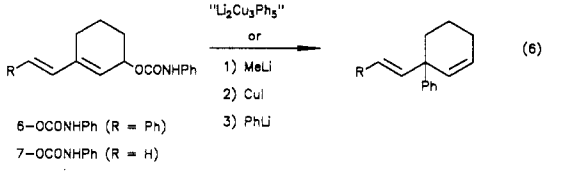
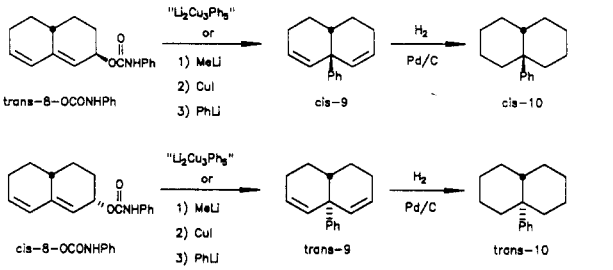
The Gallina procedure[4] involves adding an organocopper reagent "$Li_2Cu_3R_5$" (prepared by adding 5 equiv of RLi to 3 equiv CuI) to 1 equiv of carbamate in ether. Although the method is wasteful of lithium reagent, yields (with respect to carbamate) are very good and exclusive syn-γ-coupling occurs. Our procedure[5] is a three-step, one-pot process and involves initial deprotonation of the carbamate with 1 equiv of MeLi followed by complexation of the lithium carbamate with 1 equiv of CuI. The final step is the addition of 1 equiv of lithium reagent (coupling agent). Thus, only 1 equiv of coupling agent is necessary. In order to obtain good yields and to insure high regio- and stereospecificity, complete complexation (step 2) is critical.

The following examples illustrate how either method can be used to generate phenyl-substituted quaternary carbon centers regio- and stereospecifically.[7] Phenylation of 6-OCONHPh and 7-OCONHPh by either method is regiospecific and gives excellent yields of γ-coupling product (eq 6).



(6)

Phenylation of *cis*- or *trans*-8-OCONHPh[8] by either method is regio- and stereospecific (syn-γ-coupling) and yields *trans*- or *cis*-**9**, respectively (eq 7 and 8). The



(7)

(8)

stereochemistry of *cis*- and *trans*-**9** was determined by hydrogenation of each isomer to the corresponding decalin (**10**) and obtaining ^{13}C NMR spectra at room temperature and at −50 °C. The 10 ring carbons of the conformationally flexible *cis*-**10** give six signals at room temperature and ten signals at −50 °C.[9] *trans*-**10** gives six signals for the 10 ring carbons regardless of the temperature.[9]

Experimental Section

General Methods. All reagents were prepared and purified, and lithium reagents were standardized as reported earlier.[2] The high-resolution mass spectrometer and the 200-MHz NMR spectrometer used in this work have also been described.[2] General procedures for alkylation of allylic *N*-phenylcarbamates have been reported;[4,5,8] the Gallina method[4] gave comparable yields to our method[5] and ranged from 75% to 93%.

3-((*E*)-2-Phenylethenyl)-2-cyclohexenyl *N*-phenylcarbamate (6-OCONHPh) was prepared from the corresponding alcohol[10] and phenyl isocyanate in the usual manner[5,11] and recrystallized from hexane (95% yield). The carbamate had the following properties: mp 148–149 °C dec; NMR ($CDCl_3$) δ 7.0–7.4 (m, 10 H), 6.80 (d, 1 H, J = 16.1 Hz), 6.60 (d, 1 H, J = 16.1 Hz), 6.56 (m, 1 H), 5.94 (br s, 1 H), 5.42 (br s, 1 H), 2.2–2.5 (m, 2 H), 1.7–2.0 (m, 4); high-resolution mass spectrum calcd for $C_{21}H_{21}NO_2$ m/e 319.1573, found m/e 319.1568.

3-Ethenyl-2-cyclohexenyl *N*-phenylcarbamate (7-OCONHPh) was prepared as above from the corresponding alcohol[12] (94% yield) and had the following properties: mp 59–60 °C; NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H), 7.06 (t, 1 H, J = 6.6 Hz), 6.63 (br s, 1 H), 6.37 (dd, 1 H, J = 17.6, 10.8 Hz), 5.80 (br s, 1 H), 5.40 (br s, 1 H), 5.26 (d, 1 H, J = 17.6 Hz), 5.09 (d, 1 H, J = 10.8 Hz), 2.0–2.4 (m, 2 H), 1.5–2.0 (m, 4 H); high-resolution mass spectrum calcd for $C_{15}H_{17}NO_2$ m/e 243.1260, found m/e 243.1255.

