C, 74.35; H, 7.49. Found: C, 74.19; H, 7.68.

Acknowledgment. We gratefully acknowledge financial support from the National Institute of General Medical Sciences (Grant GM36336) and the National Science Foundation (Grant CHE-8800654). This project is in part funded by Wesley Foundation, Wichita, KS (Grant 8802041). We are indebted to Mr. Ken Walsh, Coal Research Center, Southern Illinois University of Carbondale, for obtaining mass spectra.

Registry No. 1, 122949-09-1; *cis*-1, 111532-83-3; 2, 122949-10-4; 3, 122949-11-5; 4, 122949-12-6; 5, 122949-13-7; 6, 122949-14-8; 7, 122949-15-9; 8, 122949-16-0; 9, 122949-17-1; 10, 122949-18-2; 11, 122949-19-3; 12, 122949-20-6; 13, 122949-21-7; 14, 122949-22-8; 15 (isomer 1), 122967-58-2; 15 (isomer 2), 122949-23-9; CH_2=C-H$(CH_2)_2$MgBr, 7103-09-5; [2-(1,3-dioxolan-2-yl)ethyl]magnesium bromide, 122949-24-0.

On the Mechanism of the Oxidation of Tosylhydrazines by *N*-Iodosuccinimide

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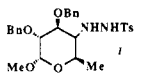
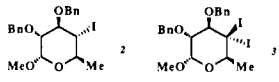
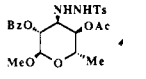
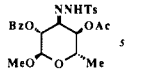
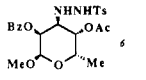
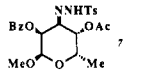
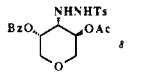
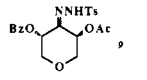
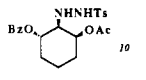
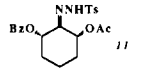
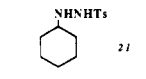
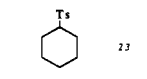
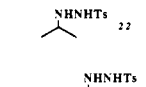
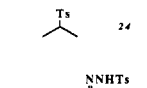
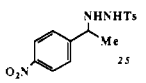
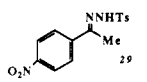
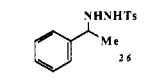
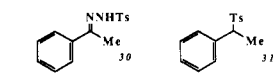
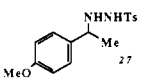
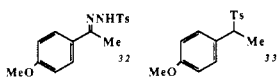
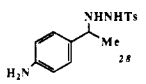
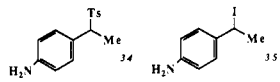
As part of our continuing efforts to study the mechanism of deoxy sugar biosynthesis at the enzymatic level,[1] it has been necessary for us to develop a general strategy for the synthesis of stereospecifically labeled deoxy sugars.[2] Reviewing the literature, we have found that hydrazines can be oxidized to the corresponding halides with defined stereochemistry by a variety of haloreagents, such as iodine, bromine, *N*-iodosuccinimide, *N*-bromosuccinimide, iodine monochloride, etc.[3] Since sugar hydrazines are readily available from the corresponding hydrazones by reduction with boron reducing agents[4] or from precursors bearing suitable leaving groups by direct nucleophilic displacement with hydrazine, a sequence involving halogen oxidation of the sugar hydrazine followed by hydride reduction of the nascent halide seems to be a compelling approach.[5] Although the key step, halogen oxidation, of this proposed sequence is an intriguing reaction, little is known about its mechanism. It has been suggested that the reaction course may involve a tautomerization step interconverting a diimide intermediate to the corresponding hydrazone.[3a,6] However, the putative hydrazone species has never been isolated, and thus, the mechanistic details of this reaction are still uncertain. In an attempt to clarify the mechanistic ambiguity of this oxidation and to test the feasibility of the proposed sequence for the preparation of stereospecifically labeled deoxy sugar molecules, we have carried out the halogen oxidation on a series of sugar tosylhydrazines. To our surprise, the major product formed in most of these experiments was not the desired halide but rather the corresponding tosylhydrazone or tolyl sulfone derivative,[7] depending on the structure of the parent pyranoside. These unexpected results have prompted us to examine tosylhydrazines of other classes to gain further insight into this oxidation. Reported in this paper are the results of these experiments and their mechanistic implications.

