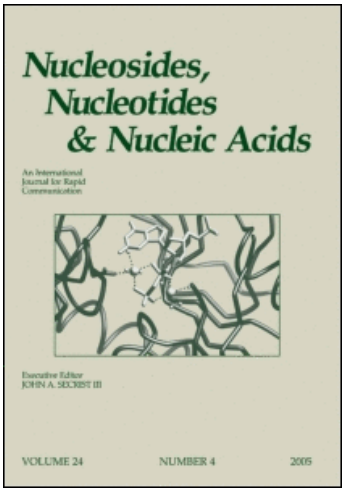

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SYNTHESIS AND REACTIONS OF SOME 3',4'-UNSATURATED 2',3'-SECOURIDINE ANALOGUES

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ABSTRACT: 2',3'-Dibromo-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (**8**) with sd-KF gave the 3',4'-didehydro-2,2'-anhydro nucleoside **9**, which was deprotected to **10**. Hydrolysis of **9** gave 3',4'-didehydro-3'-deoxy-5'-*O*-trityl-2',3'-secouridine (**11a**). Similarly, compound **9** with pyridinium halides gave the corresponding 2'-deoxy-2'-halo nucleosides (**11b-d**). Compound **11d** with azide ion gave 2'-azido analogue **11e**. Compound **9** with an excess amount of azide ion gave the 2'-azido triazole (**13**).

Since the discovery of potent antiviral activities of acyclovir,[1] numerous acyclic analogues formally derived from the parent nucleoside by cleaving one or more bonds in the furanose ring have been synthesized.[2] More recently, some 1',2'-unsaturated 2',3'-seconucleoside analogues of adenine and uracil series (**1-4**)[3] have also been introduced by analogy with 3'-deoxy-2',3'-didehydrothymidine (D4T) and other unsaturated furanose nucleosides known as anti-AIDS substances. Compounds **1** and **4** are interesting acyclic analogues related to 3'-azido-3'-deoxythymidine (AZT). As part of our interest in the chemistry of unsaturated sugar nucleosides,[4] we decided to synthesize 3',4'-unsaturated 2',3'-seconucleosides from the commercially available ribonucleosides for biological evaluation. The highly reactive electron-rich 3',4'-double bond is especially intriguing for further transformations and importantly, it would not

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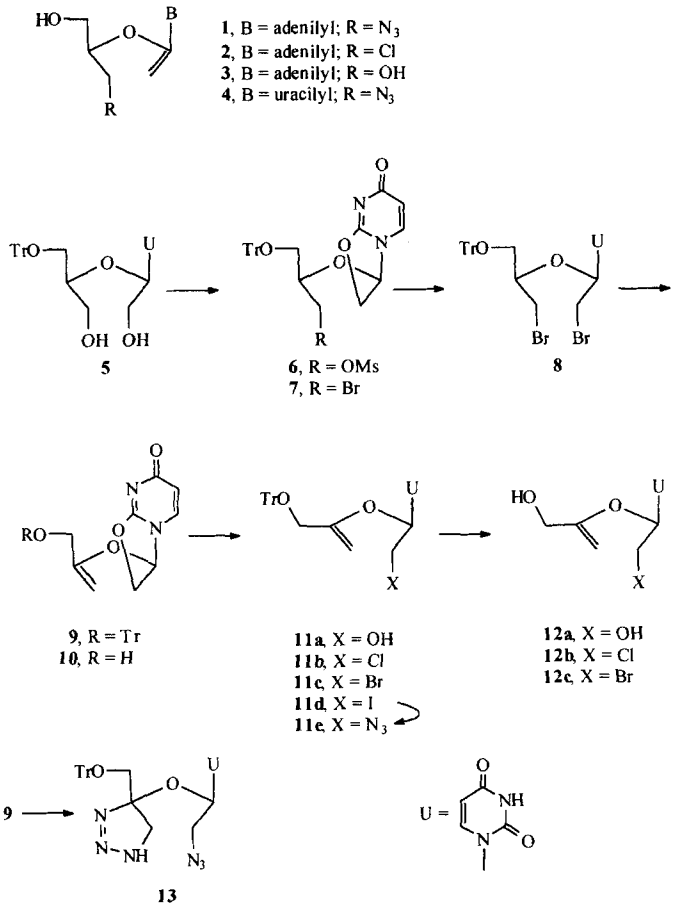

SCHEME 1

exert no allylic influence on the physico-chemical properties inherent in the natural nucleobases. Furthermore, the original anomeric configuration would be conserved in such compounds.