3-Phenyl-3-((*E*)-2-phenylethenyl)cyclohexene: NMR ($CDCl_3$) δ 7.1–7.5 (m, 10 H), 6.42 (s, 2 H), 5.98 (dt, 1 H, J = 10.1, 3.5 Hz), 5.80 (d, 1 H, J = 10.1 Hz), 2.0–2.1 (m, 4 H), 1.4–1.8 (m, 2 H); high-resolution mass spectrum calcd for $C_{20}H_{20}$ m/e 260.1566, found m/e 260.1566.

3-Ethenyl-3-phenylcyclohexene: NMR ($CDCl_3$) δ 7.2–7.4 (m, 5 H), 6.02 (dd, 1 H, J = 17.3, 10.6 Hz), 5.94 (dt, 1 H, J = 10.1, 3.6 Hz), 5.72 (br d, 1 H, J = 10.1 Hz), 5.15 (dd, 1 H, J = 10.6, 1.3 Hz), 5.09 (dd, 1 H, 17.3, 1.3 Hz), 2.0–2.1 (m, 2 H), 1.9–2.0 (m, 2 H), 1.4–1.7 (m, 2 H); high-resolution mass spectrum calcd for $C_{14}H_{16}$ m/e 184.1253, found m/e 184.1255.

***cis*-3,4,4a,5,6,8a-Hexahydro-8a-phenylnaphthalene (*cis*-9)**: NMR ($CDCl_3$) δ 7.1–7.4 (m, 5 H), 5.90 (dt, 2 H, J = 10.0, 3.7 Hz), 5.53 (dt, 2 H, J = 10.0, 2.0 Hz), 2.1–2.2 (m, 4 H), 1.89 (m, 1 H), 1.5–1.7 (m, 4 H); high-resolution mass spectrum calcd for $C_{16}H_{18}$ m/e 210.1409, found m/e 210.1408.

***trans*-3,4,4a,5,6,8a-Hexahydro-8a-phenylnaphthalene (*trans*-9)**: NMR ($CDCl_3$) δ 7.2–7.4 (m, 5 H), 5.94 (dt, 2 H, J = 9.8, 3.7 Hz), 5.67 (dt, 2 H, J = 9.8, 2.2 Hz), 2.2–2.4 (m, 4 H), 1.8–2.0 (m, 1 H), 1.2–1.4 (m, 4 H); high-resolution mass spectrum calcd for $C_{16}H_{18}$ m/e 210.1409, found m/e 210.1410.

***cis*-9-Phenyldecalin (*cis*-10)** had the following properties: ^1H NMR ($CDCl_3$) δ 7.46 (d, 2 H, J = 7.9 Hz), 7.36 (app t, 2 H, J = 7.9 Hz), 7.17 (t, 1 H, J = 7.9 Hz), 2.32 (m, 1 H), 1.2–2.0 (m, 16 H); ^{13}C NMR (−50 °C, $CDCl_3$) δ 150.2, 128.8, 126.5, 125.5, 44.5, 42.0, 37.3, 28.4, 27.4, 27.1, 26.8, 26.7, 22.9, 20.9; high-resolution mass spectrum calcd for $C_{16}H_{22}$ m/e 214.1722, found m/e 214.1720.

***trans*-9-Phenyldecalin (*trans*-10)**: ^1H NMR ($CDCl_3$) δ 7.52 (d, 2 H, J = 7.4 Hz), 7.26 (app t, 2 H, J = 7.4 Hz), 7.10 (t, 1 H, J = 7.4 Hz), 0.9–2.1 (m, 17 H); ^{13}C NMR ($CDCl_3$) δ 146.0, 129.7, 127.5, 124.7, 47.6, 44.5, 43.6, 29.8, 27.7, 22.3; high-resolution mass spectrum calcd for $C_{16}H_{22}$ m/e 214.1722, found m/e 214.1722.