The tosylhydrazines used in this study were all derived from their tosylhydrazone precursors by reduction with $NaBH_3CN$ in acidic THF–MeOH solution at 0 °C.[4,8] Initial experiments with a variety of halogen oxidizing agents showed that iodine/triphenylphosphine/imidazole in toluene at 70 °C was ineffective and iodine/*N*-methylmorpholine in chloroform at low temperature was sluggish. The most effective oxidant was found to be

Table I. Oxidation of Tosylhydrazines by *N*-Iodosuccinimide/*N*-Morpholine/$CHCl_3$

reactant	product	yield
		62% (2:3 = 2:3)
		91%
		95%
		96%
		92%
		93%
		50%
		95%
		90% (30:31 = 4:1)
		81% (32:33 = 3:2)
		56% (34:35 = 4:1)

(1) Han, O.; Liu, H. W. *J. Am. Chem. Soc.* **1988**, *110*, 7893.

(2) (a) Han, O.; Liu, H. W. *Tetrahedron Lett.* **1987**, 1073. (b) Weigel, T. M.; Liu, H. W. *Ibid.* **1988**, 4221.

(3) (a) Brown, D. M.; Jones, G. H. *J. Chem. Soc. C* **1967**, 252. (b) Campbell, J. R.; Pross, A.; Sternhell, S. *Aust. J. Chem.* **1971**, *24*, 1425. (c) Friedrich, E. C.; Falling, S. N.; Lyons, D. E. *Synth. Commun.* **1975**, *5*, 33. (d) Doyle, M. P.; Siegfried, B.; Fobare, W. F. *Tetrahedron Lett.* **1977**, 2655. (e) Barton, D. H. R.; Bashiardes, G.; Fourrey, J.-L. *Ibid.* **1983**, 1605. (f) Linholter, S.; Rosenorn, R.; Vincents, L. *Acta Chem. Scand.* **1963**, *17*, 960. (g) Cheronis, N. D.; Ma, T. S. *Organic Functional Group Analysis*; Wiley-Interscience: New York, 1964; p 289. (h) Wohl, A.; Oesterlin, C. *Chem. Ber.* **1900**, *33*, 2736.

(4) (a) Han, O.; Shih, Y.; Liu, L.-d.; Liu, H. W. *J. Org. Chem.* **1988**, *33*, 2105. (b) Caglioti, L. *Tetrahedron* **1966**, *22*, 487. (c) Nair, V.; Sinhababu, A. K. *J. Org. Chem.* **1978**, *26*, 5013.

(5) It is well-known that alkylhydrazines can be oxidized directly to the corresponding alkanes by ferricyanide, iodate, or periodate in alkaline solution (Whistler, R. L.; Shasha, B. *J. Org. Chem.* **1964**, *29*, 880. Cram, D. J.; Bradshaw, J. S. *J. Am. Chem. Soc.* **1963**, *85*, 1108. Reference 3a.) However, the stereochemical course of this direct conversion, in most cases, was not defined.

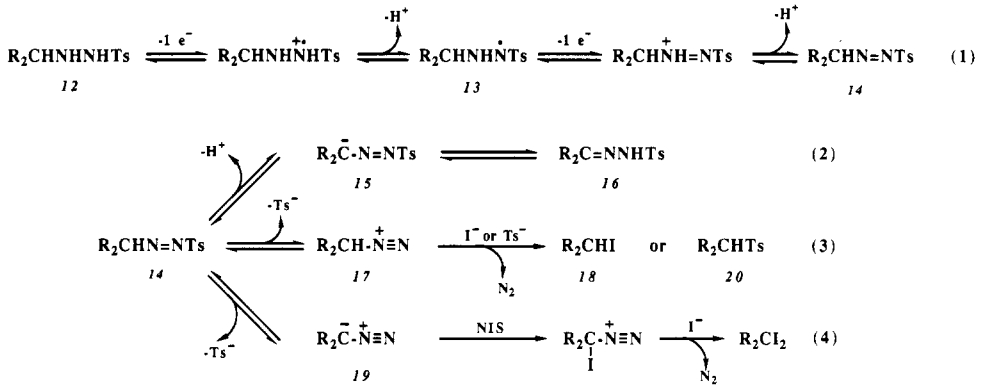
(6) Cram, D. J.; Bradshaw, J. S. *J. Am. Chem. Soc.* **1963**, *85*, 1108.

