Articles

Sugar-Modified Uridine Bisvinyl Sulfone: Synthesis of a Bifunctionalized Nucleoside Michael Acceptor and Its Use in Stereoselective Tandem Cyclization†

Sanjib Bera,‡ Graham J. Langley,§ and Tanmaya Pathak*,‡,||

Organic Chemistry Division (Synthesis), National Chemical Laboratory, Pune 411 008, India, and Department of Chemistry, The University, Southampton SO9 5NH, UK

Received March 25, 1997

A bisvinyl sulfone functionality is incorporated into the carbohydrate moiety of uridine to synthesize **6** (or **7**) which is a bifunctionalized nucleoside Michael acceptor and has the potential to form covalent bond with biological nucleophiles. This compound could be used to generate a large number and a new class of bicyclic *S*,*S*-dioxidethiazine derivatives **8**−**12** in stereoselective fashion. Compound **6** is also useful for the synthesis of a wide variety of monosubstituted compounds **13**−**15**. The structures of compounds **8**−**12** have been established unambiguously by synthesising the core structure **28** in a stereospecific fashion.

Introduction

Vinyl sulfones inhibit[1] the action of glyceraldehyde-3-phosphate dehydrogenase and vinyl sulfone containing dipeptides have been shown[2] to be efficient inhibitors of cystein protease. Attempts have been made[3] in the recent past to synthesize chemically reactive analogues of AZT that may form a covalent bond to viral reverse transcriptase. Since vinyl sulfones, highly reactive Michael acceptors,[4] reportedly[1,2] show their activities by forming covalent bonds with biological nucleophiles, we decided to incorporate[5] vinyl sulfone functionality at the carbohydrate moieties of nucleosides. After studying[5] the reactivities of 3′-deoxy-3′-*S*-vinylsulfonylthymidine **16** with various nucleophiles, we envisaged that modified nucleosides equipped with a bisvinyl sulfone functional group would also have the potential to form covalent linkages with biological nucleophiles since bisvinyl sulfone has also been reported[1] to be an efficient enzyme inhibitor.

In addition to above-mentioned properties, the parent nucleoside **6** (or **7**) will be able to generate a wide range of reactive nucleosides in partially derivatized forms and could be used as a synthon[6] to produce new classes of bicyclic nucleosides by reacting it with appropriate nucleophiles. Synthesis of such carbohydrate-modified polycyclic nucleosides is of immense importance. Naturally occurring bicyclic nucleosides, such as griseolic acids, are known to inhibit nucleotide-phosphodiesterase.[7] Herbicidines and aureonucleomycin are the unusual nucleosides having furano−pyrano−pyran skeletons.[8] Synthesis of various polycyclic nucleosides has also gained momentum in recent years, either for controlling the conformational mobilities of the corresponding nucleotides incorporated in the DNA[9] or to use the modified nucleosides as HIV reverse transcriptase inhibitors.[10]

† NCL communication no. 6423.

‡ National Chemical Laboratory.

§ The University, Southampton.

|| Present address: Department of Organic Chemistry, University of Karlsruhe, Richard-Willstatter-Allee 2, D-76128 Karlsruhe, Germany.

(1) Dai Eun, S.; Sung, C.; Yun Bae, K.; Yong Han, L.; Seung Hee, K. *Biochem. Biophys. Res. Commun.* **1993**, *195*, 1224.

(2) Palmer, J. T.; Rasnick, D.; Klaus, J. L.; Bromme, D. *J. Med. Chem.* **1995**, *38*, 3193.

(3) Schreiber, S. L.; Ikemoto, N. *Tetrahedron Lett.* **1988**, *29*, 3211.

(4) Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993.

(5) Bera, S.; Sakthivel, K.; Langley, G. J.; Pathak, T. *Tetrahedron* **1995**, *51*, 7857.

(6) For the use of bisvinyl sulfone in the synthesis of various heterocycles, see: (a) Arya, V. P. *Ind J. Chem.* **1975**, *13*, 1262. (b) Minbaev, B. U.; Shostakovskii, M. F.; Kagarlitskii, A. D. *Khim. Geterotsikl. Soedin.* **1983**, 1199. *Chem. Abstr. 100*, 6422*u*. (c) Nagao, Y.; Sakurai, H. *Chem. Lett.* **1976**, 379. (d) Kropf, H.; Bernert, C.-R. *Justus Liebigs Ann. Chem.* **1951**, *793*, 151.

(7) Tulshian, D.; Doll, R. J.; Stansberry, M. F.; McPhail, A. T. *J. Org. Chem.* **1991**, *56*, 6819.

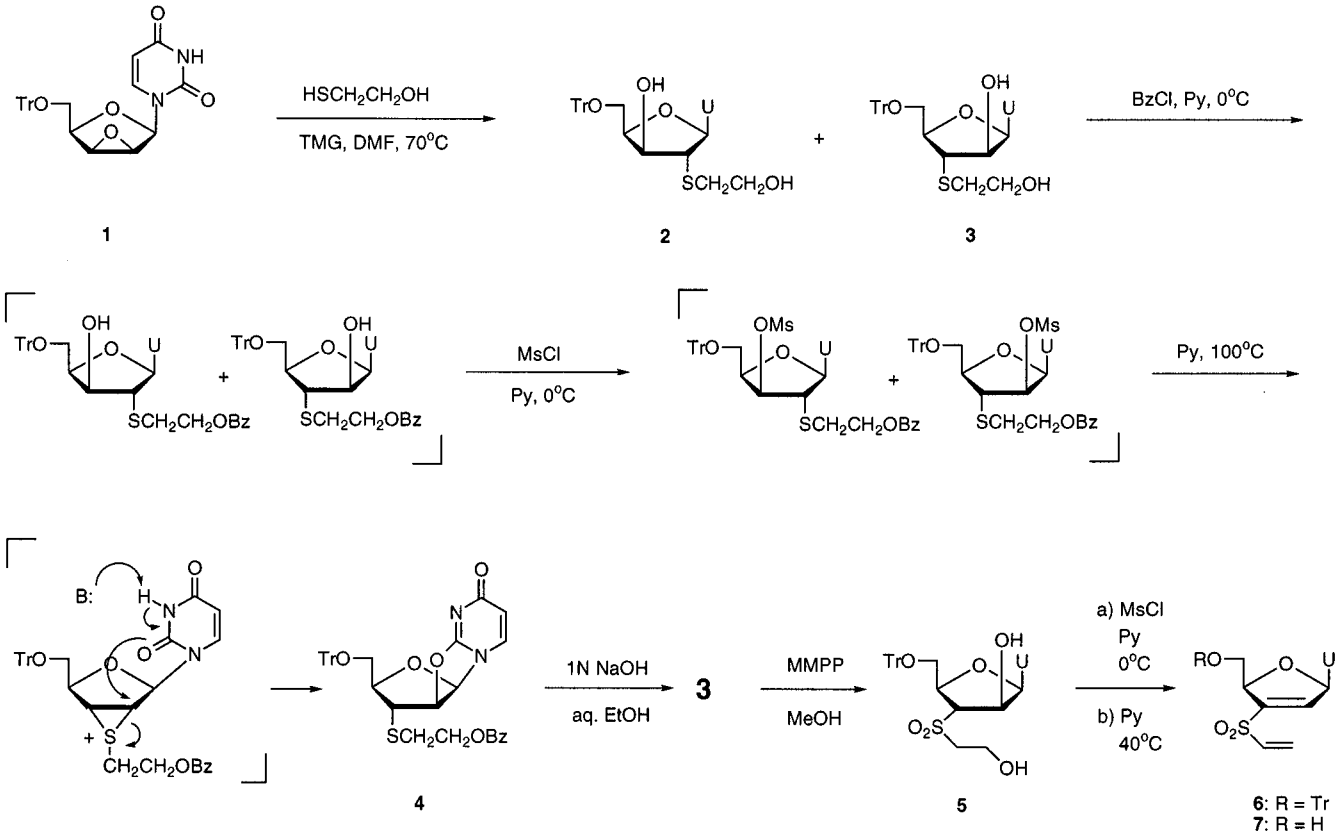
(8) Emery, F.; Vogel, P. *J. Org. Chem.* **1995**, *60*, 5843.

