7 and 4.4 Hz, C*H*OMe), 5.76 (1H, d, $J_{5,6}$= 8.1 Hz, H-5), 5.94 (1H, dd, $J_{1',2'}$= 4.0 and 6.2 Hz, H-1'), 7.82 (1H, d, H-6), 8.37 (1H, br, NH); MS *m/z* 237 (M^+–OMe), 157 (M^+–B), 126 (M^+–B–OMe). Anal. Calcd for $C_{12}H_{10}N_2O_5$: C, 53.73; H, 6.01; N, 10.44. Found: C, 53.43; H, 6.00; N, 10.37.

Compound **6** was crystallized from $CHCl_3$-hexane: mp 201-203 °C; UV (MeOH) λ_{max} 263 nm (ε 11700), λ_{min} 227 nm (ε 700); ^{1}H NMR ($CDCl_3$) δ 1.33 (1H, ddd, $J_{1'',2''}$= 7.7, $J_{2'',3''}$= 10.3, J_{gem}= 13.9 Hz, H-2''), 1.91 (1H, ddd, $J_{1'',2''}$= 2.9, $J_{2'',3''}$= 7.0, H-2''), 2.02 (1H, dt, $J_{1',2'}$= 3.7, J_{gem}= 14.1 Hz, H-2'), 2.47 (1H, m, H-3'), 2.65 (1H, dt, $J_{1',2'}$= 7.3 Hz, H-2'), 3.46 (3H, s, OMe), 3.78 (1H, dd, $J_{4',5'}$= 3.3, J_{gem}= 13.2 Hz, H-5'), 4.03 (1H, dt, $J_{4',5'}$= 3.3, $J_{3',4'}$= 6.2 Hz, H-4'), 4.21 (1H, dd, $J_{4',5'}$= 3.3 Hz, H-5'), 4.38 (1H, dd, J= 2.9 and 7.7 Hz, C*H*OMe), 5.77 (1H, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.2 Hz, H-5), 5.91 (1H, dd, $J_{1',2'}$= 3.7 and 7.3 Hz, H-1'), 7.81 (1H, d, H-6), 8.00 (1H, br, NH); MS *m/z* 268 (M^+), 237 (M^+–OMe), 157 (M^+–B), 126 (M^+–B–OMe). Anal. Calcd for $C_{12}H_{10}N_2O_5$: C, 53.73; H, 6.01; N, 10.44. Found: C, 53.86; H, 5.86; N, 10.26.

^{1}H NMR and MS data of **7**, obtained as a mixture of two diastereomers (*ca.* 1:1), are as follows: ^{1}H NMR ($CDCl_3$) δ 1.28 and 1.29 (1.5H each, d, J= 5.5 Hz, CH(OMe)*Me*), 3.27 and 3.28 (1.5H each, s, OMe), 3.60 and 3.69 (0.5H each, dd, $J_{4',5'}$= 2.9, J_{gem}=

11.0 Hz, H-5'), 3.82 and 3.88 (0.5H each, dd, $J_{4',5'}$= 2.9 and 2.6 Hz, H-5'), 4.65 and 4.66 (0.5H each, q, J= 5.5 Hz, C*H*(OMe)Me), 5.00 (1H, m, H-4'), 5.65 and 5.68 (0.5H each, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.1 Hz, H-5), 5.82, 5.83, 6.31, and 6.33 (0.5H each, dt, $J_{1',2'}$= $J_{2',4'}$= 1.6, $J_{2',3'}$= 5.9, $J_{1',3'}$= $J_{3',4'}$= 1.6 Hz, H-2' and H-3'), 7.02-7.04 (1H, m, H-1'), 7.78 and 7.79 (0.5H each, d, H-6), 8.49 (1H, br, NH); FAB-MS *m/z* 237 (M^+–OMe), 193 (M^+–$CH_2OCH(OMe)Me$), 125 (M^+–B–MeOH).