(7) One should keep in mind that the hydrazines used in all of the previous studies were plain aliphatic and/or aromatic hydrazines. Thus, formation of a toluenesulfinate product was not possible in these reported cases.

(8) Miller, V. P.; Yang, D.-y.; Weigel, T. M.; Han, O.; Liu, H. W. *J. Org. Chem.* **1989**, *54*, 4175.

0022-3263/89/1954-5402$01.50/0

Scheme I



N-iodosuccinimide. When a tosylhydrazine was treated with *N*-iodosuccinimide and *N*-methylmorpholine in chloroform at low temperature, it was oxidized rapidly and cleanly. Thus, the latter mixture was used as the oxidant throughout this study.

As shown in Table I, upon oxidation the sugar tosylhydrazine **1** was converted to a mixture of the iodide **2** and a diiodide species **3**. Although the desired iodide **2** was only a minor product in this case, the isolation of compound **3** as a co-product is a mechanistically significant finding. Since the formation of geminal diiodide derivatives from hydrazones via halogen oxidation has been well documented,[9] the aforementioned result argues for the existence of a hydrazone intermediate along the reaction coordinate. When the same oxidation was applied to sugar tosylhydrazines **4** and **6**, we were amazed to discover that the only product formed in each case was the corresponding tosylhydrazone, **5** and **7**. This unexpected finding was a delightful surprise, since it provides direct evidence supporting the intermediacy of a hydrazone species during this oxidation. A similar situation was also found for the oxidation of compound **8**, a 1,5-anhydroarabinitol derivative, from which tosylhydrazone **9** was isolated as the sole product. The dominance of tosylhydrazone formation is not confined to just the pyranose derivatives since oxidation of compound **10**, derived from cyclohexane-1,2,3-triol, also gave tosylhydrazone **11** as the major product.

Since a 1,2-disubstituted hydrazine can be readily oxidized to the corresponding azo species by a variety of reagents,[10] and many azo derivatives bearing α-hydrogen atoms can tautomerize to the more stable hydrazones under the influence of heat, light, or base,[11] the oxidation of tosylhydrazine to tosylhydrazone found in these experiments is likely a result of the combination of these two processes. As shown in Scheme I, the first half of the proposed sequence is the halogen oxidation of tosylhydrazine **12** to a diazene derivative **14** (eq 1). This reaction is likely a stepwise $1e^-/1e^-$ oxidation and may proceed via a hydrazyl radical intermediate **13**.[12] Such a stepwise electron-transfer process is characteristic for a *N*-iodosuccinimide-mediated reaction, and the iodide ion is formed concomitantly as the byproduct. Addition of *N*-methylmorpholine to the original reaction mixture facilitated the deprotonation during this stepwise oxidation; however, it could also promote the α-proton abstraction from the nascent diazene species. Thus, the second half of the proposed sequence is the base-induced tautomerization of diazene **14** to the corresponding tosylhydrazone **16** (eq 2). Such tautomerization is, evidently, the preferred pathway for the oxidation of hydrazines **4**, **6**, **8**, and **10**. However, recalling the fact that oxidation of tosylhydrazine **1** under the same conditions afforded the corresponding iodide **2** as one of the primary products, a second reaction route must exist. Since the diazene intermediate **14** can also release *p*-toluenesulfinic acid to form a diazonium ion **17**, coupling of **17** with the iodide ion generated in situ is an appealing alternative that will give the iodide **18** as observed with concurrent loss of nitrogen (eq 3). The proposed diazene/hydrazone intermediate at the branching point in this sequence may also serve as the precursor of compound **3**. As shown in Scheme I, a third pathway involving a diazo intermediate **19** may account for the formation of **3** (eq 4). A similar mechanism for the formation of *gem*-diiodide products from ketone hydrazones has been proposed by Barton et al.[3e,9,13]