(9) (a) Tarkoy, M.; Bolli, M.; Schweizer, B.; Leumann, C. *Helv. Chim. Acta* **1993**, *76*, 481. (b) Tarkoy, M.; Leumann, C. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1432. (c) Jones, R. J.; Swaminathan, S.; Milligan, J. F.; Wadwani, S.; Froehler, B. C.; Matteucci, M. D. *J. Am. Chem. Soc.* **1993**, *115*, 9816. (d) Tarkoy, M.; Bolli, M.; Leumann, C. *Helv. Chim. Acta* **1994**, *77*, 716. (e) Matteucci, M. D.; Zou, R. *Tetrahedron Lett.* **1996**, *37*, 941. (f) Haly, B.; Bharadwaj, R.; Sanghvi, Y. S. *Synlett* **1996**, 687. (g) Yannopoulos, C. G.; Zhou, W. Q.; Nower, P.; Peoch, D.; Sanghvi, Y. S.; Just, G. *Synlett* **1997**, 378. (h) Nielsen, P.; Pfundheller, H. M.; Wengel, *J. Chem. Commun.* **1997**, 825.

(10) (a) Altmann, K. H.; Imwinkelried, R.; Kesseiring, R.; Rihs, G. *Tetrahedron Lett.* **1994**, *35*, 7625. (b) Rong, J.; Roselt, P.; Plavec, J. Chattopadhyaya, J. *Tetrahedron* **1994**, *50*, 5273. (c) Garg, N.; Hossain, N.; Chattopadhyaya, J. *Tetrahedron* **1994**, *50*, 5273. (d) Grangier, G.; Aitken, D. J.; Guillaume, D.; Husson, H.-P. *Tetrahedron Lett.* **1994**, *35*, 4355. (e) Chang, H. S.; Bergmeir, S. C.; Frick, J. A.; Bathe, A.; Rapoport, H. *J. Org. Chem.* **1994**, *59*, 5336. (f) Ezzitouni, A.; Barchi, J. J. Jr.; Marquez, V. E. *J. Chem. Soc. Chem. Commun.* **1995**, 1345. (g) Chao, Q.; Nair, V. *Tetrahedron Lett.* **1995**, *36*, 7375. (h) Jeong, L. S.; Marquez, V. E. *Tetrahedron Lett.* **1996**, 37, 2353. (i) Endova, M.; Masojidkova, M.; Budesinsky, M.; Rosenberg, I. *Tetrahedron Lett.* **1996**, *37*, 3497. (j) Chao, Q.; Nair, V. *Tetrahedron* **1997**, *53*, 1957. (k) Ezzitouni, A.; Marquez, V. E. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1073.

S0022-3263(97)00557-4 CCC: $15.00
Published on Web 02/26/1998

Scheme 1



Moreover, synthesis of this new class of bicyclic nucleosides equipped with *S*,*S*-dioxide moiety will be interesting as several heterocycles containing this functionality, as part of the ring, have been synthesized. For example, 1-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranose *S*,*S*-dioxide,[11] an analogue of 1-*O*-acetylglucopyranose; a thiadiazine *S*,*S*-dioxide diacyclonucleoside;[12] and the sulfone of 4′-thiothymidine[13] have been synthesized to study their biological and biophysical properties.

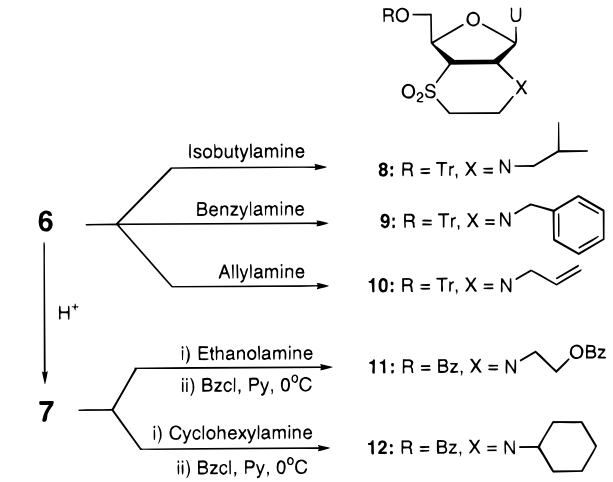
Results and Discussion

Synthesis of 5′-*O*-Trityl-2′,3′-dideoxy-2′-ene-3′-*S*-(1-vinylsulfonyl)uridine 6. 5′-*O*-Trityl-2′,3′-*O*-anhydro-*lyxo*-uridine **1**[14] was reacted with mercaptoethanol in the presence of TMG to generate a mixture of 2′-deoxy-2′-*S*-(2-hydroxyethylthio)-5′-*O*-trityl-*xylo*-uridine **2** and 3′-deoxy-3′-*S*-(2-hydroxyethylthio)-5′-*O*-trityl-*ara*-uridine **3**. As all efforts to separate the isomers failed, the primary hydroxyl group of the hydroxyethylthio moieties of **2** and **3** were benzoylated selectively at 0 °C. After workup, 2′(3′)-hydroxyl groups of the crude benzoylated products were mesylated at 0 °C. The resulting mesylated products were heated at 100 °C in pyridine; intramolecular 2′,3′-epithiiranium ion formation followed by the attack of C-2 oxygen at the C-2′ center resulted in the formation of the 2,2′-*O*-anhydro derivative **4** in 50% overall yield in four steps. Compound **4** was debenzoylated and the 2,2′-*O*-anhydro bridge was hydrolyzed by aqueous NaOH treatment to produce **3** in 96% yield. Oxidation of **3** with magnesium monoperphthalate (MMPP) produced 3′-deoxy-3′-*S*-(2-hydroxyethylsulfonyl)-5′-*O*-trityl-*ara*-uridine **5** in 86% yield. Both the hydroxyl groups of **5** were mesylated and the crude product obtained after workup was heated at 40 °C in pyridine; elimination of the mesylates produced the desired bisvinylsulfonyl uridine **6** in 86% yield (Scheme 1). Detritylation of compound **6** with 80% aqueous acetic acid produced compound **7**; however, for the sake of convenience, crude **7** (after removing tritanol by triturating the detritylating mixture of **6** with ether) was treated directly with nucleophiles. The products were isolated as the corresponding benzoylated derivatives.