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(7) The same methods have been used to stereospecifically generate methyl-substituted quaternary carbons (see ref 8), and butyl-substituted quaternary carbon centers (unpublished results by T. L. Underiner).
(8) Underiner, T. L.; Goering, H. L. *J. Org. Chem.* **1987**, *52*, 897.
(9) Dalling, D. K.; Grant, D. M.; Paul, E. G. *J. Am. Chem. Soc.* **1973**, *95*, 3718.
(10) Kuhn, D. E.; Lillya, C. P. *J. Am. Chem. Soc.* **1972**, *94*, 1682.
(11) McElvain, S. M. *The Characterization of Organic Compounds*; MacMillan: New York, 1953; p 199.
(12) Corey, E. J.; Mayers, A. G. *Tetrahedron Lett.* **1984**, *25*, 3559.

Synthesis of 3′-Cyano-2′,3′-dideoxyadenosine and 2′,3′-Dideoxy-3′-formyladenosine

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Despite the growing recognition that unnatural 2′-deoxynucleosides modified in the sugar portion often exhibit powerful antiviral properties,[1] synthetic methods to replace the natural C–O bond at the 3′-position of the deoxynucleoside with a C–C bond are scarce. The principal synthetic problems have been (1) the instability of 3′-keto-2′-deoxynucleosides, which undergo rapid elimination of the heterocyclic base,[2] precluding the use of traditional C–C bond forming methods such as the aldol

(1) For leading references, see: Mansuri, M. M.; Martin, J. C. *Ann. Rep. Med. Chem.* **1987**, *22*, 147.
(2) Hansske, F.; Robins, M. J. *Tetrahedron Lett.* **1983**, *24*, 1589. Hansske, F.; Madej, D.; Robins, M. J. *Tetrahedron* **1984**, *40*, 125.

0022-3263/89/1954-3240$01.50/0

2 3

Figure 1. Key NOE interactions observed for compounds **2** and **3** allowing assignment of 3′-configuration. Similar results were obtained for compounds **4–8**.

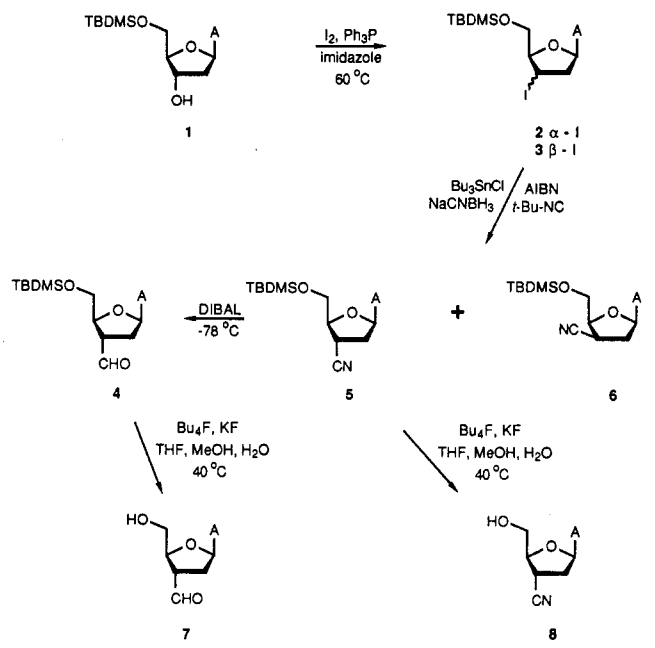
or Wittig reaction, and (2) variable success in effecting S_N2 reaction at the secondary 3′-carbon of 2′-deoxynucleosides.[3] In this paper we report that the radical cyanation reaction developed by Stork and Sher[4,5] is a simple and efficient way to introduce a C–C bond at the 3′-position of 2′-deoxyadenosine nucleosides[6] and illustrate this with a synthesis of 2′,3′-dideoxy-3′-cyanoadenosine (**8**) and 2′,3′-dideoxy-3′-formyladenosine (**7**) from 2′-deoxyadenosine in four and five steps, respectively. The latter compound is expected to be a valuable synthetic intermediate in the synthesis of a wide variety of 3′-substituted 2′-deoxyadenosines.