The known 5'-*O*-trityl-2',3'-secouridine (**5**)[5] was mesylated to the 2',3'-*O*-dimesylate,[5] which was *in situ* treated with an excess amount of triethylamine in acetone to afford 2,2'-anhydro-3'-*O*-mesyl-5'-*O*-trityl-2',3'-secouridine (**6**)[5] in a high yield. Initial trials to introduce a 3',4'-double bond into compound **6** or its 3'-bromo analogue (**7**)[5] by application of potassium t-butoxide, sodium hydride or DBU have failed, only complex mixtures having been obtained probably due to the attack of these reagents on the anomeric carbon[6] and further reactions.[7] Finally, spray-dried potassium fluoride (sd

KF) proved to be a reagent of choice. Thus, treatment of 2',3'-dibromo-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (**8**)[5] readily obtainable from **6** with an excess amount of sd KF gave 2,2'-anhydro-3',4'-didehydro-3'-deoxy-5'-*O*-trityl-2',3'-secouridine (**9**) in 53% yield. This is a regioselective 3',4'-elimination reaction in contrast with the recorded regioselective 1',2'-elimination of the 2',3'-di-*O*-tosylates of protected 2',3'-seconucleosides.[3] The less nucleophilic fluoride barely rescued the 2,2'-anhydro bond. The application of this reagent to compound **8** is more favorable than to compound **7** by unknown reason. Furthermore, compound **6** with sd-KF gave a complex mixture. Deprotection of **9** with 80% acetic acid gave 2,2'-anhydro-3',4'-didehydro-3'-deoxy-2',3'-secouridine (**10**) as a major product. The 3',4'-didehydro structures of **9** and **10** were confirmed by their ^{1}H NMR spectral data (see experimental section). Treatment of **9** with 1N NaOH/H_2O-acetone gave a good yield of 3',4'-didehydro-3'-deoxy-5'-*O*-trityl-2',3'-secouridine (**11a**), while treatment of **9** with pyridine hydrochloride afforded 2'-chloro-3',4'-didehydro-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (**11b**). Similarly, 2'-bromo (**11c**) and 2'-iodo analogues (**11d**) were synthesized. Compound **11d** with a slight excess of tetraethylammonium azide gave a moderate yield of 3'-azido-3',4'-didehydro-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (**11e**) together with the recyclized product **9**. Deprotection of **11a** gave 3',4'-didehydro-3'-deoxy-2',3'-secouridine (**12a**). Similarly, 2'-chloro (**12b**) and 2'-bromo analogues (**12c**) were obtained. Unexpectedly, these deprotected compounds resisted crystallization. Repeated attempts to isolate the deprotected forms of **11d** and **11e** in analytical purity have failed owing to their glassy nature, although mass spectrometry provided their corresponding [M + H] ions. Heating compound **9** with an excess amount of lithium azide gave 2'-azido-2',3'-dideoxy-3'-C,4'-C-triazeno-5'-*O*-trityl-2',3'-secouridine (**13**) in a moderate yield.[8] The absolute stereochemistry at the 4'-position is unknown at present. Attempts to deprotect **13** with the use of 80% acetic acid or zinc bromide in methylene chloride[3]gave a complex mixture.

Experimental Section

Mps were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. UV spectra were measured on a JASCO Ubest V-560DS spectrophotometer. The 200 MHz ^{1}H NMR spectra were recorded on a GEMINI-200 FT NMR spectrometer. Elemental analyses were conducted using a Perkin-Elmer 240B elemental analyser. For preparative scale thick-layer chromatography, glass plates coated with 2-mm thickness of Wakogel B-5F silica gel were used after activation at 100 ℃ for 10-12 h. For column chromatography, Wakogel C-300 silica gel was used. All evaporations were carried out under reduced pressure at or below 40 ℃.