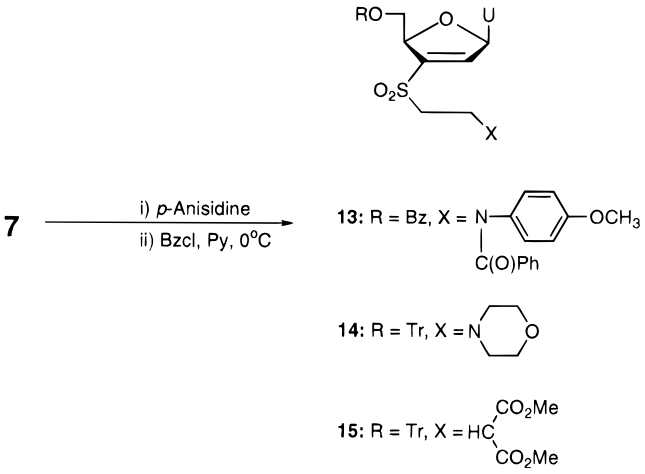
Reactions of 6 and 7 with Nucleophiles. Compounds **6** and **7** were reacted with six primary amines in methanol. All amines except allylamine were slow to react (around 2 days at room temperature), but the reactions[15] produced bicyclic derivatives **8**−**12** in high yields in stereoselective fashion (Scheme 2). Structures of all compounds were established unambiguously through alternative synthesis (see later text). To the best of our knowledge, this group of bicyclic thiazine derivatives is the first of its kind in the literature. One equivalent of *p*-anisidine reacted with **7** to produce a single compound. Attempted cyclization of this compound was unsuccessful, even at elevated temperature. The product was isolated as its dibenzoyl derivative **13**. Morpholine and dimethyl malonate/sodium hydride, reacted[16] with **6** to produce **14**

(11) Yuasa, H.; Takenaka, A.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3473.
(12) Esteban, A. I.; Juanes, O.; Marz, A.; Conde, S. *Tetrahedron* **1994**, *50*, 13865.
(13) Lousi Hancox, E.; Hamor, T. A.; Walker, R. T. *Tetrahedron Lett.* **1994**, *35*, 1291.
(14) Bera, S.; Pathak, T.; Langley, G. J. *Tetrahedron* **1995**, *51*, 1459.
(15) Selection of solvent was important for these reactions. For example, when **6** was reacted with isobutylamine in chloroform no cyclized product was obtained.
(16) Bera, S. *Ph.D. Thesis*, University of Poona, Pune, India, 1997.

Scheme 2



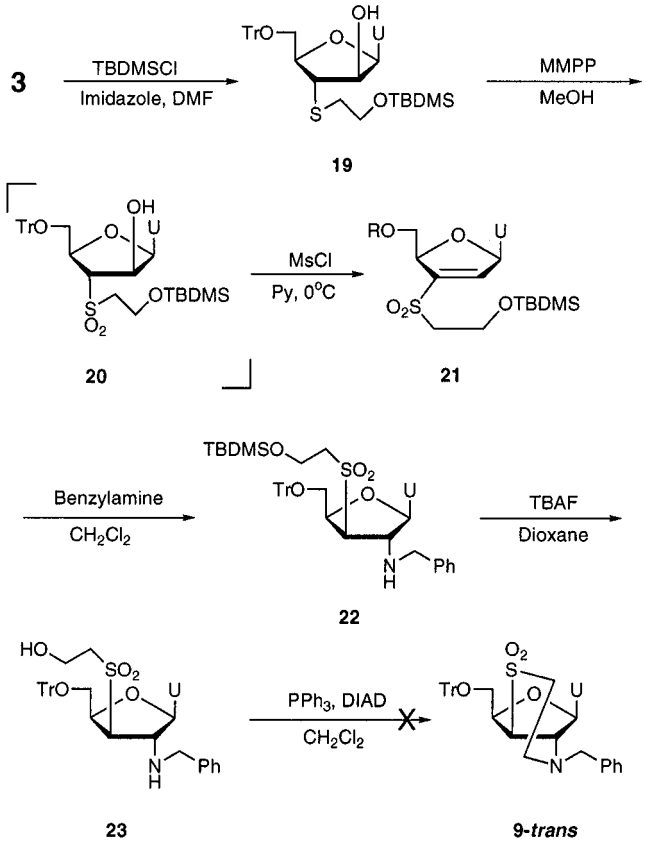
Scheme 3



and **15** in 92 and 86% yields, respectively. All these reactions (Scheme 3) demonstrated that the exocyclic vinyl sulfone group of **6** or **7** was more reactive than the endocyclic one.

Structural Elucidation. To establish the structures of **8**−**12** unambiguously, we decided to synthesize some of these compounds through different routes. The most important requirement of such a synthesis would be regio- and stereospecific construction of C-2′−N and C-3′−S bonds. We assumed that in the case of **8**−**12**, the C-2′−N bond was α to the plane of the furan ring because it was demonstrated earlier[17] that nucleophiles attacked C-2′ of 1-(5-*O*-trityl-2,3-dideoxy-3-toluenesulfonyl-*β*-D-glyceropent-2-enofuranosyl)uracil (and adenosine) exclusively from the α-side due to the presence of a bulky heterocycle at the C-1′ position in the *β* configuration. It was also known that intermolecular Michael type addition of thiophenol to 1-*p*-tolylsulfonylcyclopentene[18] and benzylamine to nucleosides[17] equipped with endocyclic vinyl sulfone functionalities exclusively produced the trans product due to steric strain. Compound **21**, with only one vinyl sulfone group available for reaction was, therefore, selected as the key starting material for producing C-2′−Nα and C-3′−S*β* linkages. Synthesis of **21** began with the selective protection of the primary

Scheme 4



hydroxyl group of **3** with TBDMS to produce **19** in 93% yield. Compound **19** was oxidized to **20**. Compound **21** was obtained by mesylating **20** and heating the reaction mixture at 40 °C. On reaction with benzylamine in dichloromethane, **21** generated **22** exclusively in 79% yield.[19] Deprotection of **22** produced **23**. All attempts to cyclize **23** were unsuccessful (Scheme 4). However, **23** was needed for cross-checking the structure of **29**.

Since **23** could not be cyclized, we turned our attention to the synthesis of **29**. We expected that by having both C-2′−N and C-3′−S bonds in α configurations, the cyclization of **29** would be easier than that of **23**. For the synthesis of **29** we started with the anhydro derivative **4**, as it was having the desired configurations at both the C-2′ and C-3′ positions. The C-3′−S linkage in **4** was already α due to the opening of *lyxo*-epoxide **1** by mercaptoethanol from the α face. The 2,2′-*O*-anhydro linkage, on the other hand, would allow a nucleophile, such as azide, to attack the C-2′ position exclusively from the α side. Compound **24** was thus obtained by the azidolysis of **4** at elevated temperature in 70% yield. Debenzoylation of **24** produced **25**. Compound **25** was oxidized to the sulfone derivative **26** in high yield. The presence of the azido group in **24**, **25**, and **26** was confirmed by the appearance of sharp peaks at 2130, 2140, and 2125 cm^{-1}, respectively in the IR spectra. The azido group of **26** was reduced and the crude amino derivative **27** was cyclized under Mitsonubo conditions.[20]