2',3'-Didehydro-2',3'-dideoxy-5'-*O*-(2-propynyl)uridine (4). To a solution of **2** (74.3 mg, 0.35 mmol) in THF (3.6 mL)/DMF (1.2 mL), NaH (60% oil suspension, 35 mg, 0.88 mmol) was added. After sonication for 0.5 h, propargyl bromide (30 μL, 0.35 mmol) was added to the mixture and the whole was stirred at 7 °C for 10 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and evaporated. The resulting whole residue was chromatographed on a silica gel column (hexane/EtOAc= 2/1) to give **4** (61.6 mg, 70%) and **8** (10.3 mg, 10%). Compound **4** was crystallized from $CHCl_3$-hexane: mp 144-146 °C; UV (MeOH) λ_{max} 267 nm (ε 10500), λ_{min} 236 nm (ε 1400); ^{1}H NMR ($CDCl_3$) δ 2.47 (1H, t, J= 2.4 Hz, C≡CH), 3.76 (1H, dd, $J_{4',5'}$= 2.8, J_{gem}= 10.8 Hz, H-5'), 3.79 (1H, dd, $J_{4',5'}$= 2.8 Hz, H-5'), 4.15-4.16 (1H, m, O*C*H_2C≡CH), 4.99 (1H, m, H-4'), 5.69 (1H, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.1 Hz, H-5), 5.84 and 6.31 (2H, each as m, $J_{2',3'}$= 6.2 Hz, H-2' and H-3'), 7.02-7.03 (1H, m, H-1'), 7.75 (1H, d, H-6), 8.68 (1H, br, NH); FAB-MS *m/z* 249 (M^++H), 193 (M^+–OCH_2C≡CH). Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 57.77; H, 4.81; N, 11.08.

^{1}H NMR and MS data of **8** are as follows: ^{1}H NMR ($CDCl_3$) δ 2.17 (1H, t, J= 2.4 Hz, NCH_2C≡C*H*), 2.46 (1H, t, J= 2.4 Hz, OCH_2C≡C*H*), 3.75 (1H, dd, $J_{4',5'}$= 3.7, J_{gem}= 11.0 Hz, H-5'), 3.79 (1H, dd, $J_{4',5'}$= 2.9 Hz, H-5'), 4.15 (2H, d, J= 2.6 Hz, O*C*H_2C≡CH), 4.69 and 4.74 (2H, each as dd, J_{gem}= 16.5 Hz, N*C*H_2C≡CH), 5.00 (1H, m, H-4'), 5.76 (1H, d, $J_{5,6}$= 8.1 Hz, H-5), 5.85 and 6.31 (2H, each as dt, $J_{2',3'}$= 5.9 Hz, H-2' and H-3'), 7.07 (1H, t, $J_{1',2'}$= $J_{1',3'}$= 1.8 Hz, H-1'), 7.73 (1H, d, H-6); FAB-MS *m/z* 287 (M^++H), 231 (M^+–OCH_2C≡CH).

Radical-mediated cyclization of 4. Formation of 9 and 10. A solution of **4** (75.7 mg, 0.31 mmol) in THF (2 mL) was diluted with benzene (13.4 mL). While refluxing this solution, a mixture of Bu_3SnH (0.25 mL, 0.92 mmol) and AIBN (5.1 mg, 0.03 mmol) in benzene (7.3 mL) was added over 6 h by a syringe pump. Florisil column chromatography (hexane and then EtOAc) followed by preparative TLC (hexane/EtOAc= 3/1) of the reaction mixture gave **9** (105.5 mg, 64%) as a syrup and **10** (28.4 mg, 17%) as a powder.

TABLE 2. Atomic Coordinates and B_{iso}/B_{eq} Used for Crystallographic Analysis of **5**.