It is worth noting that the α-C of the transient species **15** formed during the base-catalyzed tautomerization is nucleophilic in nature. By contrast, the reaction center bearing the diazonium moiety in **17** becomes electrophilic during the conversion of **14** to **18**. Since the separate pathways leading to the formation of tosylhydrazone and iodide functionalities are expected to establish opposite charge distribution on the imino carbon at the transition stage, the mechanistic diversity of this oxidation may be directly correlated to the electronic character of the transition state at the branching point. Thus, factors that stabilize the characteristic charges of these transition states may also play a key role in controlling the reaction flux. Examining the structures of hydrazines **4**, **6**, **8**, and **10**, it is evident that the general structural feature shared by these compounds is the array of two α-ester groups located separately on each side of the hydrazino moiety. The alteration of the reaction mechanism to favor the formation of tosylhydrazone for these hydrazines may be attributed to the ability of the inductive effect imposed by the α,-α'-diester functionality to stabilize the electron-rich transition state. In the absence of electron-withdrawing substituents, the reaction course is directed to the productive route that yields the anticipated iodide product. This hypothesis is consistent with the observation that **1** is converted to a mixture of **2** and **3**. It is further supported by the outcome of the oxidation of simple tosylhydrazines **21** and **22** whose structures are devoid of substituents on

(9) (a) Barton, D. H. R.; O'Brien, R. E.; Sternhell, S. *J. Chem. Soc.* **1962**, 470. (b) Pross, A.; Sternhell, S. *Aust. J. Chem.* **1970**, *23*, 989 and ref 3.

(10) Barton, D. H. R.; Ollis, W. D. *Comprehensive Organic Chemistry: The Synthesis and Reactions of Organic Compounds*; Pergamon Press: Oxford, 1979; Vol. 2, p 231.

(11) Buckingham, J. *Quart. Rev.* **1969**, *23*, 37.

(12) (a) Nelsen, S. F.; Landis, R. T., II *J. Am. Chem. Soc.* **1974**, *96*, 1788. (b) Lemal, D. M. In *Nitrenes*; Lwowski, W., Ed.; Interscience: New York, 1970; p 345. (c) Forrester, A. R.; Hay, J. M.; Thomson, R. H. *Organic Chemistry of Stable Free Radicals*; Academic: London, 1968.

(13) However, it is not immediately clear why the diiodide product was found only in the oxidation of hydrazine **1**, but not in other examples.

either side of the hydrazino carbon. As expected, no tosylhydrazone was discernible in the reaction mixture. Instead, the corresponding tolyl sulfones, **23** and **24**, were isolated as the sole product in each case. Since toluenesulfinate is released during the conversion of the diazene intermediate **14** to the diazonium ion **17**, it can couple with **17**, giving compound **20** as observed (Scheme I). As it is likely that the toluenesulfinate anion never completely disassociates from the nascent diazonium derivative **17** in these cases, its proximity could allow it to preempt the attachment of the iodide anion to the electrophilic diazonium ion **17**.[14]

To further explore the electronic nature of the transition state and to assess its affect on the course of the reaction mechanism, a series of tosylhydrazines (**25–28**) of substituted acetophenones was examined under the same conditions. As shown in Table I, the preference of the reaction flux to advance via these two alternate routes is indeed directly related to the electronic nature of the substituent at the para position of each tosylhydrazine. Namely, with a strong electron-withdrawing substituent, the reaction favors the tautomerization pathway, while with a strong electron-donating substituent, the reaction prefers the route via a diazonium intermediate. The outcomes of the oxidation of hydrazines **25** and **28**, bearing a para nitro and amino substituent respectively, well illustrate such an electronic effect of opposite extremes. The co-production of **34** and **35** from **28** further supports that the tolyl sulfone and iodide products are derived from a common precursor, the diazonium intermediate **17**. The fact that both tosylhydrazone and tolyl sulfone (**30/31, 32/33**) were isolated from the reaction of **26** and **27** is most significant, since it unequivocally confirms the presence of two competing mechanisms in this oxidation.

Experimental Section

Melting points were determined with a Mel-Temp apparatus and are uncorrected. Mass spectra were obtained with a VG 7070E-HF spectrometer. ^1H and ^{13}C NMR spectra were recorded on an IBM NR/200 or NR/300 spectrometer. Chemical shifts are reported in ppm on the δ scale relative to internal standard (tetramethylsilane or appropriate solvent peaks) with coupling constants given in hertz. NMR assignments labeled with an asterisk (*) may be interchangeable. Flash chromatography was performed in columns of various diameters with J. T. Baker (230–400 mesh) silica gel by elution with the solvents reported. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60 G-254 plates (25 mm) and developed with the solvents mentioned. TLC spots were visualized either with UV light or by dipping the plates into staining solutions of vanillin/ethanol/H_2SO_4 (1:98:1) or phosphomolybdic acid (7% EtOH solution) and then heating them. Solvents, unless otherwise specified, were reagent grade and distilled once prior to use. Preparations of most of the tosylhydrazines employed in this study have already been summarized.[8]