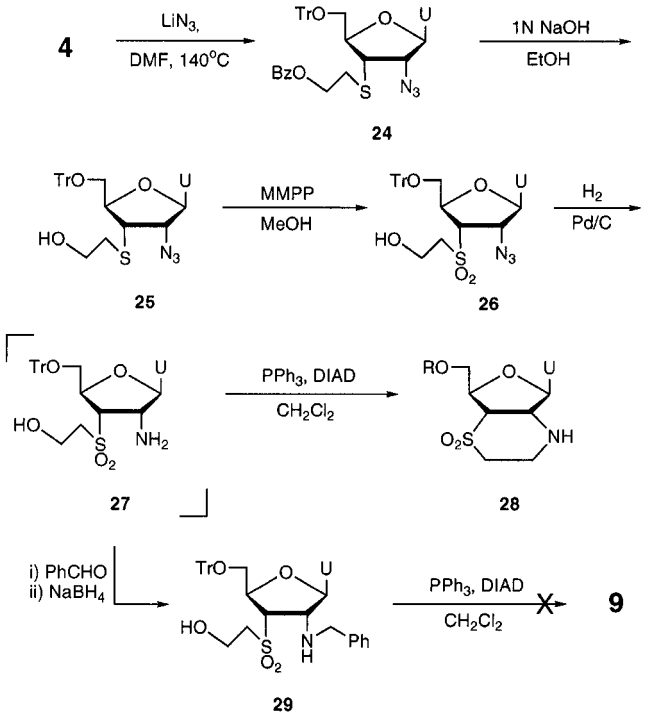
(17) Wu, J.-C.; Pathak, T.; Tong, W.; Remaud, G.; Chattopadhyaya, J. *Tetrahedron* **1988**, *44*, 6705.

(18) Truce, W. E.; Levy A. J. *J. Org. Chem.* **1963**, *28*, 679.

(19) This reaction also demonstrated that by using a system represented by **21**, it would be possible to incorporate various functionalities preferentially into the endocyclic vinyl sulfone moiety of nucleosides. The exocyclic vinyl sulfone functionality may be generated later from compound **23**. This methodology will produce a wide variety of partially functionalized vinyl sulfone derivatives.

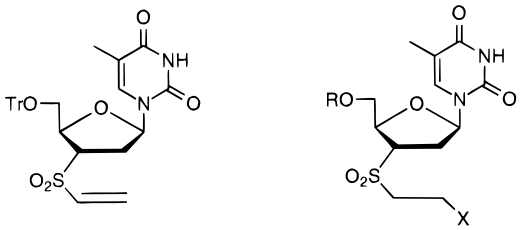
(20) Mitsunobu, O. *Synthesis* **1981**, 1.

Scheme 5



The required *S*,*S*-dioxide thiazine derivative **28** was obtained in 80% yield. In an attempt to synthesize **9**, **27** was benzylated[21] in 40% yield. The cyclization of **29**, like the cyclization of its isomer **23** was also unsuccessful (Scheme 5). However, compound **9** was debenzylated in 75% yield by reacting it with 4% formic acid and Pd/C in refluxing methanol. The debenzylated product of **9** was identical to the thiazine derivative **28**. Furthermore, **28** on treatment with allyl bromide in the presence of silver oxide produced previously synthesized allyl derivative **10** (Scheme 6). These experiments proved unambiguously that the bicyclic derivatives **8**−**12** were cis-fused.

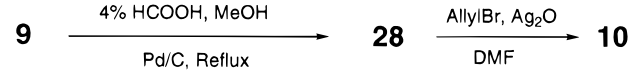
The structures of **13**−**15** were established very easily by comparing their spectroscopic signals with those of **16**, **17**, or **18**.[5] In all cases, proton signals at around 6.8



ppm (H-2′) were present, whereas the characteristic signal of the methylene group of the vinyl sulfone function (6.42 ppm for **16**)[5] was absent. Moreover, the signals at 5.78 ppm (for **6**) characteristic of SO_2CH of the vinyl sulfone group (6.13 ppm in case of **16**)[5] was also absent in the ^{1}H NMR spectra[16] of **13**−**15**. On the other hand, methylene carbons[16] attached to the sulfone groups of **13**, **14**, and **15** appeared at 52.8, 51.6, and 52.3 ppm,

(21) Celewiz, L.; Urjasz, W.; Golankiwick, K. *Nucleosides Nucleotides* **1994**, *12*, 951.

Scheme 6



respectively. These values compared well with the same methylene carbons of **17** (51.8 ppm when X = morpholinyl; 49.4 ppm when X = dimethylmalonatyl).[5]

Research is currently in progress to extend the present observations in the area of carbohydrates and to use the bisvinyl sulfone modified nucleosides as building blocks in the synthesis of backbone-modified oligonucleotides.

Experimental Section

General Information. See refs 5 and 14.

5′-*O*-Trityl-2,2′-*O*-anhydro-3′-deoxy-3′-*S*-(2-*O*-benzoylethyl)uridine 4. To a solution of mercaptoethanol (3.9 g, 50 mmol) in DMF (25 mL), TMG (1,1,3,3-tetramethylguanidine) (2.3 g, 20 mmol) was added and the mixture was heated at 70 °C for 10 min. To this mixture, epoxide **1**[14] (4.68 g, 10 mmol) was added and the reaction mixture was heated at 70 °C for 2 h. It was then cooled to room temperature and poured into saturated $NaHCO_3$ solution with vigorous stirring. The mixture was filtered and the residue was washed with water and dissolved in EtOAc. The EtOAc part was dried over Na_2SO_4 and filtered. The filtrate was evaporated to dryness and the solid residue was purified over silica gel. This purified mixture of isomers **2** and **3** (8.5 mmol) was dissolved in pyridine (40 mL) and cooled at 0 °C. Benzoyl chloride (1.4 g, 9.5 mmol) in pyridine (20 mL) was added dropwise for a period of 1 h. After the consumption of the starting material (TLC), the reaction mixture was poured into saturated $NaHCO_3$ solution with stirring. The residue was filtered, washed with water and then dissolved in EtOAc. The EtOAc solution was dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness. The crude monobenzoylated product was dissolved in pyridine (40 mL) and mesyl chloride (2.86 g, 25 mmol) in pyridine (10 mL) was added dropwise at 0 °C. After the completion of addition, the reaction mixture was kept at 4 °C overnight. The reaction mixture was then poured into saturated $NaHCO_3$ solution. The residue was filtered, washed with water, dried, and dissolved in EtOAc. The EtOAc solution was dried over Na_2SO_4 and filtered. The filtrate was evaporated to dryness. The solid residue was then dissolved in anhydrous pyridine (75 mL) and heated at 100 °C for 26 h. The reaction mixture was then cooled to room temperature and poured into saturated $NaHCO_3$ solution. The residue was filtered, washed with water, air-dried, and dissolved in EtOAc. The EtOAc part was dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness. The white residue was purified over silica gel to produce compound **4** (3.16 g, 50%, for four steps). Mp: 74−76 °C. ^{1}H NMR ($CDCl_3$): δ 8.02 (m, 2H), 7.61−7.19 (m, 19H), 6.15 (d, 5.8 Hz, 1H), 5.98 (d, 7.6 Hz, 1H), 5.31 (m, 1H), 4.50 (t, 2H), 4.26 (q, 1H), 3.71 (m, 1H), 3.11 (d, 5.6 Hz, 2H), 3.02 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 171.6, 166.2, 159.2, 143.2, 134.8, 133.3, 129.7, 128.6, 128.4, 128.1, 127.4, 110.3, 90.5, 88.9, 87.1, 86.2, 63.3, 49.4, 31.0. HRMS (EI, M^+): for $C_{37}H_{32}N_2O_6S$ calcd 632.1981, obsd 632.1946.