The starting 5′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyadenosine (**1**) is readily prepared from 2′-deoxyadenosine by the literature procedure.[7] Reaction of this alcohol with triphenylphosphine, iodine, and imidazole in toluene–acetonitrile[8,9] at 55–60 °C for 12 h provided a mixture of epimeric iodides **2** and **3** in 44% combined yield. As expected,[8] the 3′-β isomer **3** resulting from inversion of configuration predominated over the 3′-α isomer **2** in a ratio of 3.1/1. When the reaction was performed at higher temperatures or for extended times the ratio of **3** to **2** decreased significantly. Presumably, iodide formed during the reaction converts the kinetic product **3** to the thermodynamic product **2** by nucleophilic substitution at the higher temperature.

Replacement of the iodine by a nitrile group was accomplished by the method of Stork and Sher.[4,5] Treatment of either iodide **2** or **3** with *n*-Bu_3SnCl, $NaBH_3CN$, and catalytic 2,2′-azobisisobutyronitrile (AIBN) in *tert*-butyl isocyanide solvent[10] at 85 °C provided a mixture of nitriles **5** and **6** in 68% yield as well as a trace of the reduction product, 5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-dideoxyadenosine. The ratio of products **5** and **6** was essentially the same (8:7) regardless of the configuration of the starting iodide, as expected for a free-radical reaction.

Conversion of the cyano group in **5** to an aldehyde function was accomplished by reaction with diisobutylaluminum hydride in THF at −78 °C, followed by in situ hydrolysis of the resulting imine with aqueous acetic acid.[11] Deprotection of the 5′-position with Bu_4NF–KF readily

Scheme I



provided 2′,3′-dideoxy-3′-formyladenosine (**7**, 5% overall from **1**). Similar deprotection of **5** provided 3′-cyano-2′,3′-dideoxyadenosine (**8**, 11% overall from **1**).

The configurations of compounds **2–8** at the 3′-carbon could not be readily deduced by examining the ^1H–^1H coupling constants in the NMR spectra because of the conformational mobility of the furanose ring.[12] However, the 3′-configurations were unequivocally determined by NOE difference spectroscopy (Figure 1). Signals for the deoxyribose ring hydrogens were assigned by assuming that the doublet of doublets resonating between 6.0 and 6.5 ppm was the 1′-hydrogen and mapping the remaining hydrogens around the ring by decoupling experiments (data not shown). The two 2′-hydrogens were assigned on the basis of the NOE experiments; the 2′-α-hydrogen showed a strong enhancement upon irradiation of the 1′-hydrogen. The compounds that exhibited NOE interactions between the 2′-β, 3′-β, and 5′ hydrogens were assigned to have the 3′-substituent in the α-configuration (e.g. **2**, Figure 1), while those that showed NOE interactions between the 2′-α, 3′-α, and 4′ hydrogens were assigned as 3′-β-substituted (e.g. **3**, Figure 1).

In conclusion, we have described short syntheses of two 3′-carbon-substituted deoxyadenosine nucleosides, which we anticipate will serve as valuable synthetic intermediates in the preparation of more elaborate nucleoside analogues with potential medicinal applications. The compounds described herein are currently being evaluated for antiviral activity.

Experimental Section

Tetrahydrofuran (THF) was distilled from sodium benzophenone. Toluene and acetonitrile were dried with P_2O_5 and then distilled. Other reagents were reagent grade and were used without further purification. Thin-layer chromatography (TLC) was performed on Merck glass-backed silica gel plates with fluorescent indicator (0.25 mm thickness). All preparative separations were performed by flash chromatography[13] on Baker silica gel (40 μm). ^1H NMR spectra were recorded on a Bruker AM-300 spectrometer in $CDCl_3$ or Me_2SO-d_6 with Me_4Si as internal standard. NOE

(3) Calvo-Mateo, A.; Camarasa, M.-J.; Díaz-Ortíz, A.; De las Heras, F. G. *Tetrahedron Lett.* **1988**, *29*, 941.
(4) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765.
(5) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303.
(6) The synthesis of 3′-cyano-3′-deoxythymidine by several methods was reported during the course of this study: Parkes, K. E. B.; Taylor, K. *Tetrahedron Lett.* **1988**, *29*, 2995. Reference 3. Schreiber, S. L.; Ikemoto, N. *Tetrahedron Lett.* **1988**, *29*, 3211. Okabe, M.; Sun, R.-C.; Tam, S. Y.-K.; Todaro, L. J.; Coffen, D. L. *J. Org. Chem.* **1988**, *53*, 4780. In the report listed first essentially the same methodology as that reported herein was developed independently.
(7) Ogilvie, K. K. *Can. J. Chem.* **1973**, *51*, 3799.
(8) Garegg, P. J.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866. Garegg, P. J.; Johansson, R.; Ortega, C.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1982**, 681.
(9) For a related reaction with thymidine, see: Loibner, H.; Zbiral, E. *Liebigs Ann. Chem.* **1978**, 78.
(10) The use of solvents other than neat *tert*-butyl isocyanide resulted in the exclusive formation of the reduction product, 5′-(butyldimethylsilyl)-2′,3′-dideoxyadenosine.
(11) Marshall, J. A.; Andersen, N. H.; Schlicher, J. W. *J. Org. Chem.* **1970**, *35*, 858.
(12) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984; p 55.
(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