Atom	X	Y	Z	*Beq* (Å^2)
O (1)	-0.4536(8)	0.0425(5)	-0.467(1)	4.8(2)
O (2)	-0.3881(9)	-0.0878(5)	0.062(1)	3.8(2)
O (3)	-0.1406(7)	-0.2344(4)	-0.211(1)	3.6(2)
O (4)	-0.2419(8)	-0.3197(5)	-0.546(1)	4.1(2)
O (5)	-0.3821(8)	-0.4231(4)	-0.484(1)	4.0(2)
N (1)	-0.424(1)	-0.0246(6)	-0.209(2)	3.3(2)
N (2)	-0.2986(8)	-0.1361(5)	-0.202(1)	2.5(2)
C (1)	-0.277(1)	-0.1297(6)	-0.392(2)	3.3(3)
C (2)	-0.329(1)	-0.0691(7)	-0.486(2)	3.3(3)
C (3)	-0.405(1)	-0.0150(6)	-0.404(2)	3.1(2)
C (4)	-0.371(1)	-0.0844(6)	-0.110(2)	3.6(3)
C (5)	-0.231(1)	-0.1960(6)	-0.091(2)	3.7(3)
C (6)	-0.176(1)	-0.3158(6)	-0.216(2)	2.9(2)
C (7)	-0.323(1)	-0.3202(7)	-0.155(2)	3.1(3)
C (8)	-0.330(1)	-0.2564(7)	-0.019(2)	3.8(3)
C (9)	-0.142(1)	-0.3437(8)	-0.406(3)	4.6(3)
C (10)	-0.377(1)	-0.3415(6)	-0.501(2)	3.6(3)
C (11)	-0.423(1)	-0.3075(7)	-0.319(2)	3.3(3)
C (12)	-0.344(2)	-0.464(1)	-0.650(3)	6.7(5)
H (1)	-0.47(1)	0.020(7)	-0.15(2)	5(3)
H (2)	-0.23(1)	-0.170(6)	-0.44(2)	3(2)
H (3)	-0.31(1)	-0.074(7)	-0.64(2)	5(3)
H (4)	-0.17(1)	-0.163(6)	0.00(2)	4(3)
H (5)	-0.30(1)	-0.278(7)	0.12(2)	6(3)
H (6)	-0.42(1)	-0.240(7)	-0.01(2)	6(3)
H (7)	-0.12(1)	-0.348(6)	-0.14(2)	4(2)
H (8)	-0.34(1)	-0.371(6)	-0.10(2)	2(2)
H (9)	-0.14(1)	-0.403(7)	-0.41(2)	6(3)
H (10)	-0.04(1)	-0.317(7)	-0.45(2)	7(3)
H (11)	-0.44(1)	-0.318(7)	-0.60(2)	6(3)
H (12)	-0.51(1)	-0.330(6)	-0.30(2)	4(2)
H (13)	-0.43(1)	-0.247(6)	-0.33(1)	2(2)
H (14)	-0.36(2)	-0.527(9)	-0.64(3)	10(4)
H (15)	-0.41(2)	-0.449(9)	-0.74(2)	7(4)
H (16)	-0.26(2)	-0.447(7)	-0.70(2)	7(3)

Physical data of **9** are as follows: UV (MeOH) λ_{max} 263 nm (ε 8900), λ_{min} 247 nm (ε 4800); ^{1}H NMR ($CDCl_3$) δ 0.82-0.99 (15H, m, $SnCH_2(CH_2)_2Me$), 1.25-1.39 (6H, m, $SnCH_2CH_2CH_2Me$), 1.42-1.54 (6H, m, $SnCH_2CH_2CH_2Me$), 2.45-2.57 (2H, m, H-2'), 3.21 (1H, m, H-3'), 3.65 (1H, dd, $J_{4',5'}$= 2.4, J_{gem}= 13.0 Hz, H-5'), 4.07 (1H, d, J_{gem}= 13.7 Hz, H-1''), 4.15 (1H, d, H-5'), 4.23 (1H, m, H-4'), 4.37 (1H, d, H-1''), 5.66 (1H, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.1 Hz, H-5), 5.87 (1H, d, J= 1.5 Hz, H-3''), 6.08 (1H, dd, $J_{1',2'}$= 4.8 and 6.2 Hz, H-1'), 7.82 (1H, d, H-6), 8.46 (1H, br, NH); MS (isotope peaks

TABLE 3. Atomic Coordinates and B_{iso}/B_{eq} Used for Crystallographic Analysis of **6**.