1-[5-*O*-Trityl-3-deoxy-3-*S*-(2-hydroxyethyl)-*β*-D-*ara*-furanosyl]uracil 3. To a solution of **4** (3.16 g, 5 mmol) in EtOH (40 mL) and water (10 mL), was added 1 N NaOH (15 mL) solution. The reaction mixture was stirred at room temperature. After 2 h, the reaction mixture was neutralized with 1 N HCl solution under cold conditions. The residue thus obtained was filtered, washed with water, air-dried, and dissolved in EtOAc. The EtOAc solution was dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness and the white residue was purified over silica gel to give **3** (2.62 g, 96%). Mp: 99−100 °C. ^{1}H NMR ($CDCl_3$): δ 8.18 (d, 8.2 Hz, 1H), 7.46−7.25 (m, 15H), 6.15 (d, 5.9 Hz, 1H), 5.33 (d, 8.1 Hz, 1H), 4.55 (t, 1H), 3.84−3.39 (m, 7H), 2.77 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 164.6, 151.6, 143.4, 142.1, 129.0,

128.2, 127.6, 101.8, 87.7, 85.0, 81.5, 78.2, 62.1, 61.6, 47.7, 34.8. HRMS (EI, M^+) for $C_{30}H_{30}N_2O_6S$ calcd 546.1825, obsd 546.1778.

1-[5-*O*-Trityl-3-deoxy-3-*S*-(2-hydroxyethylsulfonyl)-*β*-D-*ara*-furanosyl]uracil 5. To a solution of **3** (1.63 g, 3 mmol) in MeOH (30 mL) was added MMPP (4.5 g, 9 mmol) and the reaction mixture was stirred at room temperature for 4−5 h. The white residue was filtered and washed with MeOH. The filtrate was evaporated to dryness under reduced pressure. The residue was triturated with saturated $NaHCO_3$ solution and filtered. The residue was washed with $NaHCO_3$ solution followed by water and dried. The solid mass was then dissolved in EtOAc, dried over Na_2SO_4, and filtered. The filtrate was evaporated to dryness and the white residue was purified over silica gel to give **5** (1.49 g, 86%). Mp: 154−155 °C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 7.58 (d, 8.1 Hz, 1H), 7.27−7.03 (m, 15H), 5.91 (d, 5.4 Hz, 1H), 5.74 (d, 1H), 5.03 (d, 8.1 Hz, 1H), 4.63 (m, 2H), 4.30 (m, 1H), 4.06 (m, 1H), 3.84 (m, 2H), 3.45−2.94 (m, 4H). ^{13}C NMR ($CDCl_3$ + DMSO-d_6): δ 162.5, 149.4, 142.3, 140.7, 127.4, 126.7, 126.0, 99.3, 85.7, 84.1, 73.2, 70.1, 66.8, 62.8, 54.2, 54.1. HRMS (EI, M^+) for $C_{30}H_{30}N_2O_8S$ calcd 578.1723, obsd 578.1672.

1-[5-*O*-Trityl-2,3-dideoxy-3-*S*-(vinylsulfonyl)-*β*-D-glyceropent-2-enofuranosyl]uracil 6. Compound **5** (1.15 g, 2 mmol) was dissolved in pyridine (20 mL), and mesyl chloride (1.4 g, 12 mmol) in pyridine (5 mL) was added dropwise at 0 °C. After the addition, the reaction mixture was left at 4 °C overnight. It was then poured into saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The dichloromethane part was evaporated to dryness under reduced pressure and the residue was coevaporated with toluene. The brown residue was partitioned between EtOAc (80 mL) and water (70 mL). The EtOAc part was dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in anhydrous pyridine (30 mL) and heated at 40 °C for 1.5 h. The solution was poured into saturated $NaHCO_3$ solution (100 mL) and extracted with dichloromethane (3 × 25 mL). The dichloromethane part was evaporated and the residual pyridine was coevaporated with toluene under reduced pressure. The residue was purified over silica gel to give **6** (0.93 g, 86%). Mp:195−198 °C. ^{1}H−^{1}H COSY NMR ($CDCl_3$): δ 9.10 (bs, 1H) NH; 7.90 (d, 8.0 Hz, 1H) H-6; 7.68−7.24 (m, 15H) trityl; 7.15 (m, 1H) H-1′; 6.80 (bs, 1H) H-2′; 6.52−6.23 (m, 2H) =CH_2; 5.78 (d, 9.2 Hz, 1H) SO_2CH; 5.16 (m, 1H) H-4′; 4.65 (d, 8.1 Hz, 1H) H-5; 3.83 (m, 1H), 3.66 (m, 1H) H-5′, H-5″. ^{13}C NMR ($CDCl_3$ + DMSO-d_6): δ 163.4, 150.8, 146.1, 142.9, 141.2, 138.5, 136.8, 131.4, 129.1, 128.1, 127.6, 102.3, 88.1, 87.7, 83.7, 63.3. HRMS (EI, M^+) for $C_{30}H_{26}N_2O_6S$ calcd 542.1512, obsd 542.1467.

General Procedure for the Synthesis of 8−10. A mixture of **6** (0.271 g, 0.5 mmol) and the corresponding amine (0.5 mmol) in MeOH (20 mL) was stirred at room temperature for 22−72 h. MeOH was removed under reduced pressure. The residue was purified over silica gel (**8**) or basic alumina (**9** and **10**).

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-isobutyl-4*H*-2,3,5,6-tetrahydro-1,4-thiazine-1,1-dioxides-*β*-D-*ribo*-furanosyl]uracil 8 (0.25 g, 83%). Mp: 134−138 °C; ^{1}H NMR ($CDCl_3$): δ 7.86 (d, 8.2 Hz, 1H), 7.37−7.27 (m, 15H), 6.31 (d, 6.1 Hz, 1H), 5.22 (d, 8.1 Hz, 1H), 4.80 (m, 1H), 3.81 (t, 1H), 3.64 (m, 4H), 3.10 (m, 3H), 2.73 (m, 1H), 2.28 (m, 1H), 1.65 (m, 1H), 0.87 (d, 6H). ^{13}C NMR ($CDCl_3$): δ 163.6, 150.6, 142.9, 139.6, 128.7, 128.3, 127.8, 102.6, 88.4, 83.3, 75.4, 69.2, 64.3, 62.5, 58.5, 47.7, 47.2, 27.3, 20.3, 20.2. HRMS (CI, M + H^+) for $C_{34}H_{38}N_3O_6S$ calcd 616.2481, obsd 616.2432.

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-benzyl-4*H*-2,3,5,6-tetrahydro-1,4-thiazine-1,1-dioxides-*β*-D-*ribo*-furanosyl]uracil 9 (0.27 g, 83%). Mp: 143−144 °C. ^{1}H−^{1}H COSY NMR ($CDCl_3$): δ 7.81 (d, 8.2 Hz, 1H) H-6; 7.43−7.22 (m, 20H) aromatic, 6.31 (d, 4.5 Hz, 1H) H-1′; 5.13 (d, 8.2 Hz, 1H) H-5; 4.82 (m, 1H) H-4′; 4.30 (d, 14.4 Hz, 1H) one of benzyl CH_2; 3.79−3.52 (m, 6H) H-3′, H-5′, H-5″, SO_2CH_2 and one of benzyl CH_2; 3.20−3.09 (m, 3H) H-2′, NCH_2. ^{13}C NMR ($CDCl_3$): δ 163.7, 150.6, 142.9, 139.5, 137.6, 128.9, 128.8, 128.3, 128.2, 127.9, 127.7, 102.6, 88.3, 84.4, 76.4, 68.7, 63.5, 58.4, 47.7. HRMS (EI, M^+) for $C_{37}H_{35}N_3O_6S$ calcd 649.2247, obsd 649.2189.