difference spectra were obtained as described by Hall and Sanders[14] using a pulse width of 8 μs (90°), a 10-s delay for NOE buildup, a 10-s delay for relaxation, two dummy scans and eight transients per cycle per frequency, and 16-32 cycles. IR spectra were recorded of neat thin films of analyte on NaCl plates on a Perkin-Elmer 727B spectrophotometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. FAB-HRMS spectra were obtained at the Regional MS Facility located at MIT on a Finnigan MAT 8200 spectrometer.

9-(5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′-dideoxy-3′-iodo-β-D-*erythro*-pentofuranosyl)adenine (2) and 9-(5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′-dideoxy-3′-iodo-β-D-*threo*-pentofuranosyl)adenine (3). A solution of iodine (125 mg, 0.49 mmol), triphenylphosphine (215 mg, 0.81 mmol), and imidazole (37 mg, 0.54 mmol) in 2.0 mL of toluene-acetonitrile (9:1) was added to a solution of 5′-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyadenosine[7] (1, 100 mg, 0.27 mmol) in 2 mL of toluene-acetonitrile (1:9) at ~40 °C under argon. After stirring for 12 h at 60 °C, the resulting suspension of a white solid in a colorless solution was evaporated to dryness and chromatographed ($CHCl_3$/EtOH, 96:4) to give **2**, 14 mg (11%), and **3**, 43 mg (33%).

For **2**: TLC ($CHCl_3$/EtOH, 96:4) R_f = 0.20; mp 142-144 °C; ^1H NMR δ 8.32 (1 H, s, H-8 or H-2), 8.28 (1 H, s, H-2 or H-8), 6.33 (1 H, dd, J = 6.7, 2.4 Hz, H-1′), 5.75 (2 H, s, NH_2), 4.46 (1 H, ddd, J = 10.1, 8.4, 6.8 Hz, H-3′), 4.33 (1 H, dψt, J = 8.5, 2.4, 2.4 Hz, H-4′), 4.04 (1 H, dd, J = 11.8, 2.5 Hz, H-5′a), 3.95 (1 H, dd, J = 11.8, 2.4 Hz, H-5′b), 3.01 (1 H, ddd, J = 13.7, 6.8, 2.4 Hz, H-2′β), 2.87 (1 H, ddd, J = 13.7, 10.1, 6.7 Hz, H-2′α), 0.91 (9 H, s, t-Bu), 0.11 (6 H, s, Me_2Si); FAB-HRMS (m/z) calcd for $C_{16}H_{26}IN_5O_2Si$ + H 476.0979, found 476.0977.

For **3**: TLC ($CHCl_3$/EtOH, 96:4) R_f = 0.14; mp 148-149 °C; ^1H NMR δ 8.32 (1 H, s, H-8 or H-2), 8.31 (1 H, s, H-2 or H-8), 6.36 (1 H, dd, J = 7.2, 4.5 Hz, H-1′), 5.66 (2 H, s, NH_2), 4.51 (1 H, ddd, J = 6.8, 4.9, 4.8 Hz, H-3′), 4.05 (1 H, dd, J = 10.7, 4.7 Hz, H-5′a), 3.86 (1 H, dd, J = 10.7, 4.9 Hz, H-5′b), 3.64 (1 H, dd, J = 4.9, 4.8 Hz, H-4′), 3.25 (1 H, ddd, J = 14.7, 7.4, 6.9 Hz, H-2′α), 2.98 (1 H, dψt, J = 14.7, 4.6, 4.6 Hz, H-2′β), 0.89 (9 H, s, t-Bu), 0.11 (6 H, s, Me_2Si). Anal. Calcd for $C_{16}H_{26}IN_5O_2Si$: C, 40.42; H, 5.51; N, 14.73. Found: C, 40.42; H, 5.43; N, 14.47.