Atom	X	Y	Z	*Beq* (Å^2)
O (1)	0.2775(4)	0.5080(1)	0.2822(4)	4.59(7)
O (2)	0.4654(3)	0.3600(1)	-0.1291(4)	3.76(6)
O (3)	0.4249(3)	0.2337(1)	0.1689(4)	3.71(6)
O (4)	0.3295(3)	0.1220(1)	0.4330(4)	4.37(7)
O (5)	0.4092(4)	0.1066(1)	0.7374(4)	5.29(8)
N (1)	0.3740(4)	0.4329(1)	0.0830(4)	2.99(7)
N (2)	0.5014(3)	0.3412(1)	0.1918(4)	2.72(6)
C (1)	0.4797(5)	0.3628(2)	0.3761(5)	2.86(8)
C (2)	0.4092(5)	0.4183(2)	0.4174(5)	3.03(9)
C (3)	0.3483(5)	0.4566(2)	0.2661(6)	3.01(8)
C (4)	0.4485(4)	0.3766(2)	0.0369(5)	2.66(8)
C (5)	0.5570(5)	0.2756(2)	0.1506(6)	3.32(9)
C (6)	0.6833(5)	0.2479(2)	0.2804(7)	3.58(9)
C (7)	0.6227(4)	0.1807(2)	0.3316(6)	3.20(8)
C (8)	0.4924(5)	0.1705(2)	0.1860(6)	3.56(9)
C (9)	0.5607(5)	0.1747(2)	0.5359(6)	3.53(10)
C (10)	0.4647(5)	0.1147(2)	0.5528(6)	3.9(1)
C (11)	0.3726(6)	0.1215(2)	0.2368(6)	4.1(1)
C (12)	0.3387(9)	0.0444(3)	0.7672(10)	6.1(2)
H (1)	0.333(4)	0.457(2)	-0.020(5)	4.1(9)
H (2)	0.514(4)	0.336(2)	0.481(5)	3.9(9)
H (3)	0.404(5)	0.434(2)	0.550(6)	4.7(9)
H (4)	0.587(5)	0.275(2)	0.017(5)	4.1(10)
H (5)	0.784(5)	0.246(2)	0.217(6)	5.0(10)
H (6)	0.698(5)	0.275(2)	0.397(6)	4.6(10)
H (7)	0.702(4)	0.148(2)	0.316(5)	3.6(8)
H (8)	0.539(5)	0.157(2)	0.063(6)	4(1)
H (9)	0.647(5)	0.176(2)	0.629(6)	5(1)
H (10)	0.499(4)	0.214(2)	0.567(6)	3.9(9)
H (11)	0.523(4)	0.076(2)	0.508(6)	5(1)
H (12)	0.410(5)	0.078(2)	0.210(6)	5(1)
H (13)	0.275(5)	0.130(2)	0.162(6)	5(1)
H (14)	0.307(6)	0.041(3)	0.893(8)	8(1)
H (15)	0.252(7)	0.040(3)	0.678(8)	8(1)
H (16)	0.416(6)	0.013(3)	0.744(8)	8(1)

corresponding to ^{120}Sn, ^{118}Sn, and ^{116}Sn are shown) *m/z* 483, 481, and 479 (M^+–Bu), 371, 369, and 367 (M^+–B–Bu). Anal. Calcd for $C_{24}H_{40}N_2O_4Sn$: C, 53.45; H, 7.48; N, 5.19. Found: C, 53.61; H, 7.61; N, 5.05.