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-allyl-4*H*-2,3,5,6-tetrahydro-1,4-thiazine-1,1-dioxides-*β*-D-*ribo*-furanosyl]uracil 10 (0.22 g, 73%). Mp: 135−137 °C. ^{1}H−^{1}H COSY NMR ($CDCl_3$): δ 7.94 (d, 8.2 Hz, 1H) H-6; 7.43−7.27 (m, 15H) trityl; 6.27 (d, 4.8 Hz, 1H) H-1′; 5.76 (m, 1H) =CH; 5.21 (m, 3H) =CH_2, H-5; 4.76 (m, 1H) H-4′; 3.85−3.49 (m, 6H) H-2′, H-3′, H-5′, H-5″, SO_2CH_2; 3.13 (m, 4H) CH_2NCH_2. ^{13}C NMR ($CDCl_3$): δ 163.7, 150.5, 142.9, 139.9, 134.2, 128.8, 128.3, 127.7, 118.8, 102.6, 88.3, 83.9, 76.1, 68.2, 63.6, 58.8, 57.3, 47.9, 47.3. HRMS (EI, M^+) for $C_{33}H_{33}N_3O_6S$ calcd. 599.2090, obsd 599.2081.

General Procedure for the Synthesis of 11−13. A solution of **6** (0.73 mmol) in 80% aqueous HOAc (50 mL) was heated at 75 °C for 45 min. HOAc was removed under reduced pressure and the residual HOAc was coevaporated with EtOH. The solid residue was triturated with ether. The detritylated product **7** was dissolved in MeOH (15 mL). Appropriate amine (0.73 mmol) was added to the mixture. The suspension was stirred at room temperature for 22−72 h. MeOH was removed under reduced pressure. The residue was dissolved in anhydrous pyridine (15 mL) and benzoyl chloride (0.75 g, 5 mmol) was added dropwise at 0 °C. The reaction mixture was stirred at 0 °C. After 2 h the mixture was poured into saturated $NaHCO_3$ solution (60 mL) and extracted with chloroform (3 × 20 mL). The chloroform part was evaporated to dryness and the residual pyridine was coevaporated with toluene. The product was purified over silica gel.[22]

1-[5-*O*-Benzoyl-2,3-dideoxy-2-*N*-(2-*O*-benzoylethyl)-4*H*-2,3,5,6-tetrahydro-1,4-thiazine-1,1-dioxides-*β*-D-*ribo*-furanosyl]uracil 11 (0.235 g, 56%). Mp: 109−111 °C. ^{1}H NMR ($CDCl_3$): δ 8.05 (m, 4H) and 7.68−7.35 (m, 7H), 6.13 (d, 3.1 Hz, 1H), 5.40 (dd, 8.2 Hz, 1H), 4.85−4.53 (m, 4H), 4.29 (m, 1H), 3.84 (m, 1H), 3.63 (m, 3H), 3.20 (m, 3H), 2.80 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 166.5, 165.8, 163.5, 150.5, 139.0, 133.8, 133.3, 129.7, 129.6, 129.4, 129.1, 128.7, 128.5, 102.7, 86.1, 75.6, 68.4, 64.0, 61.8, 58.6, 52.5, 48.2. HRMS (CI, M + H^+): for $C_{27}H_{28}N_3O_9S$ calcd 570.1546, obsd 570.1577.

1-[5-*O*-Benzoyl-2,3-dideoxy-2-*N*-cyclohexyl-4*H*-2,3,5,6-tetrahydro-1,4-thiazine-1,1-dioxides-*β*-D-*ribo*-furanosyl]uracil 12 (0.16 g, 58%). Mp: 125−127 °C. ^{1}H NMR ($CDCl_3$): δ 8.86 (bs, 1H), 8.05−7.47 (m, 6H), 6.37 (d, 7.5 Hz, 1H), 5.60 (d, 8.1 Hz, 1H), 5.11 (m, 1H), 4.77 (m, 2H), 3.79 (m, 2H), 3.47 (m, 2H), 3.03 (m, 2H), 2.63 (m, 1H), 1.64 (m, 4H), 1.05 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 165.9, 163.5, 150.5, 138.9, 133.9, 129.5, 129.1, 128.8, 102.9, 82.5, 73.0, 65.8, 64.2, 62.4, 58.9, 48.3, 44.7, 32.8, 31.4, 25.6, 25.4. HRMS (CI, M + H^+): for $C_{24}H_{30}N_3O_7S$ calcd 504.1804, obsd 504.1796.

1-[5-*O*-Benzoyl-2,3-dideoxy-3-*S*-(2-*N*-benzoyl-*p*-methoxyanilinoethylsulfonyl)-*β*-D-glyceropent-2-enofuranosyl]uracil 13 (0.19 g, 63%). Mp: 112−114 °C; ^{1}H NMR ($CDCl_3$): δ 9.20 (bs, 1H), 7.99 (m, 2H), 7.60−6.70 (m, 15H), 5.57 (m, 1H), 5.18 (d, 8.1 Hz, 1H), 4.95 (2d, 1H), 4.65 (2d, 1H), 4.28 (m, 2H), 3.75 (s, 3H), 3.63 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 171.0, 165.9, 163.3, 158.6, 150.6, 144.9, 139.9, 139.1, 135.0, 134.8, 133.6, 130.2, 129.5, 128.8, 127.9, 114.8, 103.2, 88.2, 82.7, 63.9, 55.4, 51.6, 44.7. HRMS (EI, M^+): for $C_{32}H_{29}N_3O_9S$ calcd 631.1625, obsd 631.1600.

1-[5-*O*-Trityl-3-deoxy-3-*S*-(2-*O*-*tert*-butyldimethylsilylethyl)-*β*-D-*ara*-furanosyl]uracil 19. To a solution of **3** (1 g, 1.8 mmol) and imidazole (0.27 g, 4 mmol) in DMF (10 mL) was added *tert*-butyldimethylsilyl chloride (2.5 mmol) and the reaction mixture was stirred at room temperature for 8 h. The solution was then poured into ice-cold water and filtered. The residue was dissolved in EtOAc, dried over Na_2SO_4, and filtered. The filtrate was evaporated to dryness and the white residue was purified over silica gel to give **19** (1.1 g, 93%). Mp: 77−79 °C. ^{1}H NMR ($CDCl_3$): δ 9.50 (bs, 1H), 8.11 (d, 8.2 Hz, 1H), 7.46−7.27 (m, 15H), 6.16 (d, 5.2 Hz, 1H), 5.34 (d, 8.1 Hz, 1H), 4.72 (d, 1H), 4.55 (m, 1H), 3.83 (m, 3H), 3.50 (m, 3H), 2.79 (m, 2H), 0.88 (s, 9H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$)

(22) Compound **11** was synthesized in 0.73 mmol scale. Compounds **12** and **13** were prepared in 0.55 mmol scale. In the preparation of **13**, the suspension of **7** and *p*-methoxyaniline in MeOH was stirred at room temperature followed by heating under reflux for 10 h to initiate cyclization.

δ 164.8, 151.4, 143.5, 142.4, 128.9, 128.2, 127.5, 101.4, 87.5, 85.6, 81.7, 78.1, 63.3, 62.4, 48.3, 34.2, 26.1, 18.5, −5.0. HRMS (EI, M^+): for $C_{36}H_{44}N_2O_6SSi$ calcd 660.2690, obsd 660.2648.