9-(5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′-dideoxy-3′-cyano-β-D-*erythro*-pentofuranosyl)adenine (5) and 9-(5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′-dideoxy-3′-cyano-β-D-*threo*-pentofuranosyl)adenine (6). A solution of dried iodo compound **2** (30 mg, 0.063 mmol), tributyltin chloride (4.1 mg, 0.013 mmol), 2,2′-azobisisobutyronitrile (AIBN, 2.1 mg, 0.013 mg), and sodium cyanoborohydride (7.8 mg, 0.12 mmol) in 0.7 mL *tert*-butyl isocyanide was deoxygenated by repeated evacuation and admission of argon, then warmed to 87 °C for 1.5 h. The solvent was removed in vacuo, and the residue was chromatographed (EtOAc/EtOH, 94:6) to give **5** (8.5 mg, 36%) and **6** (7.4 mg, 32%).

Reaction of iodo isomer **3** (134 mg, 0.28 mmol) under identical conditions provided **5** (33 mg, 31%) and **6** (30 mg, 29%).

For **5**: TLC (EtOAc/EtOH, 94:6) R_f = 0.64; mp 135-136 °C; IR 2240 cm^{-1} (weak); ^1H NMR δ 8.30 (1 H, s, H-8 or H-2), 8.04 (1 H, s, H-2 or H-8), 6.32 (1 H, dd, J = 7.2, 2.6 Hz, H-1′), 5.59 (2 H, s, NH_2), 4.34 (1 H, m, H-4′), 4.09 (1 H, dd, J = 7.2, 14.6 Hz, H-5′a), 3.98 (1 H, dd, J = 3.5, 14.6, H-5′b), 3.86 (1 H, m, H-3′), 3.07 (1 H, ddd, J = 10.5, 7.9, 2.6 Hz, H-2′β), 2.84 (1 H, ddd, J = 13.6, 10.6, 7.2 Hz, H-2′α), 0.88 (9 H, s, t-Bu), 0.04 (6 H, s, Me_2Si); FAB-HRMS (m/z) calcd for $C_{17}H_{26}N_6O_2Si$ + H 375.1965, found 375.1943.

For **6**: TLC (EtOAc/EtOH, 94:6) R_f = 0.76; IR (neat) 2251 cm^{-1}; ^1H NMR δ 8.36 (1 H, s, H-8 or H-2), 8.30 (1 H, s, H-2 or H-8), 6.35 (1 H, dd, J = 6.4, 3.2 Hz, H-1′), 5.52 (2 H, s, NH_2), 4.35 (1 H, dψt, J = 8.0, 2.9 Hz, H-4′), 4.05 (1 H, dd, J = 11.5, 3.0 Hz, H-5′a), 3.81 (1 H, dd, J = 11.5, 3.0 Hz, H-5′b), 3.64 (1 H, m, H-3′), 2.84 (2 H, m, H-2′α and H-2′β), 0.91 (9 H, s, t-Bu), 0.09 (6 H, s, Me_2Si); FAB-HRMS (m/z) calcd for $C_{17}H_{26}N_6O_2Si$ + H 375.1965, found 375.1947.

9-(5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′-dideoxy-3′-formyl-β-D-*erythro*-pentofuranosyl)adenine (4). To a solution of dry **5** (15 mg, 0.04 mmol) in 0.4 mL of THF at -78 °C was added diisobutylaluminum hydride (17 mg, 0.12 mmol), and the mixture was stirred at -78 °C for 1 h and then at 25 °C for 1.5 h. Acetic acid (0.8 mL of a 0.5 M aqueous solution) was added, and the reaction was stirred for 3 h. The mixture was extracted with chloroform and chromatographed ($CHCl_3$/EtOH, 92:8) to give **4**: 6.5 mg (43%); TLC (dioxane/CH_2Cl_2, 1:2) R_f = 0.25; mp 108-109 °C; IR (neat) 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.80 (1 H, d, J = 1.6 Hz, C*H*O), 8.31 (1 H, s, H-8 or H-2), 8.14 (1 H, s, H-2 or H-8), 6.29 (1 H, dd, J = 3.8, 6.7 Hz, H-1′), 5.68 (2 H, s, NH_2), 4.38 (1 H, ddd, J = 3.5, 4.6, 7.1 Hz, H-4′), 3.96 (1 H, dd, J = 4.6, 10.9 Hz, H-5′a), 3.83 (1 H, dd, J = 3.5, 10.9 Hz, H-5′b), 3.64 (1 H, m, H-3′), 2.87 (1 H, m, H-2′α), 2.77 (1 H, m, H-2′β), 0.88 (9 H, s, t-Bu), 0.21 (6 H, s, Me_2Si); FAB-HRMS (m/z) calcd for $C_{17}H_{27}N_5O_3Si$ + H 378.1962, found 378.1935.