Modified Synthesis of 2,2'-Anhydro-3'-*O*-mesyl-5'-*O*-trityl-2',3'-secouridine (6). To a stirred, ice-cooled solution of compound **5** (8.24 g, 16.9 mmol) and triethylamine (5.2 ml, 37 mmol) in acetone (80 ml) was added in portions methanesulfonyl chloride (MsCl) (2.86 ml, 37 mmol). The mixture was allowed to warm up to room temperature gradually. After overnight stirring, the consumption of the starting material and formation of a single less polar product (dimesylate of **5**) was confirmed by TLC (silica; $CHCl_3$/EtOH, 9:1). Then, further triethylamine (11.8 ml, 84.3 mmol) was added and the mixture stirred for 21 h. At this stage, the less polar intermediate was shown to have changed to more polar **6**. The mixture was evaporated and the residue partitioned between EtOAc (370 ml) and water (100 ml). The EtOAc layer was again washed with water (2 × 40 ml). The separated organic layer was dried over sodium sulfate and appropriately evaporated to give totally 7.36 g (77.3%) of TLC-homogeneous **6**, identical with an authentic sample.[5]

2,2'-Anhydro-3',4'-didehydro-3'-deoxy-5'-*O*-trityl-2',3'-secouridine (9). A mixture of compound **8** (4.92 g, 8.01 mmol) and sd-KF (3.81 g, 65.6 mmol) in DMF (29 ml) was stirred at 95-100 ℃ for 17 h and the solvent evaporated off. The residue was partitioned between EtOAc (150 ml) and water (50 ml). After repeated washing with water (2 × 20 ml), the organic layer was separated, dried over sodium sulfate and evaporated. Silica gel column chromatography (3 × 26 cm; $CHCl_3$/EtOH, 95 : 5) with the residue gave 1.92 g (52.8%) of **9** of mp 105-108 ℃ after recrystallization from MeOH. λmax (MeOH) nm (ε) 222 (20800, shoulder) and 249 (8300, shoulder); ^{1}H NMR ($CDCl_3$) δ 3.60 (2H, s, H-5'), 4.19 (1H, d, J_{gem} = 3.6, H-3'a), 4.57 (1H, dd, $J_{2'a,1'}$ = 2.2, J_{gem} = 10.8, H-2'a), 4.78 (1H, d, J_{gem} = 3.6, H-3'b), 4.80 (1H, dd, $J_{2'b,1'}$ = 6.2, J_{gem} = 10.8, H-2'), 6.03 (1H, d, $J_{5,6}$ = 7.4, H-5), 6.15 (1H, dd, $J_{1',2'a}$ = 2.2, $J_{1',2'b}$ = 6.2, H-1'), 7.26-7.45 (16H, m, 5'-Tr and H-6). *Anal.* Calcd for $C_{28}H_{24}N_2O_4$: C, 74.32; H, 5.36; N, 6.19. Found: C, 74.53; H, 5.34; N, 5.99.

2,2'-Anhydro-3',4'-didehydro-3'-deoxy-2',3'-secouridine (10). A solution of compound **9** (200 mg, 0.44 mmol) in 80% AcOH (14 ml) was left at room temperature overnight and the mixture evaporated. The residue was repeatedly co-evaporated with EtOH (5 × 6 ml) and the residue fractionated on a silica gel plate (20 × 20 cm; CHCl3/MeOH, 85 : 15, developed 3 times). The major fraction was eluted with MeOH to give 40 mg (43.3%) of crystals (**10**) of mp 172-174 ℃ after recrystallization from MeOH. λmax (MeOH) nm (ε) 226 (9600) and 248 (8300); ^{1}H NMR (Me_2SO-d_6) δ 3.83 (2H, d, J = 5.8, H-5'), 4.28 (1H, d, J_{gem} = 2.4, H-3'a), 4.44 (1H, d, J_{gem} = 2.4, H-3'b), 4.61 (1H, dd, $J_{2a',1'}$ = 1.6, J_{gem} = 10.6, H-2'a), 4.91 (1H, dd, $J_{2'b,1'}$ = 5.4, J_{gem} = 10.6, H-2'b), 5.22 (1H, t, J = 5.8, 5'-OH), 5.92 (1H, d, $J_{5,6}$ = 7.4, H-5), 6.39 (1H, dd, $J_{1',2'a}$ = 1.6, $J_{1',2'b}$ = 5.4, H-1'), 7.90 (1H, d, $J_{6,5}$ = 7.4, H-6). *Anal.* Calcd for $C_9H_{10}N_2O_4$: C, 51.42; H, 4.80; N, 13.33. Found: C, 51.43; H, 4.84; N, 13.28.