1-[5-*O*-Trityl-2,3-dideoxy-3-*S*-(2-*O*-*tert*-butyldimethylsilylethylsulfonyl)-β-D-glyceropent-2-enofuranosyl]-uracil 21. Compound **19** (0.9 g, 1.36 mmol) was oxidized with MMPP (2.5 g, 5.5 mmol) in MeOH (25 mL) following the same method as described for **5** to give **20** (0.85 g, 90%). To a solution of compound **20** (0.8 g, 1.18 mmol) in pyridine (10 mL) was added mesyl chloride (0.3 mL, 3.6 mmol) dropwise at 0 °C. After the addition the reaction mixture was kept at 4 °C overnight. Water (2 mL) was added to the reaction mixture. The mixture was then heated at 40 °C for 1.5 h. The mixture cooled to room temperature and was poured into saturated $NaHCO_3$ solution. The residue was filtered, washed with water, and then dissolved in EtOAc. The EtOAc part was dried over Na_2SO_4 and filtered. The filtrate was evaporated to dryness under reduced pressure and the residue was purified over silica gel to give **21** (0.67 g, 86%). Mp: 87−90 °C. ^{1}H NMR ($CDCl_3$): δ 7.90 (d, 8.0 Hz, 1H), 7.41−7.27 (m, 15H), 7.09 (m, 1H), 6.78 (t, 1H), 5.20 (m, 1H), 4.79 (d, 8.1 Hz, 1H), 4.02 (t, 2H), 3.75 (m, 2H), 3.30 (m, 2H), 0.92 (s, 9H), 0.10 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 163.3, 150.6, 147.8, 142.8, 140.8, 137.3, 129.1, 128.6, 127.6, 102.9, 88.4, 87.7, 84.4, 63.1, 58.4, 56.9, 25.9, 18.3, −5.4. HRMS (CI, M + H^+): for $C_{36}H_{43}N_2O_7SSi$ calcd 675.2560, obsd 675.2608.

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-benzylamino-3-*S*-(2-*O*-*tert*-butyldimethylsilylethylsulfonyl)-β-D-*xylo*-furanosyl]uracil 22. Compound **21** (0.52 g, 0.77 mmol) was treated with benzylamine (1.3 g, 12 mmol) in dichloromethane (20 mL) for 3 days. Dichloromethane was removed under reduced pressure and the gummy residue was triturated with petroleum ether. The white residue was purified over silica gel to give **22** (0.48 g, 79%). Mp: 92−94 °C. ^{1}H NMR ($CDCl_3$): δ 7.58 (d, 8.2 Hz, 1H), 7.51−7.22 (m, 20H), 5.94 (d, 4.4 Hz, 1H), 5.62 (d, 8.2 Hz, 1H), 4.61 (m, 1H), 3.94−3.63 (m, 9H), 3.02 (m, 2H), 0.90 (s, 9H), 0.05 (2s, 6H). ^{13}C NMR ($CDCl_3$): δ 163.5, 150.9, 143.5, 140.4, 138.8, 128.9, 128.2, 128.1, 127.6, 127.4, 102.9, 89.1, 87.9, 78.1, 69.2, 64.5, 62.6, 57.7, 56.4, 51.5, 26.0, 18.4, −5.4. HRMS (CI, M + H^+): $C_{43}H_{52}N_3O_7SSi$ calcd 782.3295, obsd 782.3276.

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-benzylamino-3-*S*-(2-hydroxyethylsulfonyl)-β-D-*xylo*-furanosyl]uracil 23. Compound **22** (0.35 g, 0.44 mmol) was treated with tetrabutylammonium fluoride (0.18 g, 0.68 mmol) in dioxane (10 mL) for 0.5 h. The reaction mixture was then poured into ice cold water (50 mL) and extracted with dichloromethane (2 × 20 mL). The combined dichloromethane part was dried over anhydrous Na_2SO_4 and filtered. The gummy residue was purified over silica gel to produce **23** (0.25 g, 90%). Mp: 125−126 °C. ^{1}H NMR ($CDCl_3$): δ 7.56 (d, 8.1 Hz, 1H), 7.46−7.28 (m, 20H), 5.97 (d, 4.3 Hz, 1H), 5.63 (d, 8.1 Hz, 1H), 4.60 (m, 1H), 3.97−3.64 (m, 8H), 3.05 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 163.8, 150.9, 143.6, 143.3, 140.6, 138.6, 128.7, 128.3, 128.0, 127.4, 103.1, 88.6, 87.8, 77.5, 68.1, 63.9, 62.2, 56.2, 51.1. HRMS (EI, M^+): for $C_{37}H_{37}N_3O_7S$ calcd 667.2352, obsd 667.2341.

Attempted Cyclization of 23. To a solution of **23** (0.3 g, 0.45 mmol) and Ph_3P (0.15 g, 0.57 mmol) in dichloromethane (20 mL) was added diisopropyl azadicarboxylate (0.14 mL, 0.7 mmol) dropwise at 0 °C. After the completion of addition, the reaction mixture was stirred at room temperature for 6 h. The reaction mixture afforded a complex mixture of products (TLC).

1-[5-*O*-Trityl-2,3-dideoxy-2-azido-3-*S*-(2-*O*-benzoylethyl)-β-D-*ribo*-furanosyl]uracil 24. To a solution of **4** (2 g, 3.15 mmol) in DMF (30 mL) was added LiN_3 (2 g, 40 mmol) and the reaction mixture was heated at 140 °C for 3 h. The mixture was cooled to room temperature and poured into saturated $NaHCO_3$ solution. The white precipitate was filtered, washed with water, dried, and dissolved in EtOAc. The EtOAc part was dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness and the residue was purified over silica gel to give **24** (1.5 g, 70%). Mp: 81−83 °C. IR: 2130 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.10 (bs, 1H), 8.19 (d, 8.2 Hz, 1H), 7.99 (m, 2H) and 7.64−7.27 (m, 18H), 5.91 (s, 1H), 5.25 (d, 8.2 Hz, 1H), 4.44 (m, 1H), 4.30 (m, 2H), 4.08 (d, 10.8 Hz, 1H), 3.86 (d, 11.4 Hz, 1H), 3.67 (m, 1H), 3.52 (d, 11.4 Hz, 1H), 2.74 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 166.2, 163.9, 150.4, 142.7, 139.5, 133.4, 129.6, 128.8, 128.5, 128.3, 127.6, 102.1, 89.6, 87.7, 84.2, 69.6, 63.9, 59.9, 45.7, 31.0. HRMS (CI, M + H^+): for $C_{37}H_{34}N_5O_6S$ calcd 676.2230, obsd 676.2239.

