Diastereoselective Addition of Amines to Vinyl Sulfone Modified Carbohydrates: A Highly Flexible Methodology for the Synthesis of New Classes of Deoxyaminosugars

Bindu Ravindran,[†] Kandasamy Sakthivel,[§] Cheravakkattu. G. Suresh,[‡] and Tanmaya Pathak*,[†]

[a]*Organic Chemistry Division (Synthesis) and* [b]*Division of Biochemical Sciences, National Chemical Laboratory, Pune 411 008, India*

Received August 31, 1999

Methyl 2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-*erythro*-hex-2-enopyranoside (**5α**) and methyl 2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-*β*-D-*erythro*-hex-2-enopyranoside (**5*β***) have been subjected to Michael addition reaction with various amines to develop a new methodology for the synthesis of new classes of aminosugars. Compound **5α** reacted with primary amines to generate gluco- derivatives, but secondary amines produced both gluco- (major) and manno- (minor) isomers. Compound **5*β***, on the other hand, produced only gluco- isomers with both primary and secondary amines. The stereochemical course of addition of some of the amines to **5α** and **5*β*** are significantly different from that of the addition of amines to 3-nitroenopyranoses. The present route to the syntheses of various aminosugars with gluco- configurations from **5α** and **5*β*** constitutes a novel method for the introduction of *N*-monoalkylated and *N*,*N*-dialkylated amines to the C-2 carbon of pyranoses in equatorial configurations.

Introduction

Aminosugars are one of the most important classes of modified carbohydrates.[1] The most common methods for the synthesis of aminosugars involve the reactions of amines with sugar-derived epoxides, tosylates, and ketones, although several other minor methods are also reported.[1] Nucleophilic addition (Michael) to double bonds activated by electron-withdrawing groups as part of carbohydrates could, in theory, serve as a useful methodology for the functionalization of monosaccharides. Several examples of Michael addition of nitrogen nucleophiles including amines to hex-2-enose[2] and 3-nitro-hex-2-enopyranosides[3,4] have been reported. 2,3-Dideoxy-hex-2-en-4-ulopyranosides, for example, have been reacted with azide,[2a] partially protected amino acids and benzylamine[2b] to generate several new classes of aminosugars. The major drawbacks of using 4-uloses as starting materials are that (a) the products will always be 2,3-dideoxy derivatives and (b) the stereochemical outcome of the reduction of the carbonyl group (C-4) is dependent on the orientation of the C-2 substituent.[2] Such limitations made this route less attractive for synthetic work. The studies on the addition of nitrogen nucleophiles to 3-nitro-hex-2-enopyranosides, however, have remained limited mostly to gluco- and galactopyranoses,[3] and except for the preparation of a few diamino- and triaminosugars,[4] these nitrosugar derivatives have not been utilized as intermediates for further synthetic manipulations.

Results and Discussion

During the course of our studies on the synthesis of carbohydrate modified monovinyl sulfone[5a] and bisvinyl sulfone substituted nucleosides,[5b] we envisaged that as a result of the high reactivities of vinyl sulfones toward a wide variety of nucleophiles, vinyl sulfone modified carbohydrates could be utilized to generate a wide variety of modified monosaccharides. Vinyl sulfone modified carbohydrates are expected to offer the following advantages: (a) Almost all carbohydrates, either in pyranose or furanose forms, could be converted to their vinyl sulfone derivatives very easily, the first step being the simple nucleophilic displacements of sulfonylates[1b] or regioselective opening of epoxides[1b] by alkyl or aryl mercaptans at various positions. (b) Since sulfone chemistry has been exploited extensively over decades and its compatibility with a wide variety of simple and complex molecules and reaction conditions are well established,[6] vinyl sulfone modified carbohydrates could be used

[†] Organic Chemistry Division (Synthesis).
[‡] Division of Biochemical Sciences.
[§] Present address: The Skaggs Institute for Chemical Biology and the Department of Molecular Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037.

(1) Ferrier, R. J. (Senior Reporter). *Carbohydrate Chemistry*; The Royal Society of Chemistry, Cambridge: 1968−1996; Vols. 1−28. (b) Collins, P. M.; Ferrier, R. J. *Monosaccharides: Their Chemistry and Their Roles in Natural Products*; John Wiley & Sons: Chichester, 1996.

(2) Jegou, E.; Cleophax, J.; Leboul, J.; Gero, S. D. *Carbohydr. Res.* **1975**, *45*, 323. (b) Apostolopoulos, C. D.; Couladouros, E. A.; Georgiadis, M, P. *Liebigs Ann. Chem*. **1994**, 781. (c) Couladouros, E. A.; Constantinou-Kokotou, V.; Georgiadis, M. P Kokotos, G. *Carbohydr. Res.* **1994**, *254*, 317.

(3) Nakagawa, T.; Sakakibara, T.; Kumazawa, S. *Tetrahedron Lett.* **1970**, *11*, 1645. (b) Rajabalee, F. J−M. *Carbohydr. Res.* **1973**, *26*, 219. (c) Sakakibara, T.; Sudoh, R. *Carbohydr. Res.* **1976**, *50*, 191. (d) Sakakibara, T.; Sudoh, R. *J. Org. Chem.* **1977**, *42*, 1746. (e) Sudoh, R. *Tetrahedron* **1984**, *40*, 1533. (f) Sakakibara, T.; Ohkita, N.; Nakagawa, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 446.