3',4'-Didehydro-3'-deoxy-5'-*O*-trityl-2',3'-secouridine (11a). A solution of **9** (300 mg, 0.66 mmol) in a mixture of acetone (15 ml) and 2N NaOH (15 ml) was stirred at room temperature for 2 h and then neutralized with 1N AcOH/EtOH. The mixture was evaporated, repeatedly co-evaporated with MeOH/EtOH (1:1) and the residue fractionated on 2 sheets of silica plates (20 × 20 cm; $CHCl_3$/EtOH, 4:1, twice developed). The major band was eluted with MeOH to give 255 mg (82.0%) of **11a** as crystals of mp 204-206 °C after recrystallization from MeOH: λmax (MeOH) 259.6 nm (ε 9700); ^{1}H NMR (Me_2SO-d_6) δ 3.41 (2H, s, H-5'), 3.66 (2H, m, H-2'), 4.33 (1H, d, J_{gem} = 2.4, H-3'a), 4.57 (1H, d, J_{gem} = 2.4, H-3'b), 5.30 (1H, s, 2'-OH), 5.62 (1H, d, J = 8.2, H-5), 6.08 (1H, t, $J_{2',1'}$ = 5.3, H-1'), 7.20-7.40 (15H, m, 5'-Tr), 7.55 (1H, d, J = 8.2, H-6), 11.45 (1H, s, 3-NH). *Anal.* Calcd for $C_{28}H_{26}N_2O_5$: C, 71.47; H, 5.57; N, 5.95. Found: C, 71.49; H, 5.43; N, 5.87.

2'-Chloro-3',4'-didehydro-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (11b). A mixture of **9** (300 mg, 0.66 mmol) and pyridine hydrochloride (62 mg, 0.79 mmol) in DMF (10 ml) was stirred at 60 °C for 1 h. The mixture was evaporated and the residue fractionated on a silica plate (20 × 20 cm; $CHCl_3$/EtOAc, 9:1, developed 3 times). The major fraction was eluted with MeOH and recrystallized from the same solvent to give 271 mg (84.0 %) of **11b**, mp 182-184 °C: λmax (MeOH) 259.6 nm (ε 6740); ^{1}H NMR ($CDCl_3$) δ 3.61 (2H, d, J = 1.6, H-5'), 3.78 (1H, dd, J_{gem} = 12.1, $J_{2'a,1'}$ = 4.6, H-2'a), 3.85 (1H, dd, J_{gem} = 12.1, $J_{2'b,1'}$ = 4.4, H-2'b), 4.31 (1H, d, J_{gem} = 3.4, H-3'a), 4.46 (1H, d, J_{gem} = 3.4, H-3'b), 5.76 (1H, dd, J = 8.2, $J_{5,NH}$ = 2.2, H-5), 6.40 (1H, t, $J_{1',2'a}$ = 4.6, $J_{1',2'b}$ = 4.4, H-1'), 7.26-7.48 (16H, m, Tr and H-6), 8.67 (1H, br s, 3-NH). *Anal.* Calcd for $C_{28}H_{25}ClN_2O_4$: C, 68.78; H, 5.15; N, 5.73. Found: C, 68.78; H, 5.18; N, 5.74.

2'-Bromo-3',4'-didehydro-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (11c). A mixture of **9** (300 mg, 0.66 mmol) and pyridine hydrobromide (127 mg, 0.79 mmol) in DMF (10 ml) was stirred at 60 °C for 2 h and evaporated. The residue was directly fractionated on a silica plate (20 × 20 cm; $CHCl_3$/EtOAc, 4:1, twice developed) to give 178 mg (50.0%) of **11c** as crystals of mp 170-171 °C after elution with MeOH and recrystallization from the same solvent: λmax (MeOH) 258.4 nm (ε 10100); ^{1}H NMR ($CDCl_3$) δ 3.61 (2H, d, J = 2.8, H-5'), 3.62 (1H, dd, J_{gem} = 11.2, $J_{2'a,1'}$ = 4.6, H-2'a), 3.69 (1H, dd, J_{gem} = 11.2, $J_{2'b,1'}$ = 4.8, H-2'b), 4.31 (1H, d, J_{gem} = 3.5, H-3'a), 4.58 (1H, d, J_{gem} = 3.5, H-3'b), 5.76 (1H, dd, $J_{5,6}$ = 8.2, $J_{5,NH}$ = 2.2, H-5), 6.37 (1H, t, $J_{1',2'a}$ = 4.6, $J_{1',2'b}$ = 4.8, H-1'), 7.22-7.47 (16H, m, Tr and H-6), 8.70 (1H, br s, 3-NH). *Anal.* Calcd for $C_{28}H_{25}BrN_2O_4$: C, 63.05; H, 4.72; N, 5.25. Found: C, 62.98;H, 4.84;N, 5.20.