Physical data of **10** are as follows: UV (MeOH) λ_{max} 260 nm (ε 11000), λ_{min} 235 nm (ε 5600); ^{1}H NMR ($CDCl_3$) δ 0.87-0.96 (15H, m, $SnCH_2(CH_2)_2Me$), 1.25-1.39 (6H, m, $SnCH_2CH_2CH_2Me$), 1.45-1.57 (6H, m, $SnCH_2CH_2CH_2Me$), 2.13 (1H, ddd, $J_{2'\beta,3'}$= 11.7, $J_{1',2'\beta}$= 8.8, J_{gem}= 12.8 Hz, H-2'β), 2.41 (1H, ddd, $J_{2'\alpha,3'}$= 8.6, $J_{1',2'\alpha}$= 5.5 Hz,

TABLE 4. Atomic Coordinates and B_{iso}/B_{eq} Used for Crystallographic Analysis of **11**.

Atom	X	Y	Z	*Beq* (Å^2)
O (1)	0.7836(7)	0.0015(2)	0.1295(7)	5.3(1)
O (2)	0.8010(8)	0.1786(2)	-0.2899(7)	4.8(1)
O (3)	0.9413(5)	0.2984(2)	0.1160(8)	4.2(1)
O (4)	0.809(1)	0.3289(4)	0.5110(9)	9.1(2)
N (1)	0.7868(8)	0.0913(3)	-0.0724(8)	3.3(1)
N (2)	0.8027(7)	0.2021(3)	0.0408(7)	2.8(1)
C (1)	0.796(1)	0.1762(3)	0.231(1)	3.5(2)
C (2)	0.793(1)	0.1107(3)	0.273(1)	4.0(2)
C (3)	0.7964(10)	0.0635(3)	0.116(1)	3.7(2)
C (4)	0.7869(9)	0.1592(3)	-0.1188(10)	3.3(2)
C (5)	0.8126(10)	0.2751(3)	0.0079(10)	3.1(2)
C (6)	0.6804(9)	0.3153(3)	0.086(1)	3.7(2)
C (7)	0.7510(10)	0.3821(4)	0.153(1)	4.1(2)
C (8)	0.9088(9)	0.3624(4)	0.207(1)	4.2(2)
C (9)	0.6695(9)	0.4149(4)	0.326(1)	4.3(2)
C (10)	0.684(2)	0.3775(6)	0.516(2)	7.7(3)
C (11)	0.938(1)	0.3577(7)	0.423(2)	6.9(3)
C (12)	0.597(1)	0.4723(5)	0.312(2)	6.8(3)
H (1)	0.776(9)	0.060(3)	-0.19(1)	5(1)
H (2)	0.794(9)	0.212(3)	0.33(1)	5(1)
H (3)	0.786(9)	0.093(3)	0.405(10)	5(1)
H (4)	0.831(8)	0.281(3)	-0.137(9)	4(1)
H (5)	0.598(7)	0.322(3)	-0.02(1)	3(1)
H (6)	0.631(7)	0.288(3)	0.195(10)	3(1)
H (7)	0.748(8)	0.0414(3)	0.041(10)	4(1)
H (8)	0.983(7)	0.397(3)	0.16(1)	4(1)
H (10)	0.59(1)	0.350(4)	0.54(2)	9(1)
H (11)	0.70(1)	0.406(4)	0.64(2)	10(1)
H (12)	0.92(1)	0.402(5)	0.52(2)	10(2)
H (13)	1.021(8)	0.327(3)	0.45(1)	6(1)
H (15)	0.54(1)	0.490(5)	0.44(2)	9(1)
H (16)	0.583(10)	0.494(4)	0.18(1)	6(1)