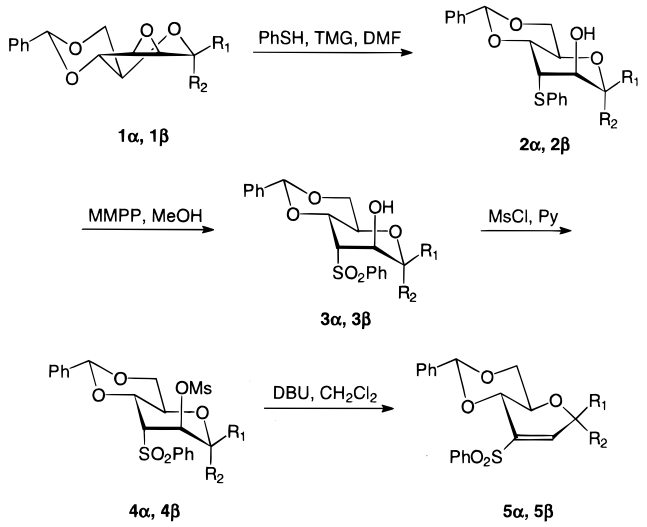
(4) Baer, H. H.; Neilson, T. *J. Org. Chem.* **1967**, *32*, 1068. (b) Lichtenthaler, F. W.; Vors, P.; Mayer, N. *Angew. Chem., Int. Ed.* **1969**, *8*, 211.

(5) Bera, S.; Sakthivel, K.; Langley, G. J.; Pathak, T. *Tetrahedron* **1995**, *51*, 7857. (b) Bera, S.; Langley, G. J.; Pathak, T. *J. Org. Chem.* **1998**, *63*, 1754.

(6) Schank, K. In *The Chemistry of Sulphones & Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: New York, 1988. (b) Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993.

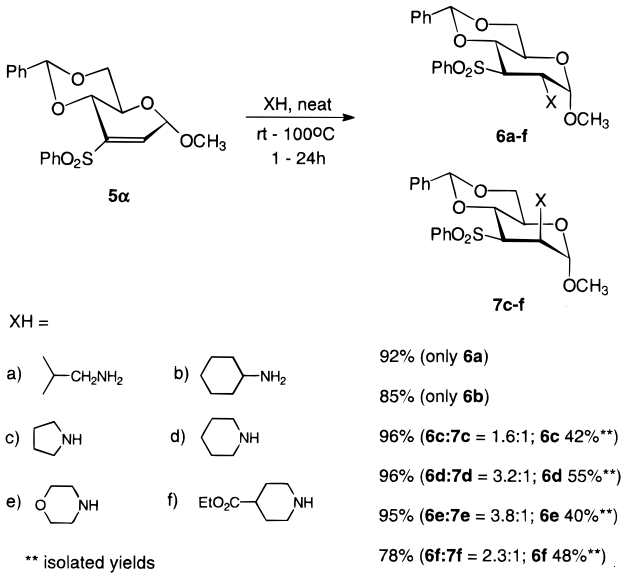
10.1021/jo991380d CCC: $19.00
Published on Web 03/30/2000

Scheme 1

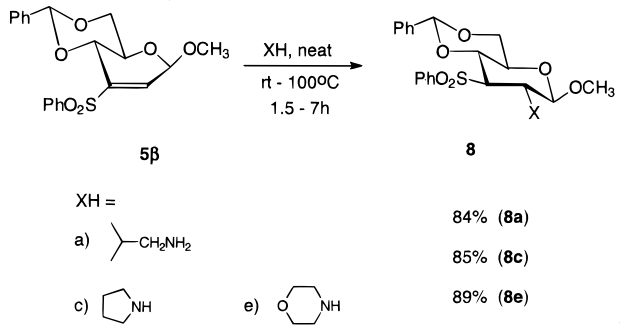


α: R_1 = H, R_2 = OCH_3 overall yield of **5α** from **1α** 88%
β: R_1 = OCH_3, R_2 = H overall yield of **5β** from **1β** 75%

Scheme 2



Scheme 3



extensively as versatile synthons. (c) After using the vinyl sulfone moiety as a tool for functionalization, whenever necessary, the sulfone group could be removed oxidatively[6b,7] or reductively[6b,8] with ease to regenerate a hydroxyl group or methylene group, respectively, on the carbon carrying the sulfone group. (d) Sulfur dioxide extrusion reactions[6] could be applied to cyclic and acyclic derivatives to access further modified monosaccharides. Thus, a more thorough study of the synthetic application of the Michael addition to vinyl sulfones derived from carbohydrates is highly desirable. To initiate a systematic study on the reaction patterns of endocyclic monovinyl sulfones derived from carbohydrates,[9] the easily accessible anomers methyl 2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-*erythro*-hex-2-enopyranoside (**5α**) and methyl 2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-*β*-D-*erythro*-hex-2-enopyranoside (**5*β***) were selected as the first set of candidates.

Compounds **5α** and **5*β*** were, therefore, synthesized in high yields from the known epoxides **1α** and **1*β***, respectively (Scheme 1). Epoxide **1α**[10] was reacted with thiophenol in the presence of 1,1,3,3-tetramethylguanidine (TMG) to afford **2α**. The corresponding sulfone derivative **3α** was generated in quantitative yield by oxidizing **1α** with magnesium monoperoxypthalate (MMPP). Compound **3α** was mesylated at 0 °C using methanesulfonyl chloride (MsCl) in pyridine. The crude mesylated product **4α** was subjected to an elimination reaction with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in dichloromethane to produce **5α** in 88% overall yield (four steps from **1α**). Similarly, thiophenol in the presence of TMG opened epoxide **1*β***[11] at the 3-position to generate **2*β***. Oxidation of **2*β***, followed by mesylation and DBU treatment, generated the desired compound **5*β*** in 75% overall yield (four steps from **1*β***).