9-(2′,3′-Dideoxy-3′-formyl-β-D-*erythro*-pentofuranosyl)adenine (7). A solution of **4** (5 mg, 0.013 mmol), tetrabutylammonium fluoride (100 mg, 0.38 mmol), and KF (20 mg, 0.34 mmol) in 1.5 mL of THF/H_2O/MeOH (1:1:1) was stirred at 40 °C for 30 h. The solvent was evaporated, and the residue was chromatographed ($CHCl_3$/EtOH, 92:8) to give **7**: 2.0 mg (60%); mp 210-212 °C; IR 1750 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 9.73 (1 H, s, C*H*O), 8.36 (1 H, s, H-8 or H-2), 8.14 (1 H, s, H-2 or H-8), 7.32 (2 H, s, NH_2), 6.23 (1 H, t, J = 6.0 Hz, H-1′), 5.30 (1 H, br s, OH), 4.29 (1 H, m, H-4′), 3.90 (1 H, m, H-3′), 3.65 (2 H, m, H-5′), 2.70 (2 H, m, H-2′α,β); FAB-HRMS (m/z) calcd for $C_{11}H_{13}N_5O_3$ + H 264.1097, found 264.1068.

9-(3′-Cyano-2′,3′-dideoxy-β-D-*erythro*-pentofuranosyl)adenine (8). Protected nitrile **5** (8.4 mg, 0.22 mmol) was treated exactly as for **7** above, to give **8**: 4 mg (67%); mp 194-195 °C; TLC ($CHCl_3$/EtOH, 94:6) R_f = 0.20; IR 2240 cm^{-1} (weak); ^1H NMR (Me_2SO-d_6) δ 8.32 (1 H, s, H-8 or H-2), 8.14 (1 H, s, H-2 or H-8), 7.12 (2 H, s, NH_2), 6.36 (1 H, dd, J = 3.9, 6.6 Hz, H-1′), 5.30 (1 H, t, J = 5.6 Hz, OH), 4.25 (1 H, dψt, J = 4.1, 8.5 Hz, H-4′), 3.91 (1 H, m, H-3′), 3.60 (2 H, m, H-5′), 3.15 (1 H, m, H-2′α), 2.92 (1 H, m, H-2′β); FAB-HRMS (m/z) calcd for $C_{11}H_{12}N_6O_2$ + H 261.1100, found 261.1060.

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(14) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703.

Annelation Reaction via Tandem Michael-Claisen Condensations. 3. Synthesis of the Hydrindan System

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We have recently reported a new 4C + 2C annelation reaction based on the tandem Michael-Claisen condensation of 3-(phenylthio)-1-(trimethylsiloxy)-1-methoxy-1,3-butadiene (**1**) with a number of α,β-unsaturated ketones.[1,2] The reaction is formally similar to the Diels-Alder reaction but offers the advantage that even relatively unreactive dienophiles can undergo the annelation reaction. The usefulness of the reaction was demonstrated by the construction of the 9-methyldecalin system[1] and the syntheses of two sesquiterpenes, aristolone and fukinone.[2]

In trying to extend the reaction to the synthesis of the hydrindan system by the condensation of **1** with cyclopent-2-enone (**3**) according to Scheme I, the yield of the Michael adduct **4** was found to be poor.[1] Because of the presence of the hydrindan structure in many natural

(1) Chan, T. H.; Prasad, C. V. C. *J. Org. Chem.* **1987**, *52*, 110.
(2) Prasad, C. V. C.; Chan, T. H. *J. Org. Chem.* **1987**, *52*, 120.

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