General Procedure of *N*-Iodosuccinimide Oxidation. To a *N*-iodosuccinimide (1.2 equiv) suspension/solution in chloroform was added dropwise a mixture of tosylhydrazine (1 equiv) and *N*-methylmorpholine (2 equiv) in chloroform solution at low temperature under nitrogen. A yellow color developed instantaneously. This mixture was stirred at low temperature until the reaction was complete. At the end of the reaction, the solution turned reddish brown. The excess iodine was quenched by the addition of sodium bisulfite solution (10%). The organic layer was separated, washed with water and brine, dried over anhydrous sodium sulfate, and concentrated in vacuo. The reaction products were then purified by flash chromatography. The oxidation was conducted at 0 °C for aliphatic and sugar tosylhydrazines and at −50 °C for aromatic tosylhydrazines. The reaction was generally complete in 5–30 min.

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-4-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-galactopyranoside (1). This compound was prepared from methyl 2,3-di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (**36**)[2b,15] via a sequence involving oxidation of the C-4 hydroxyl group to a keto moiety (**36** to **37**),[16] coupling of the C-4 keto group with toluenesulfonhydrazide (**37** to **38**), and reduction of the tosylhydrazone by $NaBH_3CN$ (**38** to **1**).[8] Experimental details of these steps are summarized below.

Methyl 2,3-Di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (36). This compound was synthesized from methyl glucoside according to a published procedure:[2b,15] ^1H NMR ($CDCl_3$) δ 7.39–7.27 (10 H, m, Ar H's), 5.03, 4.74 (1 H each, d, J = 11.5, benzyl H's), 4.74, 4.65 (1 H each, d, J = 12.1, benzyl H's), 4.59 (1 H, d, J = 3.4, 1-H), 3.77 (1 H, dd, J = 9.6, 9.3, 3-H), 3.66 (1 H, dq, J = 9.3, 6.2, 5-H), 3.52 (1 H, dd, J = 9.6, 3.4, 2-H), 3.38 (3 H, s, OMe), 3.16 (1 H, dt, J = 9.3, 2.9, 4-H), 2.62 (1 H, d, J = 2.9, OH), 1.26 (3 H, d, J = 6.2, 5-Me); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.2, 128.6, 128.5, 128.1, 127.9 (Ar-C's), 98.0 (C-1), 81.4 (C-2)*, 80.2 (C-3)*, 75.5, 75.3 (benzyl C's), 73.0 (C-4), 67.0 (C-5), 55.1 (OMe), 17.8 (C-6).

Methyl 2,3-Di-*O*-benzyl-6-deoxy-α-D-*xylo*-hexopyranosid-4-ulose (37). To a chilled (0 °C) orange suspension of pyridinium chlorochromate (2 g, 9.5 mmol), sodium acetate (1.17 g, 14.2 mmol), and 3-Å molecular sieves (2 g, activated at 250 °C for 24 h) in 30 mL of dry methylene chloride was added compound **36** (850 mg, 2.37 mmol) in one portion. The reaction mixture was allowed to warm up gradually to room temperature and stirred under nitrogen for 2 h. After completion, the reaction mixture was treated with anhydrous ether. The black precipitate was filtered off via a pad of silica gel and washed with ether. The combined filtrates were evaporated, and the oily residue was purified by flash chromatography (15% EtOAc/hexane) to give the desired product (white solid) in 83% yield: ^1H NMR ($CDCl_3$) δ 7.44–7.23 (10 H, m, Ar H's), 4.96, 4.66 (1 H each, d, J = 11.4, benzyl H's), 4.84, 4.66 (1 H each, d, J = 12.1, benzyl H's), 4.73 (1 H, d, J = 3.4, 1-H), 4.45 (1 H, d, J = 10.1, 3-H), 4.17 (1 H, q, J = 6.4, 5-H), 3.78 (1 H, dd, J = 10.1, 3.4, 2-H), 3.44 (3 H, s, OMe), 1.27 (3 H, d, J = 6.4, 5-Me); ^{13}C NMR ($CDCl_3$) δ 203.3 (C-4), 138.0, 130.0, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8 (Ar-C's), 98.4 (C-1), 82.8 (C-3)*, 80.7 (C-2)*, 74.2, 73.8 (benzyl C's), 69.1 (C-5), 56.0 (OMe), 13.8 (C-6); high-resolution FAB-MS calcd for $C_{21}H_{25}O_5$ $(M + H)^+$ 357.1702, found 357.1696.