The α-vinyl sulfone derivative **5α** was reacted with various primary and secondary amines. Reaction conditions and yields are summarized in Scheme 2. Primary amines, such as isobutylamine and cyclohexylamine, were found to add diastereoselectively to produce single isomers **6a** and **6b**, respectively. The secondary amines, pyrrolidine, piperdine, morpholine, and ethyl isonipecotate, on the other hand, generated a mixture of C-2 isomers having **6c**, **6d**, **6e**, and **6f** as the major isomers, respectively. The ratios of the isomers were determined on the crude mixture (^{1}H NMR) to avoid loss of any of the isomers during column purification. The major gluco-isomers, **6c**−**f**, were separated by crystallization. The minor manno- isomer **7c** was isolated to unambiguously establish its structure.

Similarly, the anomeric *β*-vinyl derivative **5*β*** was treated with isobutylamine, pyrrolidine, and morpholine. These primary and secondary amines were found to add diastereoselectively to produce single isomers **8a**, **8c**, and **8e**, respectively (Scheme 3).

The ^{1}H NMR data of the Michael adducts are consistent with the assigned structures. The $J_{1,2}$ values (3.1−3.6 Hz) of compounds **6a**−**f** are comparable to those of methyl 2-*N*-alkylamino-2,3-dideoxy-3-nitro-4,6-*O*-(phen-

(7) Little, R. D.; Myong, S. O. *Tetraheron Lett.* **1980**, *21*, 3339. (b) Mujica, M. T.; Afonso, M. M.; Galindo, A.; Palenzuela, J. A. *J. Org. Chem.* **1998**, *63*, 9728.

(8) Brow, A. C.; Carpino, A. L. *J. Org. Chem.* **1985**, *50*, 1749.

(9) Cassidy, J. F.; Williams, J. M. *Tetrahedron Lett.* **1986**, *27*, 4355. (b) Sakakibara, T.; Takaki, I.; Tachimori, Y.; Yamamoto, A.; Ishido, Y.; Sudoh, R. *Carbohydr. Res.* **1987**, *160*, C3. (c) Wu, J.-C.; Pathak, T.; Tong, W.; Vial, J. M.; Remaud, G.; Chattopadhyaya, J. *Tetrehedron* **1988**, *44*, 6705. (d) Takai, I.; Yamamoto, A.; Ishido, Y.; Sakakibara, T.; Yagi, E. *Carbohydr. Res.* **1991**, *220*, 195. (e) Marot, C.; Rollin, P. *Phosphorus, Sulfur Silicon Relat. Elem.* **1994**, *95*−*96*, 503.

(10) Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203.

(11) Kim, K. S.; Vyas, D. M.; Szarek, W. A. *Carbohydr. Res.* **1979**, 72, 25.

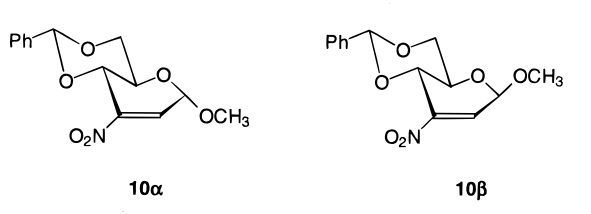


Figure 1.

ylmethylene)-α-D-glucopyranosides (2.9−3.7 Hz).[3b] For the minor isomer **7c**, H-1 appeared as a singlet, which is consistent with the very small $J_{1,2}$ values (equatorial H-1−equatorial H-2 arrangement) reported for methyl 2-azido-2,3-dideoxy-3-nitro-4,6-*O*-(phenylmethylene)-α-D-mannopyranoside (1 Hz) and the corresponding 2-cyano-α-mannopyranoside (1.3 Hz).[3c] In case of **8a**, **8c**, and **8e**, H-1 signals appeared as doublets with large coupling constant ($J_{1,2}$) values of 4.6−6.8 Hz, which are in line with the large values reported for methyl 2-*N*-alkylamino-2,3-dideoxy-3-nitro-4,6-*O*-(phenylmethylene)-*β*-D-glucopyranosides (7.7−8.5 Hz).[3b]

It has been reported that the addition of *p*-toluenethiol to 1-*p*-tolylsulfonylcyclohexene produced *cis*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane and *not* the thermodynamically more stable trans product. It was established that, because an arylsulfonyl group had a much larger steric requirement than an arylmercapto group, the former should tend to occupy an equatorial position.[12] The stereochemistry of nucleophilic addition reactions to more complicated systems such as 3-nitro-hex-2-enopyranosides **10α** and **10*β*** (Figure 1),[3] however, has been discussed in terms of electrostatic interactions,[3d] stereoelectronic control,[3d] steric hindrance,[3d] $A^{(1,3)}$ strain,[3e] and also hydrogen bonding.[3e] A generalization that the axial attack predominates over equatorial attack for **10α** and the converse is true for **10*β*** has been arrived at on the basis of reactions of **10α** and **10*β*** with several nucleophiles.[3d] Interestingly, one of the earliest works in this area contradicted this generalization by reporting that, irrespective of the anomeric configuration of the Michael acceptor and steric bulk/nucleophilicity of the incoming nucleophiles, addition of amines to **10α** and **10*β*** produced thermodynamically more stable C-2 equatorial products.[3b] Sterically demanding purine bases, however, added to **10α** and **10*β*** from the β[3c] and α[3a] sides, respectively. 2,3-Dideoxy-hex-2-en-4-ulopyranosides, on the other hand, always produced epimeric mixture at C-2.[2]

In light of the above observations, it can be stated that the stereochemical course of addition of amines to **5** does not fully obey any of the precedence. Structural analysis by ^{1}H NMR spectroscopy showed that in a partially rigid bicyclic system of **5** the sterically bulky phenylsulfonyl group will always occupy the equatorial position. In case of **5α**, primary amines always attacked the C-2 center from the equatorial direction to produce thermodynamically more stable diequatorial products. Interestingly, however, sterically bulky secondary amines on reaction with **5α** produced a mixture of products, epimeric at C-2, in comparison with the work of Rajabalee and coworkers[3b] that produced only C-2 equatorial products with both **10α** and **10*β***. To explain the formation of a mixture of products **6c−f** and **7c−f**, one has to bear in mind the established rules that (a) secondary amines carrying nonbonded electron pairs would face electrostatic repulsion by C_1-O_1 and C_1-O_5 bonds[3d] and (b) thermodynamically more stable diequatorial products should predominate.[3d] Nevertheless to explain the formation of manno- isomers (such as **7c**), it is necessary to assume the existence of a stereoelectronic factor responsible for repelling the incoming secondary amines from equatorial direction, although the exact nature of the hindrance cannot be rationalized at this point.