1-[5-*O*-Trityl-2,3-dideoxy-2-azido-3-*S*-(2-hydroxyethyl)-β-D-*ribo*-furanosyl]uracil 25. To a solution of **24** (1.25 g, 1.84 mmol) in ethanol (50 mL) and water (10 mL) was added 1 N NaOH solution (10 mL) and the reaction mixture was stirred at room temperature for 2 h. The mixture was then neutralized with 1 N HCl. Saturated $NaHCO_3$ solution was added to the mixture followed by water (100 mL). The precipitate was filtered, washed with water, and air-dried. The residue was dissolved in EtOAc, dried over anhydrous Na_2SO_4, and filtered. The filtrate was evaporated to dryness and the residue was purified over silica gel to give **25** (1 g, 95%). Mp: 87−88 °C. IR: 2140 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.54 (bs, 1H), 8.17 (d, 8.1 Hz, 1H), 7.44−7.27 (m, 15H), 5.87 (s, 1H), 5.28 (d, 8.1 Hz, 1H), 4.49 (d, 5.1 Hz, 1H), 4.05 (d, 10.0 Hz, 1H), 3.80 (m, 4H), 3.54 (d, 1H), 2.64 (t, 2H), 2.45 (bs, 1H). ^{13}C NMR ($CDCl_3$): δ 164.1, 150.7, 143.1, 140.1, 128.8, 128.1, 127.6, 101.9, 89.7, 87.6, 83.9, 69.5, 62.6, 60.4, 46.0, 35.1. HRMS (CI, M + H^+): for $C_{30}H_{30}N_5O_5S$ calcd 572.1968, obsd 572.1925.

1-[5-*O*-Trityl-2,3-dideoxy-2-azido-3-*S*-(2-hydroxyethylsulfonyl)-β-D-*ribo*-furanosyl]uracil 26. Compound **25** (0.86 g, 1.5 mmol) was oxidized with MMPP (2.8 g, 5.6 mmol) in MeOH (30 mL) following the same method as described for **5** to give **26** (0.79 g, 87%). Mp: 110−112 °C. IR: 2125 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.54 (bs, 1H), 8.05 (d, 8.3 Hz, 1H), 7.50−7.20 (m, 15H), 5.94 (d, 0.8 Hz, 1H), 5.31 (d, 8.1 Hz, 1H), 4.79 (m, 2H), 4.47 (m, 1H), 3.96 (m, 3H), 3.56 (d, 1H), 2.97 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 163.5, 150.2, 142.4, 139.1, 128.5, 127.8, 127.3, 102.1, 88.5, 87.6, 65.7, 61.6, 61.1, 56.9, 55.6. HRMS (EI, M^+): for $C_{30}H_{29}N_5O_7S$ calcd 603.1788, obsd 603.1772.

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-4*H*-2,3,5,6-tetrahydro-1,4-thiazine-1,1-dioxides-β-D-*ribo*-furanosyl]uracil 28. Compound **26** (0.5 g, 0.82 mmol) was dissolved in EtOAc (7 mL) and Pd/C (10% Pd, 0.08 g) was added. The reaction mixture was then shaken under hydrogen pressure of 30 lbs/in. for 4 h. Pd/C was filtered off and the filtrate was evaporated to dryness to produce **27**. To a solution of the crude product **27** and Ph_3P (0.24 g, 0.9 mmol) in dichloromethane (20 mL) was added diisopropyl azadicarboxylate (0.2 mL, 1 mmol) dropwise at 0 °C. After the addition, the reaction mixture was stirred at room temperature for 2 h. The organic solvent was removed under reduced pressure and the gummy residue was purified over silica gel column to give **28** (0.34 g, 74%). Mp: 162−165 °C. ^{1}H NMR ($CDCl_3$): δ 9.46 (bs, 1H), 8.15 (d, 8.2 Hz, 1H), 7.46−7.25 (m, 15H), 5.66 (s, 1H), 5.11 (d, 8.1 Hz, 1H), 4.75 (d, 10.2 Hz, 1H), 3.91 (m, 3H), 3.62 (d, 10.2 Hz, 1H), 3.40−3.06 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 163.7, 150.8, 142.9, 139.8, 128.7, 128.1, 127.5, 101.9, 89.3, 88.0, 79.2, 64.9, 61.5, 59.3, 50.9, 42.6. HRMS (CI, M + H^+) for $C_{30}H_{30}N_3O_6S$ calcd 560.1855, obsd 560.1830.

1-[5-*O*-Trityl-2,3-dideoxy-2-*N*-benzylamino-3-*S*-(2-hydroxyethylsulfonyl)-β-D-*ribo*-furanosyl]uracil 29. Compound **26** (0.33 g, 0.55 mmol) was reduced to compound **27** following the same method as described above. To a solution of crude **27** in EtOH (50 mL) were added water (6 mL) and acetate buffer (1.4 mL) [prepared from NaOAc·3H_2O (2.5 g), glacial HOAc (8.4 mL), and water (25 mL)] followed by the addition of benzaldehyde (0.15 g, 1.4 mmol). The reaction mixture was stirred at 0−5 °C for 0.5 h and then $NaBH_4$ (0.15 g, 5 mmol) was added portionwise over a period of 1 h. The solvent was removed under reduced pressure. To the residue was added water (25 mL) and the mixture was extracted with chloroform (3 × 20 mL). The combined organic extracts were washed with water (25 mL), dried over Na_2SO_4, and filtered, and the filtrate was evaporated under reduced pressure. The product was purified over silica gel to give **29** (0.15 g, 40%). Mp: 77−79 °C. ^{1}H NMR ($CDCl_3$): δ 8.86 (bs, 1H), 7.67 (d, 8.0 Hz, 1H), 7.30 (m, 20H), 6.14 (d, 6.5 Hz, 1H), 5.30 (d, 8.2 Hz, 1H), 4.86 (m, 1H), 4.10−3.25 (m, 10H). ^{13}C NMR ($CDCl_3$ + DMSO-d_6): δ 163.3, 151.0, 143.5, 140.1, 139.6, 128.7, 128.3, 128.1, 127.5, 127.2, 102.3, 87.5, 87.4, 75.7, 64.9, 63.1, 62.9, 56.5,

55.5, 51.5. HRMS (EI, M^+) for $C_{37}H_{37}N_3O_7S$ calcd 667.2352, obsd 667.2332.

Compound 28 from Compound 9. To a solution of **9** (0.42 g, 0.64 mmol) in 4% formic acid in methanol (25 mL) was added Pd/C (0.3 g, 10% Pd) and the solution was heated at 80 °C for 10 min. The suspension was filtered. Excess aqueous NH_3 solution was added to the filtrate and the solution was evaporated to dryness. The residue was partitioned between EtOAc and water. The EtOAc part was dried over Na_2SO_4 and evaporated to dryness. The solid residue was purified over silica gel to give compound **28** (0.27 g, 75%).

Compound 10 from Compound 28. To a solution of **28** (0.11 g, 0.19 mmol) and allyl bromide (0.05 g, 0.41 mmol) in DMF (2 mL) was added Ag_2O (0.06 g) and the reaction mixture was stirred at room temperature for 1.25 h. After allowing the precipitate to settle, DMF solution was slowly decanted off. The precipitate was washed with chloroform (3 × 5 mL). The combined organic part (DMF and $CHCl_3$) was washed with 0.5% aqueous NaCN solution (50 mL). The aqueous part was washed with chloroform (2 × 10 mL). The combined chloroform part was then washed thoroughly with water, dried over Na_2SO_4, and evaporated to dryness. The residue was purified over silica gel to yield **10** (0.1 g, 87%).

Acknowledgment. S.B. thanks UGC, New Delhi, India, for a fellowship.

Supporting Information Available: Copies of both ^1H and ^{13}C NMR spectra of **3**, **5**, **6**, **9**, **10**, **14**, **15**, and **28** and copies of ^1H NMR of **4**, **8**, **11**, **12**, **15**, **19**, **21**, **22**, **23**, **24**, **25**, **26** and **29** (31 pages). This material is contained in libraries on microfiche, immediately follows this article in this microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9705576