Methyl 2,3-Di-*O*-benzyl-6-deoxy-α-D-*xylo*-hexopyranosid-4-ulose (*p*-Tolylsulfonyl)hydrazone (38). To a well-agitated solution of **37** (600 mg, 1.68 mmol) in 10 mL of methylene chloride was added *p*-toluenesulfonhydrazide (320 mg, 1.68 mmol) in portions. The reaction mixture was then stirred for 2 h at room temperature. After completion, the excess solvent was evaporated, and the crude product was purified by flash chromatography (12% EtOAc/hexane). The yield was 79%: ^1H NMR ($CDCl_3$) δ 7.69, 7.23 (2 H each, d, J = 8.2, Ts H's), 7.43–7.28 (10 H, m, Ar H's), 4.83, 4.74 (1 H each, d, J = 9.6, benzyl H's), 4.75, 4.60 (1 H each, d, J = 12.0, benzyl H's), 4.66 (1 H, d, J = 9.8, 3-H), 4.59 (1 H, d, J = 3.5, 1-H), 4.21 (1 H, q, J = 6.3, 5-H), 3.62 (1 H, dd, J = 9.8, 3.5, 2-H), 3.37 (3 H, s, OMe), 2.39 (3 H, s, Ts-Me), 1.22 (3 H, d, J = 6.3, 5-Me); ^{13}C NMR ($CDCl_3$) δ 148.0 (C-4), 143.7–127.9 (Ar-C's), 97.7 (C-1), 81.2 (C-2)*, 80.8 (C-3)*, 75.9, 73.4 (benzyl C's), 66.9 (C-5), 55.7 (OMe), 21.6 (Ts-Me), 16.3 (C-6); high-resolution FAB-MS calcd for $C_{28}H_{33}N_2O_6S$ $(M + H)^+$ 525.2059, found 525.2046.

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-4-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-galactopyranoside (1). To a stirred mixture of compound **38** (400 mg, 0.76 mmol) and a trace amount of methyl orange in a solution of 1:1 THF–MeOH (4 mL) under nitrogen was added $NaBH_3CN$ (1 M in dry THF) and HCl (0.1 N in dry MeOH) dropwise via two syringes until the color of the solution had just changed to yellow. Additional amounts of acid and reducing agent were added in two to three portions over the

(14) It is likely that the corresponding toluenesulfinate product was also formed in the oxidation of tosylhydrazine **1**. However, the reaction product was a complex mixture and attempts to isolate products other than **2** and **3** were futile.

(15) Stevens, C. L.; Blumbergs, P.; Otterbach, D. H. *J. Org. Chem.* **1966**, *31*, 2817.

(16) (a) Herscovici, J.; Egron, M.; Antonakis, K. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1967. (b) Czernecki, S.; Georgoulis, C.; Stevens, C. L.; Vijayakakumaran, K. *Synth. Commun.* **1986**, *16*, 11.