Compound **5*β***, on the other hand, on reaction with both primary and bulky secondary amines produced thermodynamically more stable diequatorial products. In this case, it is difficult to establish conclusively whether the electrostatic repulsion between attacking amines, C_1-O_1 and C_1-O_5 bonds directed the nucleophiles to attack the C-2 position of **5*β*** from the equatorial direction, resulting in the formation of single isomers **8**. This observation, nevertheless, falls more in line with the generalized rule that in the case of an *β*-anomeric substrate, a nucleophile should approach the C-2 site preferably from the equatorial direction.[3d]

Conclusion

We have established that vinyl sulfone modified carbohydrates are very useful intermediates for the synthesis of several new deoxyaminosugars. The present study acquires greater importance in view of the significant role of C−N equatorial bonds in carbohydrates. Thus, naturally occurring aminosugars, such as D-glucosamine,[1b] D-galactosamine,[1b] D-lividosamine,[1b,13] etc, which are vital components of biologically important macromolecules, have their C−N bonds at C-2 in equatorial configurations. *N*-Alkyl- and *N*,*N*-dialkyl-D-glucosamine derivatives, for example, have been synthesized in the past by *N*-alkylation or *N*,*N*-dialkylation of glucosamine in a linear fashion.[14] The other most commonly used methods for the synthesis of aminosugars involved the opening of epoxides **1α** or **1*β*** by amines which always produced the C-3 deoxy C-3 aminosugars and not the C-2 deoxy C-2 aminosugars.[15] Reactions of primary and secondary amines with methyl 2,3-anhydro-4,6-*O*-(phenylmethylene)-D-allopyranoside, on the other hand, produced exclusively the C-2 deoxy C-2 amino products with the C−N bond in an axial configuration.[16] Syntheses of compounds **6** and **8** from **5α** and **5*β*** respectively, therefore, constitute one of the few examples of the introduction of *N*-monoalkylated and *N*,*N*-dialkylated amines to the C-2 carbon of pyranoses in equatorial configurations. Carbon nucleophiles also add to **5α** and **5*β*** with equal ease but with a different pattern of diastereoselectivity, leading to the synthesis of novel branched sugars; this subject will be dealt with separately in a forthcoming publication.[17] Application of this methodology to various other pyranose and furanose sugars is also currently in progress.[18]

(12) Truce, W. E.; Levy, A. J. *J. Am. Chem. Soc.* **1961**, *83*, 4641.

(13) Mori, T.; Ichyanasi, T.; Kondo, H.; Tokkunasa, T.; Oda, T.; Munakata, T. *J. Antibiot. Ser. A* **1971**, *24*, 339.

(14) Takeda, R.; Ryu, S. Y.; Park, J. H.; Nakanishi, K. *Tetrahedron*, **1990**, *46*, 5533. (b) Vega-Perez, J. M.; Espartero, J. L.; Alkudia, F. *J. Carbohydr. Chem.* **1993**, *12*, 477.

(15) Willams, N. R. *Adv. Carbohydr. Chem. Biochem.* **1970**, *25*, 109.

(16) Vega-Perez, J. M.; Candela, J. I.; Vega, M.; Iglesias-Guerra, F. *Carbohydr., Res.* **1995**, *279*, C5.

(17) Sanki, A.; Pathak, T., unpublished results.

(18) Compounds **6** and **8** undergo desulfonation reactions to generate derivatives and analogues of D-lividosamine (2-amino-2,3-dideoxy-D-glucose). This topic will be discussed separately in a forthcoming publication.

Experimental Section

General Methods. Melting points were determined in open-end capillary tubes and are uncorrected. All chemicals were obtained from commercial suppliers and are used without purification. TLC was carried out on precoated plates (Merck silica gel 60, f_{254}), and the spots were visualized with UV light. Column chromatography was performed on silica gel (silica gel 60, 230−400 mesh). ^{1}H NMR spectra were recorded at 200 and 300 MHz in $CDCl_3$ using the residual $CHCl_3$ as standard, and ^{13}C NMR were recorded at 50.3 and 75 MHz in $CDCl_3$ using the triplet centered at δ 77.0 as the standard. Optical rotation was recorded at 589 nm.