H-2'α), 3.18 (1H, ddd, $J_{3',4'}$= 9.2 Hz, H-3'), 3.48 (1H, dd, $J_{4',5'}$= 2.6, J_{gem}= 13.0 Hz, H-5'), 3.86 (1H, d, H-5'), 4.26-4.31 (2H, m, H-4' and H-1''), 4.69 (1H, dd, $J_{1'',3''}$= 1.5, J_{gem}= 14.7 Hz, H-1''), 5.76 (1H, dd, J= 1.5 and 2.2 Hz, H-3''), 5.81 (1H, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.1 Hz, H-5), 6.31 (1H, dd, H-1'), 7.81 (1H, d, H-6), 8.31 (1H, br, NH); MS (isotope peaks corresponding to ^{120}Sn, ^{118}Sn, and ^{116}Sn are shown) *m/z* 483, 481, and 479 (M^+–Bu), 371, 369, and 367 (M^+–B–Bu). Anal. Calcd for $C_{24}H_{40}N_2O_4Sn$: C, 53.45; H, 7.48; N, 5.19. Found: C, 53.53; H, 7.68; N, 5.23.

Protonolysis of 9 leading to 11. A solution of **9** (145.1 mg, 0.26 mmol) in 10% AcOH/MeOH (25 mL) was refluxed for 6.5 h and then neutralized with saturated

aqueous $NaHCO_3$. Extraction of the reaction mixture with $CHCl_3$ followed by preparative TLC (hexane/EtOAc= 1/1) gave **11** (53.4 mg, 82%), which was crystallized from $CHCl_3$-hexane: mp 195-196 °C; UV (MeOH) λ_{max} 260 nm (ε 9800), λ_{min} 237 nm (ε 7500); ^1H NMR ($CDCl_3$) δ 2.50 (1H, dt, $J_{1',2'}$= $J_{2',3'}$= 3.7, J_{gem}= 13.9 Hz, H-2'), 2.56 (1H, ddd, $J_{1',2'}$= 6.2, $J_{2',3'}$= 7.3 Hz, H-2'), 3.09-3.13 (1H, m, H-3'), 3.71 (1H, dd, $J_{4',5'}$= 2.0, J_{gem}= 13.2 Hz, H-5'), 4.05 (1H, d, J_{gem}= 13.6 Hz, H-1"), 4.19 (1H, dd, $J_{3',4'}$= 6.8, $J_{4',5'}$= 2.0 Hz, H-4'), 4.21 (1H, d, H-5'), 4.37 (1H, d, H-1"), 4.93 and 4.98 (2H, each as s, H-3"), 5.68 (1H, dd, $J_{5,NH}$= 2.2, $J_{5,6}$= 8.1 Hz, H-5), 6.05 (1H, dd, H-1'), 7.84 (1H, d, H-6), 8.83 (1H, br, NH); FAB-MS *m/z* 251 (M^++H), 139 (M^+−B). Anal. Calcd for $C_{12}H_{14}N_2O_4$: C, 57.59; H, 5.64; N, 11.19. Found: C, 57.58; H, 5.70; N, 11.07.

Data used for X-ray analyses of 5, 6, and 11.

Compound **5**: space group $P2_12_12_1$ (orthorhombic), Z= 4, a= 9.819(2), b= 17.66(2), c= 7.240(4) Å, V= 1255(1) Å^3, Dc= 1.419 g/cm^3, R= 0.100.

Compound **6**: space group $P2_12_12_1$ (orthorhombic), Z= 4, a= 8.6381(7), b= 20.726(1), c= 6.969(2) Å, V= 1247.7(3) Å^3, Dc= 1.428 g/cm^3, R= 0.038.

Compound **11**: space group $P2_12_12_1$ (orthorhombic), Z= 4, a= 8.949(1), b= 19.751(1), c= 6.760(2) Å, V= 1194.9(2) Å^3, Dc= 1.391 g/cm^3, R= 0.061.

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