next 3–6 h until the reaction was complete. The total amount of $NaBH_3CN$ added was 3–4 molar equiv of that of the tosylhydrazone **38**. Workup consisted of neutralization with saturated sodium bicarbonate and extraction with methylene chloride. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and evaporated. The crude mixture was purified by flash chromatography (15% EtOAc/hexane). The major product isolated was the desired tosylhydrazine **1**. The corresponding C-4 epimer, methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-glucopyranoside, was also found as a minor product. The ratio of these products was 3:1, and the total yield was 89%: ^1H NMR ($CDCl_3$) of compound **1** δ 7.73, 7.23 (2 H each, d, J = 8.2, Ts H's), 7.63–7.14 (10 H, m, Ar H's), 4.83, 4.73 (1 H each, d, J = 11.4, benzyl H's), 4.77, 4.63 (1 H each, d, J = 11.9, benzyl H's), 4.51 (1 H, d, J = 3.8, 1-H), 3.92 (1 H, dd, J = 10.2, 4.0, 3-H), 3.83 (1 H, br q, J = 6.6, 5-H), 3.62 (1 H, dd, J = 10.2, 3.8, 2-H), 3.30 (3 H, s, OMe), 3.07 (1 H, br s, 4-H), 2.41 (3 H, s, Ts-Me), 1.16 (3 H, d, J = 6.6, 5-Me); ^{13}C NMR ($CDCl_3$) of compound **1** δ 143.7, 138.1, 138.0, 129.4–128.0 (Ar-C's), 98.3 (C-1), 80.4 (C-2)*, 76.3 (C-3)*, 74.2, 73.3 (benzyl C's), 65.1 (C-5), 60.7 (C-4), 55.3 (OMe), 21.6 (Ts-Me), 17.1 (C-6); high-resolution FAB-MS of compound **1** calcd for $C_{28}H_{35}N_2O_6S$ $(M + H)^+$ 527.2216, found 527.2198. Anal. Calcd for $C_{28}H_{34}N_2O_6S$: C, 63.85; H, 6.51; N, 5.32; S, 6.08. Found: C, 63.66; H, 6.65; N, 5.36; S, 6.20. ^1H NMR ($CDCl_3$) of the minor product: δ 7.62, 7.19 (2 H each, d, J = 9.2, Ts H's), 7.40–7.33 (10 H, m, Ar H's), 4.74–4.60 (4 H, m, benzyl H's), 4.57 (1 H, d, J = 3.5, 1-H), 3.81 (1 H, t, J = 9.3, 3-H), 3.97–3.90 (1 H, m, 5-H), 3.49 (1 H, dd, J = 9.3, 3.5, 2-H), 3.35 (3 H, s, OMe), 3.07 (1 H, t, J = 9.3, 4-H), 2.43 (3 H, s, Ts-Me), 1.19 (3 H, d, J = 6.3, 5-Me); ^{13}C NMR ($CDCl_3$) of the minor product δ 143.6–128.0 (Ar-C's), 97.6 (C-1), 81.6 (C-2), 75.1 (C-3), 74.2, 72.6 (benzyl C's), 65.7 (C-5)*, 65.0 (C-4)*, 55.3 (OMe), 21.6 (Ts-Me), 18.6 (C-6).