Methyl 2,3-Dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-*erythro*-hex-2-enopyranoside (5α). To a solution of **1α** (3.20 g, 12.12 mmol) in DMF (15 mL) were added thiophenol (6.24 mL, 60.6 mmol) and TMG (4.56 g, 36.36 mmol). The reaction mixture was heated for 3 h at 80−90 °C, poured into saturated aqueous NaCl (80 mL), and extracted with EtOAc (3 × 30 mL). The EtOAc layer was washed with saturated aqueous $NaHCO_3$ (2 × 15 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The resulting syrup was purified over silica gel to yield **2α** (4.26 g, 94%). To a solution of **2α** (4.26 g, 11.4 mmol) in methanol (25−30 mL) was added MMPP (16.88 g, 34.17 mmol). The reaction mixture was stirred for 2.5 h at ambient temperature and filtered, and the filtrate was evaporated under reduced pressure. The resulting residue was neutralized with saturated aqueous $NaHCO_3$ (70 mL), extracted with EtOAc (3 × 30 mL), washed with water (3 × 15 mL), dried over anhydrous Na_2SO_4, and concentrated to dryness under reduced pressure to yield **3α** quantitatively. To a solution of **3α** in anhydrous pyridine (25 mL) was added methanesulfonyl chloride (2.82 mL, 36.45 mmol) in anhydrous pyridine (15 mL) at O°C, and the solution was left overnight at 4 °C. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (70 mL) and filtered. The residue was dissolved in dichloromethane (60 mL), and the solution was dried over anhydrous Na_2SO_4. DBU (3.41 mL, 22.78 mmol) was added to the dichloromethane solution of the mesylated product **4α**. After 5 min the solvent was evaporated under reduced pressure, and the resulting residue was purified over silica gel (eluent 40% EtOAc−petroleum ether) to yield a white crystalline solid **5α** (4.12 g, 88%; four steps from epoxide **1α**). Mp: 196−198 °C. $[\alpha]^{28.5}_D$ −54.7° (*c* 1.154, $CHCl_3$). ^{1}H NMR: δ 3.50 (s, 3H), 3.86 (m, 2H), 4.25 (m, 1H), 4.54 (m, 1H), 5.13 (dd, J = 1.2, 2.8 Hz, 1H), 5.55 (s, 1H), 6.99 (m, 1H), 7.11−7.57 (m, 8H), 7.80 (m, 2H). ^{13}C NMR: δ 56.7, 64.1, 69.0 (CH_2), 74.2, 95.8, 102.3, 126.5, 128.2, 128.7, 128.8, 129.3, 133.4, 135.5, 136.7, 140.4, 142.5. Anal. Calcd for $C_{20}H_{20}O_6S$: C, 61.84; H, 5.19; S, 8.25. Found: C, 61.73; H, 5.17; S, 8.21.

Methyl 3-Deoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfide-*β*-D-altropyranoside (2*β*). Compound **2*β*** was synthesized by treating a DMF (10 mL) solution of **1*β*** (2.64 g, 10.07 mmol) with thiophenol (5.18 mL, 50.07 mmol) in the presence of TMG (3.79 mL, 30.22 mmol) for 2.5 h at 80−90 °C. After the usual workup (vide compound **2α**), the syrup was purified over silica gel (eluent 50% EtOAc−petroleum ether) to yield a white solid **2*β*** (3.16 g, 84%). Mp: 142−143 °C. ^{1}H NMR: δ 3.54 (s, 3H), 3.82 (t, J = 11.2 Hz, 1H), 4.00 (m, 3H), 4.34 (m, 2H), 4.29 (s, 1H), 5.59 (s, 1H), 7.19−7.52 (m, 10H). ^{13}C NMR: δ 50.9, 56.9, 65.3, 69.0 (CH_2), 71.5, 75.2, 98.9, 101.8, 126.3, 127.1, 128.1, 128.9, 129.0, 131.4, 134.7, 137.4. Anal. Calcd for $C_{20}H_{22}O_5S$: C, 64.15; H, 5.92; S, 8.56. Found: C, 64.14; H, 5.92; S, 8.77.

Methyl 3-Deoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-*β*-D-altropyranoside (3*β*). Compound **2*β*** (3.16 g, 8.44 mmol) was oxidized with MMPP (12.15 g, 25.33 mmol) in methanol (20−25 mL) for 2.5 h at ambient temperature. After the usual workup, the residue was purified over silica gel (eluent 55% EtOAc−petroleum ether) to yield a white solid **3*β*** quantitatively. Mp: 156−157 °C. ^{1}H NMR: δ 3.60 (s, 3H), 3.67 (t, J = 10.2 Hz, 1H), 4.02 (dd, J = 2.6, 5.8 Hz, 1H), 4.23−4.43 (m, 2H), 4.63 (m, 1H), 4.84 (m, 1H), 5.10 (d, J = 1.4 Hz, 1H), 5.31 (s, 1H), 7.03−7.49 (m, 8H,), 7.83 (m, 2H). ^{13}C NMR: δ 56.5, 63.3, 64.8, 66.4, 69.1(CH_2), 74.3, 99.2, 101.7, 125.8, 127.4, 128.1, 128.4, 132.8, 136.3, 140.5. Anal. Calcd for $C_{20}H_{22}O_7S$: C, 59.09; H, 5.45. Found: C, 58.96; H, 5.35.

Methyl 2,3-Dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-*β*-D-*erythro*-hex-2-enopyranoside (5*β*). Compound **3*β*** (3.42 g, 8.44 mmol) in anhydrous pyridine (15 mL) was reacted with methanesulfonyl chloride (2.09 mL, 27.02 mmol) at 4 °C overnight. After the usual workup, crude mesylated product **4*β*** in dichloromethane (70 mL) was treated with DBU (2.52 mL, 16.88 mmol) for 5 min. Solvent was evaporated under reduced pressure, and the resulting residue was purified over silica gel (eluent 50% EtOAc−petroleum ether) to yield a white fluffy solid **5*β*** (7.55 g, 75%; four steps from **1*β***). Mp: highly hygroscopic. $[\alpha]^{25}_D$ −8.9° (*c* 0.333, $CHCl_3$). ^{1}H NMR: δ 3.53 (s, 3H), 3.73 (m, 1H), 3.89 (t, J = 11.3 Hz, 1H), 4.28 (dd, J = 4.3, 10.2 Hz, 1H), 4.61 (m, 1H), 5.44 (m, 1H), 5.55 (s, 1H), 6.94 (m, 1H), 7.19−7.60 (m, 8H), 7.82 (m, 2H). ^{13}C NMR: δ 55.1, 68.0 (CH_2), 69.3, 73.2, 98.3, 101.5, 125.8, 127.5, 128.2, 128.6, 132.9, 136.2, 136.8, 139.8, 142.5.