3',4'-Didehydro-2',3'-dideoxy-2'-iodo-5'-*O*-trityl-2',3'-secouridine (11d). A mixture of **9** (600 mg, 1.33 mmol) and pyridine hydroiodide (330 mg, 1.59 mmol) in DMF (10 ml) was stirred in the dark for 19 h at room temperature. TLC at this stage

indicated the formation of a single less polar product. The solvent was evaporated off and the residue partitioned between EtOAc (60 ml) and water (20 ml). The organic layer was dried over sodium sulfate and evaporated to give a paste, which gave 646 mg (83.7%) of TLC-homogeneous crystals (**11d**) on digestion with a small volume of MeOH. For analysis, a part was recrystallized from MeOH at room temperature to afford colorless fine needles of mp 138-139 ℃: λmax (MeOH) 259.4 nm (ε 7700); ^{1}H NMR (Me_2SO-d_6) δ 3.42 (2H, s, H-5'), 3.65 (1H, dd, J_{gem} = 10.8, $J_{2'a,1'}$ = 6.2, H-2'a), 3.72 (1H, dd, J_{gem} = 10.8, $J_{2'b,1'}$ = 6.8, H-2'b), 4.34 (1H, d, J_{gem} = 2.4, H-3'a), 4.55 (1H, d, J_{gem} = 2.4, H-3'b), 5.70 (1H, d, $J_{5,6}$ = 8.0, H-5), 6.21 (1H, br t, $J_{1',2'a}$ = 6.2, $J_{1',2'b}$ = 6.8, H-1'), 7.33 (15H, br m, Tr), 7.66 (1H, d, $J_{6,5}$ = 8.0, H-6), 11.56 (1H, br s, 3-NH). *Anal.* Calcd for $C_{28}H_{25}IN_2O_4$: C, 57.94; H, 4.34; N, 4.83. Found: C, 57.94; H, 4.38; N, 4.88.

3'-Azido-3',4'-didehydro-2',3'-dideoxy-5'-*O*-trityl-2',3'-secouridine (11e). A mixture of tetraethylammonium chloride (400 mg, 2.41 mmol) and sodium azide (170 mg, 2.61 mmol) in DMF (15 ml) was stirred at room temperature for 30 min under exclusion of moisture. To this mixture was added compound **11d** (1.17 g, 2.01 mmol) and the total vigorously stirred in the dark for 24 h. TLC-monitoring at this stage showed the formation of two more polar products. After having evaporated the solvent, the residue was partitioned between EtOAc (50 ml) and water (20 ml). The organic layer was again washed with water (2 × 20 ml), dried over sodium sulfate and evaporated. The residue was subjected to column chromatography (3 × 20 cm; $CHCl_3$/EtOAc, 5:1) to give from the first fraction 618 mg (62.0%) of colorless crystals (**11e**) of mp 144-146 ℃ after recrystallization from MeOH: λmax (MeOH) 260.0 nm (ε 4200); ^{1}H NMR (Me_2SO-d_6) δ 3.44 (2H, s, H-5'), 3.68 (1H, dd, J_{gem} = 13.4, $J_{2'a,1'}$ = 5.3, H-2'a), 3.92 (1H, dd, J_{gem} = 13.4, $J_{2'b,1'}$ = 6.3, H-2'b),4.35 (1H, d, J_{gem} = 2.8, H-3'a), 4.59 (1H, d, J_{gem} = 2.8, H-3'b), 5.70 (1H, d, $J_{5,6}$ = 8.0, H-5), 6.24 (1H, br t, $J_{1',2'a}$ = 5.3, $J_{1',2'b}$ = 6.3, H-1'), 7.32 (15H, br m, Tr), 7.63 (1H, d, $J_{6,5}$ = 8.0, H-6), 11.50 (1H, br s, 3-NH). *Anal.* Calcd for $C_{28}H_{25}N_5O_4$: C, 67.86; H, 5.09; N, 14.12. Found: C, 67.83; H, 5.13; N, 14.11.

The slower-moving fraction gave 218 mg (24.0%) of **9**, identical with an authentic sample of **9** in terms of IR spectroscopy and ^{1}H NMR spectrometry.