General Procedure for the Synthesis of 6a−f, 8a, 8c, and 8e. Solutions of **5α** or **5*β*** in neat amines (2−3 mL/mmol) were heated separately for 1−24 h at various temperatures. Amines were evaporated under reduced pressure. The resulting residues were dissolved in EtOAc and washed with water. EtOAc solutions were dried over anhydrous Na_2SO_4 and filtered, and the filtrates were evaporated under reduced pressure. The residue was purified over silica gel. For secondary amines, major isomers were crystallized out from mixtures of isomers. Analytical samples were prepared from methanol.

Methyl 2,3-Dideoxy-2-*N*-isobutylamino-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-glucopyranoside (6a). A solution of **5α** (0.79 g, 2.04 mmol) was heated in neat isobutylamine (3 mL) for 1 h at 50−55 °C and converted (eluent 60% EtOAc−petroleum ether) to a white solid **6a** (0.84 g, 90%). Mp: 149−150 °C. $[\alpha]^{24}_D$ +38.3° (*c* 0.405, $CHCl_3$). ^{1}H NMR: δ 0.94 (m, 6H), 1.74 (m, 1H), 2.48 (m, 2H), 3.42 (s, 3H), 3.48 (dd, J = 3.5, 10.3 Hz, 1H), 3.67−4.00 (m, 4H), 4.21 (dd, J = 3.4, 9.3 Hz, 1H), 4.83 (d, J = 3.5 Hz, 1H), 5.33 (s, 1H), 7.05 (m, 2H), 7.16−7.39 (m, 6H), 7.79 (m, 2H). ^{13}C NMR: δ 20.7, 20.8, 28.6, 55.5, 55.6 (CH_2), 57.3, 62.4, 65.0, 69.4 (CH_2), 76.5, 98.2, 101.8, 126.3, 128.0, 128.2, 128.6, 129.1, 133.1, 136.6, 142.0. MS EI *m*/*z* (%) 461 (M^+, 4), 430 ($M^+ - OCH_3$, 5), 418 ($M^+ - CH(CH_3)_2$, 100), 320 ($M^+ - SO_2Ph$, 35). Anal. Calcd for $C_{24}H_{31}NO_6S$: C, 62.45; H, 6.77; N, 3.03. Found: C, 62.43; H, 7.17; N, 3.15.

Methyl 2-*N*-Cyclohexylamino-2,3-dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-glucopyranoside (6b). A solution of **5α** (0.44 g, 1.13 mmol) in neat cylcohexylamine (3 mL) was heated for 3.5 h at 80−90 °C and converted (eluent 65% EtOAc−petroleum ether) to a white solid **6b** (0.47 g, 85%). Mp: 152−153 °C. $[\alpha]^{28.5}_D$ +30.4° (*c* 0.412, $CHCl_3$). ^{1}H NMR: δ 1.10−2.05 (m, 10H), 2.56 (m, 1H), 3.43 (s, 3H), 3.47−3.98 (m, 5H), 4.21 (dd, J = 3.3, 9.2 Hz, 1H), 4.47 (d, J = 3.3 Hz, 1H), 5.29 (s, 1H), 7.04 (m, 2H), 7.15−7.36 (m, 6H), 7.78 (m, 2H). ^{13}C NMR: δ 24.8 (CH_2), 24.9 (CH_2), 25.9 (CH_2), 32.6 (CH_2), 34.9 (CH_2), 54.7, 55.2, 62.2, 65.0, 69.1 (CH_2), 76.2, 98.8, 101.5, 126.1, 127.7, 127.8, 128.3, 128.8, 132.8, 136.4, 142.1. MS EI *m*/*z* (%) 487 (M^+, 2), 346 ($M^+ - OCH_3$, 40). Anal. Calcd for $C_{26}H_{33}NO_6S$: C, 64.04; H, 6.82; N, 2.87; S, 6.58. Found: C, 64.20; H, 7.16; N, 2.95; S, 6.97.

Methyl 2,3-Dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-2-*N*-pyrrolidino-α-D-glucopyranoside (6c). A solution of **5α** (1.01 g, 2.6 mmol) in neat pyrrolidine (4 mL) was stirred for 3 h at ambient temperature and converted to an isomeric mixture of **6c** and **7c** (1.42 g, 96%) in a ratio 1.6:1 (^{1}H NMR). **Compound 6c** (yellow solid, 0.5 g, 42%). Mp: 132−133 °C. $[\alpha]^{28.5}_D$ +91.1° (*c* 1.318, $CHCl_3$). ^{1}H NMR: δ 1.40−1.62 (m, 4H), 2.64 (m, 2H), 2.90 (m, 2H), 3.37 (s, 3H), 3.57−4.12 (m, 5H), 4.24 (dd, J = 3.4, 9.4 Hz, 1H), 4.84 (d, J = 3.2 Hz, 1H), 5.36 (s, 1H), 7.25−7.48 (m, 8H), 7.84 (m, 2H). ^{13}C NMR: δ 24.0 (CH_2), 47.7 (CH_2), 54.5, 57.8, 62.5, 69.4 (CH_2), 76.3, 98.7, 101.3, 126.1, 127.8, 128.2, 128.7, 132.5, 136.7, 142.2. MS EI *m*/*z* (%) 459 (M^+, 100), 428 ($M^+ - OCH_3$, 30), 318 ($M^+ - SO_2Ph$, 85). Anal. Calcd for $C_{24}H_{29}NO_6S$: C, 62.72; H, 6.36; N, 3.05. Found: C, 62.45; H, 6.52; N, 3.16.

Methyl 2,3-Dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-2-*N*-pyrrolidino-α-D-mannopyranoside (7c) (yellow solid, 0.5 g, 42%). Mp: 160−161 °C. **[α]**$^{28.5}_{D}$ +38.1° (*c* 0.126, CH_2Cl_2). ^{1}H NMR: *δ* 1.75−1.88 (m, 4H), 2.73 (m, 4H), 3.43 (m, 3H), 3.66 (t, *J* = 11.0 Hz, 1H), 3.84 (m, 2H), 4.30 (m, 2H), 4.75 (m, 1H), 4.85 (s, 1H), 5.40 (s, 1H), 7.18−7.47 (m, 8H), 7.79 (m, 2H). ^{13}C NMR: *δ* 23.6 (CH_2), 51.5 (CH_2), 54.5, 58.2, 61.1, 62.0, 69.7 (CH_2), 75.7, 98.9, 102.5, 126.6, 128.1, 128.3, 129.1, 129.2, 132.7, 137.1, 142.9. Anal. Calcd for $C_{24}H_{29}NO_6S$: C, 62.72; H, 6.36; N, 3.05; S, 6.63. Found: C, 62.27; H, 6.63; N, 3.06.

Methyl 2,3-Dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-2-*N*-piperidino-α-D-glucopyranoside (6d). A solution of **5α** (0.776 g, 2.0 mmol) in neat piperdine (3 mL) was heated for 9 h at 90−100 °C and converted to an isomeric mixture of **6d** and **7d** (0.90 g, 96%) in a ratio of 3.2:1 (^{1}H NMR). **Compound 6d** (pale yellow solid, 0.52 g, 55%). Mp: 120−121 °C (decomp). **[α]**$^{28.5}_{D}$ +80.5° (*c* 0.546, $CHCl_3$). ^{1}H NMR: *δ* 1.20−1.55 (m, 6H), 2.67 (m, 4H), 3.30 (dd, *J* = 3.1,11.5 Hz, 1H), 3.35 (s, 3H), 3.45−4.07 (m, 4H), 4.17 (dd, *J* = 3.1, 9.8 Hz, 1H), 4.80 (d, *J* = 3.1 Hz, 1H), 5.17 (s, 1H), 7.10−7.43 (m, 8H), 7.85 (m, 2H). ^{13}C NMR: *δ* 24.8 (CH_2), 26.2 (CH_2), 51.0 (CH_2), 54.6, 61.9, 62.8, 63.9, 69.5 (CH_2), 76.7, 98.2, 101.6, 126.3, 127.9, 128.2, 128.5, 128.9, 132.8, 136.7, 142.2. MS EI *m*/*z* (%) 473 (M^+, 40), 442 ($M^+ - OCH_3$, 15), 332 ($M^+ - SO_2Ph$, 80). Anal. Calcd for $C_{25}H_{31}NO_6S$: C, 63.40; H, 6.60; N, 2.96. Found: C, 63.28; H, 6.71; N, 2.99.

Methyl 2,3-Dideoxy-2-*N*-morpholino-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-glucopyranoside (6e). A solution of **5α** (0.39 g, 1.0 mmol) in neat morpholine (2 mL) was heated for 24 h at 80−90 °C and converted to an isomeric mixture of **6e** and **7e** (0.45 g, 95%) in a ratio of 3.8:1 (^{1}H NMR). **Compound 6e** (yellow solid, 0.19 g, 40%). Mp: 228 °C (decomp). **[α]**$^{28.5}_{D}$ +66.8° (*c* 0.435, $CHCl_3$). ^{1}H NMR: *δ* 2.84 (m, 4H), 3.42 (s, 3H), 3.85 (m, 8H), 4.06 (m, 1H), 4.19 (dd, *J* = 3.2, 9.7 Hz, 1H), 4.89 (d, *J* = 3.1 Hz, 1H), 5.12 (s, 1H), 7.05 (m, 2H), 7.20−7.32 (m, 6H), 7.85 (m, 2H). ^{13}C NMR: *δ* 49.8 (CH_2), 54.4, 61.4, 62.5, 63.0, 67.1 (CH_2), 69.1 (CH_2), 76.3, 97.7, 101.5, 126.0, 127.6, 127.9, 128.3, 128.7, 132.7, 136.3, 141.9. MS EI *m*/*z* (%) 475 (M^+, 32), 444 ($M^+ - OCH_3$, 15), 334 ($M^+ - SO_2Ph$, 100). Anal. Calcd for $C_{24}H_{29}NO_7S$: C, 60.61; H, 6.15; N, 2.94. Found: C, 60.19; H, 5.94; N, 2.90.

Methyl 2,3-Dideoxy-2-*N*-ethylisonipecotate-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-α-D-glucopyranoside (6f). A solution of **5α** (0.67 g, 1.72 mmol) in neat ethylisonipecotate (3 mL) was heated at 90−100 °C for 10 h and converted (eluent 65% EtOAc−petroleum ether) to an isomeric mixture of **6f** and **7f** (0.73 g, 78%) in a ratio of 2.3:1 (^{1}H NMR). **Compound 6f** (white solid, 0.45 g, 48%). Mp: 195 °C (decomp). **[α]**$^{28.5}_{D}$ +64.4° (*c* 0.445, $CHCl_3$). ^{1}H NMR: *δ* 1.25 (m, 3H), 1.75 (m, 4H), 2.21 (m, 1H), 2.75 (m, 2H), 2.94 (m, 2H), 3.38 (s, 3H), 3.43−3.46 (m, 1H), 3.70−3.94 (m, 3H), 4.13 (m, 4H), 4.81 (d, *J* = 3.1 Hz, 1H), 5.20 (s, 1H), 7.11−7.34 (m, 8H), 7.84 (m, 2H). ^{13}C NMR: *δ* 14.3, 28.4 (CH_2), 28.5 (CH_2), 41.4, 48.1 (CH_2), 50.2 (CH_2), 54.6, 60.1 (CH_2), 61.8, 62.6, 63.3, 69.3 (CH_2), 76.5, 98.3, 101.5, 126.2, 127.8, 128.1, 128.5, 128.9, 132.8, 136.6, 142.0, 175.1. MS EI *m*/*z* (%) 545 (M^+, 3), 404 ($M^+ - SO_2Ph$, 60). Anal. Calcd for $C_{28}H_{35}NO_8S$: C, 61.63; H, 6.46; N, 2.57. Found: C, 61.10; H, 6.80; N, 2.59.