3',4'-Didehydro-3'-deoxy-2',3'-secouridine (12a). A solution of **11a** (300 mg, 0.64 mmol) in 80% acetic acid (5 ml) was left at room temperature overnight and the solvent evaporated off. The residue was repeatedly co-evaporated with EtOH (5 × 5 ml) and subjected to preparative TLC (silica, 20 × 20 cm; $CHCl_3$/MeOH, 8:2, developed twice). The major fraction was thoroughly eluted with MeOH to give 121 mg (83.0%) of **12a** as a foam. λmax (MeOH) 260.4 nm (ε 6100); ^{1}H NMR (Me_2SO-d_6) δ 3.22 (ca. 4H, s, C**H**$_3$OH), 3.36 (2H, d, J = 5.8, H-5'), 3.50-3.74 (2H, m, H-2'), 4.23

(1H, d, J_{gem} = 2.4, H-3'a), 4.44 (1H, d, J_{gem} = 2.4, H-3'b), 5.08 (1H, t, J = 5.8, D_2O-exchangeable, 5'-OH), 5.61 (1H, d, $J_{5,6}$ = 8.0, H-5), 5.79 (1H, t, $J_{1',2'}$ = 5.4, H-1'), 7.63 (1H, d, $J_{6,5}$ = 8.0, H-6), 11.30 (1H, br s, 3-NH). *Anal.* Calcd for $C_9H_{12}N_2O_5 \cdot {}^3/_2CH_3OH$: C, 45.65; H, 6.57; N, 10.14. Found: C, 45.67; H, 6.50; N, 10.19.

2'-Chloro-3',4'-didehydro-2',3'-dideoxy-2',3'-secouridine (12b). A solution of **11b** (200 mg, 0.41 mmol) in 80% AcOH (5 ml) was left at room temperature overnight and worked up as in the case of **12a**. The finally obtained pasty residue was fractionated on a silica plate (20 × 20 cm; $CHCl_3$/EtOAc, 1:1, once developed). The major fraction was eluted with MeOH to give 69 mg (68.2%) of a homogeneous foam (**12b**). λmax (MeOH) 258.4 nm (ε 5900); ^{1}H NMR (Me_2SO-d_6) δ 3.23 (ca 4H, C**H**$_3$OH), 3.40 (2H, d, J = 5.4, H-5'), 3.94 (2H, d, $J_{2',1'}$ = 6.4, H-2'), 4.26 (1H, d, J_{gem} = 2.4, H-3'a), 4.40 (1H, d, J_{gem} = 2.4, H-3'b), 4.92 (1H, t, J = 5.4, D_2O-exchangeable, 5'-OH), 5.68 (1H, d, $J_{5,6}$ = 8.1, H-5), 5.98 (1H, t, $J_{1',2'}$ = 6.4, H-1'), 7.33 (1H, d, $J_{6,5}$ = 8.1, H-6), 11.43 (1H, br s, 3-NH). *Anal.* Calcd for $C_9H_{11}ClN_2O_4 \cdot {}^3/_2CH_3OH$: C, 42.79; H, 5.81; N, 9.51. Found: C, 42.82; H, 5.64; N, 9.65.

2'-Bromo-3',4'-didehydro-2',3'-dideoxy-2',3'-secouridine (12c). A solution of **11c** (80mg, 0.15 mmol) in 80% AcOH (1.5 ml) was left at room temperature overnight and the mixture worked up by the same procedures involving chromatography with the case of **12b** to give 30 mg (68.7%) of **12c** as a foam. λmax (MeOH) 258.4 nm (ε 5300); ^{1}H NMR (Me_2SO-d_6) δ 3.23 (ca. 4H, s, C**H**$_3$OH), 3.40 (2H, d, J = 5.4, H-5'), 3.81 (2H, d, $J_{2',1'}$ = 6.4, H-2'), 4.26 (1H, J_{gem} = 2.4, H-3'a), 4.40 (1H, d, J_{gem} = 2.4, H-3'b), 4.92 (1H, t, J = 5.4, 5'-OH), 5.69 (1H, d, $J_{5,6}$ = 8.1, H-5), 5.99 (1H, t, $J_{1',2'}$ = 6.4, H-1'), 7.73 (1H, d, $J_{6,5}$ = 8.1, H-6), 11.43 (1H, br s, 3-NH). *Anal.* Calcd for $C_9H_{11}BrN_2O_4 \cdot {}^3/_2CH_3OH$: C, 37.18; H, 5.05; N, 8.26. Found: C, 37.28; H, 5.01; N, 8.21.