Methyl 2,3-Dideoxy-2-*N*-isobutylamino-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl *β*-D-glucopyranoside (8a). A solution of **5*β*** (0.35 g, 0.902 mmol) in neat isobutylamine (3 mL) was heated at 60−65 °C for 3 h and converted (eluent 60% EtOAc−petroleum ether) to a white solid **8a** (0.76 g, 84%). Mp: 156−157 °C. **[α]**$^{26.5}_{D}$ −70.7° (*c* 0.512, $CHCl_3$). ^{1}H NMR: *δ* 0.97 (m, 6H), 1.73 (m, 1H), 2.61 (m, 1H), 2.74 (m, 1H), 3.55 (s, 3H), 3.29−3.77 (m, 4H), 3.97 (t, *J* = 9.7 Hz, 1H), 4.27 (dd, *J* = 4.8, 10.6 Hz, 1H), 4.44 (d, *J* = 6.6 Hz, 1H), 5.29 (s, 1H), 7.02 (m, 2H), 7.20−7.45 (m, 6H), 7.81 (m, 2H). ^{13}C NMR: *δ* 20.6, 20.8, 28.9, 56.1 (CH_2), 56.8, 57.5, 66.6, 66.9, 69.0 (CH_2), 75.7, 101.3, 105.7, 126.0, 127.8, 128.3, 128.7, 129.0, 133.3, 136.3, 140.6. MS EI *m*/*z* (%) 461 (M^+, 4), 418 ($M^+ - CH(CH_3)_2$, 100). Anal. Calcd for $C_{24}H_{31}NO_6S$: C, 62.45; H, 6.77; N, 3.03. Found: C, 62.68; H, 7.26; N, 3.07.

Methyl 2,3-Dideoxy-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-2-*N*-pyrrolidino-*β*-D-glucopyranoside (8c). A solution of **5*β*** (0.63 g, 1.62 mmol) in neat pyrrolidine (3 mL) was stirred for 1.5 h at ambient temperature and converted (eluent 55% EtOAc−petroleum ether) to a yellow solid **8c** (0.64 g, 86%). Mp: 136−138 °C. **[α]**$^{24}_{D}$ −27.8 (*c* 0.739, $CHCl_3$). ^{1}H NMR: *δ* 1.56 (m, 4H), 2.65 (m, 4H), 3.41 (s, 3H), 3.56−4.31 (m, 4H), 4.30 (m, 1H), 4.44 (m, 1H), 4.67 (d, *J* = 4.6 Hz, 1H), 5.49 (s, 1H), 7.28−7.40 (m, 8H), 7.84 (m, 2H). ^{13}C NMR: *δ* 23.1 (CH_2), 48.8 (CH_2), 55.3, 59.7, 65.1, 66.6, 69.3 (CH_2), 74.9, 100.7, 100.8, 125.7, 127.7, 128.3, 128.5, 132.6, 136.6, 141.5. MS EI *m*/*z* (%) 459 (M^+, 20), 318 ($M^+ - SO_2Ph$, 80). Anal. Calcd for $C_{24}H_{29}NO_6S$: C, 62.72; H, 6.36; N, 3.05. Found: C, 62.17; H, 6.39; N, 3.02.

Methyl 2,3-Dideoxy-2-*N*-morpholino-4,6-*O*-(phenylmethylene)-3-*C*-phenylsulfonyl-*β*-D-glucopyranoside (8e). A solution of **5*β*** (0.40 g, 1.03 mmol) in neat morpholine (3 mL) was heated for 2 h at 90−100 °C and converted (eluent 65% EtOAc−petroleum ether) to a yellow solid **8e** (0.49 g, 90%). Mp: 179 °C (decomp). **[α]**$^{28.5}_{D}$ −8.4° (*c* 1.042, $CHCl_3$). ^{1}H NMR: *δ* 2.69 (m, 2H), 2.84 (m, 2H), 3.51 (s, 3H), 3.30−3.85 (m, 8H), 4.15 (t, *J* = 9.5 Hz, 1H), 4.34 (dd, *J* = 4.8, 10.9 Hz, 1H), 4.61 (d, *J* = 6.8 Hz, 1H), 5.38 (s, 1H), 7.27−7.45 (m, 8H), 7.89 (m, 2H). ^{13}C NMR: *δ* 49.7 (CH_2), 56.1, 63.8, 65.2, 66.9 (CH_2), 67.8, 69.2 (CH_2), 75.2, 101.3, 102.0, 126.1, 128.1, 128.2, 128.8, 129.0, 133.2, 136.8, 142.1. MS EI *m*/*z* (%) 444 ($M^+ - OCH_3$, 4), 334 ($M^+ - SO_2Ph$, 100). Anal. Calcd for $C_{24}H_{29}NO_7S$: C, 60.61; H, 6.15; N, 2.94. Found: C, 60.51; H, 6.97; N, 2.98.

Acknowledgment. B.R and K.S thank the Council for Scientific and Industrial Research, New Delhi for fellowships. Financial support from the Department of Science and Technology, New Delhi is gratefully acknowledged.

JO991380D