2'-Azido-2',3'-dideoxy-3'-C,4'-C-triazeno-5'-*O*-trityl-2',3'-secouridine (13). A mixture of sodium azide (715 mg, 11 mmol) and lithium chloride (466 mg, 11 mmol) in DMF (25 ml) was stirred at 80 °C for 10 min. To this mixture was added compound **9** (1 g, 2.2 mmol) and the total was stirred at this temperature for 1 h. After evaporation of the solvent, the residue was partitioned between EtOAc (50 ml) and water (20 ml). The separated organic layer was again washed with water (3 × 20 ml), dried over sodium sulfate and evaporated. The residue was fractionated on two sheets of silica plates (20 × 20 cm; $CHCl_3$/EtOH, 95:5, twice developed) and the major fraction was eluted with MeOH. Recrystallization of the obtained solid from MeOH gave 671 mg (56.5%) of **13** as colorless crystals of mp 157-159 °C. IR (KBr) 2100 cm^{-1} (N_3); λmax (MeOH) 262 nm (ε 8500); ^{1}H NMR ($CDCl_3$) δ 1.60 (1H, s, D_2O-exchangeable, 3-NH), 3.21 (1H, dd, J_{gem} = 12.1, $J_{2'a,1'}$ = 5.2, H-2'a), 3.28 (1H, dd, J_{gem} = 12.1, $J_{2'b,1'}$ = 5.0, H-2'b), 3.52 (4H, complex m, H-5' and H-3'), 5.57 (1H, d, $J_{5,6}$ = 8.2, H-5), 5.95 (1H, br t, J = 5.2 and 5.0,

H-1'), 7.31 (16H, m, Tr and H-6), 8.51 (1H, br s, D_2O-exchangeable, 3-NH). *Anal.* Calcd for $C_{28}H_{26}N_8O_4$: C, 62.45; H, 4.87; N, 20.81. Found: C, 62.48; H, 4.90; N, 20.75.

REFERENCES

1. Schaeffer, H.; J, Bauchamp, L.; de Miranda, P.; Elion, G. B.; Bauer, D. J.; Collins, P. *Nature* (*London*), **1978**, *272*, 583-585.
2. Huryn, D. M.; Okabe, M. *Chem. Rev.*, **1992**, *92*, 1745-1768.
3. Vrcek, V.; Caplar, V. *Helv. Chim. Acta*, **1995**, *78*, 1797-1805.
4. (a) Sasaki, T.; Minamoto, K.; Hattori, K. *J. Org. Chem.*, **1973**, *38*, 1283-1286; (b) Sasaki, T.; Minamoto, K.; Tanizawa, S. *J. Org. Chem.*, **1973**, *38*, 2896-2899; (c) Sasaki, T.; Minamoto, K.; Hattori, K. *Tetrahedron*, **1974**, *30*, 2689-2694; (d) Minamoto, K.; Oishi, M.; Kakehi, A.; Ohta, N.; Matsuda, I.; Watanabe, K.; Yanagihara, K.; Takeuchi, T.; Tanigawa, K. *J. Chem. Soc. Perkin Trans. 1*, **1994**, 2289-2296 and literatures cited therein; (e) Ohta, N.; Minamoto, K.; Yamamoto, T.; Koide, N.; Sakoda, R. *Nuleosides Nucleotides*, **1996**, *15*(4), 833-855; (f) Tsuboike, K.; Mizuno, G.; Minamoto, K. *Collect. Czech. Chem. Commun.*, **1996**, *61*, 45-48.
5. Jones, A. S.; Walker, R. T.; Wyatt, P. G.; Balzarini, J.; de Clercq, E. *J. Chem. Res.* (*M*), **1985**, 3520-3532.
6. Robins, M. J.; Trip, E. M. *Tetrahedron Lett.*, **1974**, *38*, 3369-3372.
7. TLC-Monitoring of these reactions with the use of silica plates and $CHCl_3$/EtOH (9:1) indicated the formations of over four products.
8. We obtained a tiny amount of by-product as an amorphous powder, which seemed to be a stereoisomer of **13** on the basis of elemental analysis. However, we abandoned to pursue this compound, since we knew that the deprotected form of the crystalline major product **13** could not be obtained even with the use of zinc bromide.

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