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-4-iodo-α-D-glucopyranoside (2) and Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-4,4-diiodo-α-D-*xylo*-hexopyranoside (3). Via the method described in the general procedures, compound **1** was oxidized to give a complex mixture. The major component was isolated by repeated flash chromatography (15% EtOAc/hexane) followed by preparative TLC (EtOAc/$CHCl_3$/hexane = 4:20:76). Two products, **2** and **3** of 2:3 ratio, were purified to homogeneity through this separation sequence. The total yield was 62%. Compound **2**: ^1H NMR ($CDCl_3$) δ 7.46–7.29 (10 H, m, Ar H's), 4.93, 4.87 (1 H each, d, J = 10.1, benzyl H's), 4.78, 4.62 (1 H each, d, J = 12.1, benzyl H's), 4.58 (1 H, d, J = 3.5, 1-H), 4.05 (1 H, dq, J = 10.5, 6.2, 5-H), 3.97 (1 H, dd, J = 10.5, 9.3, 3-H), 3.65 (1 H, t, J = 10.5, 4-H), 3.45 (1 H, dd, J = 9.3, 3.5, 2-H), 3.39 (3 H, s, OMe), 1.43 (3 H, d, J = 6.2, 5-Me); high-resolution FAB-MS calcd for $C_{21}H_{24}O_4I$ $(M - H)^+$ 467.0719, found 467.0687. Compound **3**: ^1H NMR ($CDCl_3$) δ 7.54–7.30 (10 H, m, Ar H's), 5.13, 5.09 (1 H each, d, J = 10.2, benzyl H's), 4.76, 4.56 (1 H each, d, J = 12.0, benzyl H's), 4.57 (1 H, d, J = 3.8, 1-H), 3.71 (1 H, dd, J = 9.2, 3.8, 2-H), 3.39 (3 H, s, OMe), 3.37 (1 H, d, J = 9.2, 3-H), 3.11 (1 H, q, J = 6.0, 5-H), 1.57 (3 H, d, J = 6.0, 5-Me); ^{13}C NMR ($CDCl_3$) δ 147.5, 138.3, 137.8, 128.5–127.6 (Ar-C's), 98.5 (C-1), 86.3 (C-2), 80.0 (C-3), 76.1 (C-5), 73.8, 73.1 (benzyl C's), 55.6 (OMe), 22.2 (C-6); high-resolution FAB-MS calcd for $C_{21}H_{23}O_4I_2$ $(M - H)^+$ 592.9686, found 592.9658. Anal. Calcd for $C_{21}H_{24}O_4I_2$: C, 42.43; H, 4.07; I, 42.73. Found: C, 42.66; H, 4.12; I, 42.02.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-L-*arabino*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (5). This hydrazone was obtained from methyl 4-*O*-acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-α-L-altropyranoside (**4**)[2a] using the method described in the general procedures. The product was purified by flash chromatography (10% EtOAc/hexane) with a yield of 91%: ^1H NMR ($CDCl_3$) δ 9.59 (1 H, s, NH), 7.96, 7.21 (2 H each, d, J = 7.2, Ts H's), 7.72 (2 H, d, J = 8.1, ortho H's), 7.61 (1 H, t, J = 7.4, para H), 7.44 (2 H, dd, J = 8.1, 7.4, meta H's), 5.33 (1 H, br s, 2-H), 4.95 (1 H, d, J = 9.9, 4-H), 4.91 (1 H, s, 1-H), 4.11 (1 H, m, 5-H), 3.39 (3 H, s, OMe), 2.34 (3 H, s, Ts-Me), 2.04 (3 H, s, CH_3C=O), 1.29 (3 H, d, J = 6.2, 5-Me); ^{13}C NMR ($CDCl_3$) δ 169.1 (CH_3C=O), 166.5 (PhC=O), 143.9 (C-3), 144.8–127.8 (Ar C's), 98.9 (C-1), 71.0 (C-4), 67.4 (C-2)*, 66.4 (C-5)*, 55.0 (OMe), 21.6 (Ts-Me), 20.6 (CH_3C=O), 18.1 (C-6). Anal. Calcd for $C_{23}H_{26}N_2O_8S$: C, 56.32; H, 5.34; N, 5.71; S, 6.54. Found: C, 56.16; H, 5.07; N, 5.80; S, 6.52.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-L-*xylo*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (7). This hydrazone was obtained from methyl 4-*O*-acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-α-L-gulopyranoside (**6**)[8] using the method described in the general procedures. The product was purified by flash chromatography (10% EtOAc/hexane) with a yield of 95%: mp 81–82 °C; ^1H NMR ($CDCl_3$) δ 9.21 (1 H, s, NH), 8.05 (2 H, d, J = 7.1, ortho H's), 7.64 (1 H, t, J = 7.4, para H), 7.50 (2 H, dd, J = 7.4, 7.1, meta H's), 7.43, 7.79 (2 H each, d, J = 8.2, Ts H's), 5.59 (1 H, d, J = 3.8, 2-H), 5.09 (1 H, d, J = 1.8, 4-H), 4.97 (1 H, d, J = 3.8, 1-H), 4.26 (1 H, dq, J = 6.6, 1.8, 5-H), 3.43 (3 H, s, OMe), 2.25 (3 H, s, CH_3C=O), 2.12 (3 H, s, Ts-Me), 1.28 (3 H, d, J = 6.6, 5-Me); ^{13}C NMR ($CDCl_3$) δ 172.2 (CH_3C=O), 165.1 (PhC=O), 145.6 (C-3), 143.5, 134.4, 133.5, 130.1, 129.4, 129.1, 128.4, 128.1 (Ar C's), 99.1 (C-1), 68.5, 68.4, 64.6 (C-2, 4, 5), 55.6 (OMe), 21.5 (CH_3C=O), 20.3 (Ts-Me), 15.5 (C-6). Anal. Calcd for $C_{23}H_{26}N_2O_8S$: C, 56.32; H, 5.34; N, 5.71; S, 6.54. Found: C, 56.46; H, 5.40; N, 5.73; S, 6.48.

2-*O*-Acetyl-1,5-anhydro-4-*O*-benzoyl-L-*threo*-pent-3-ulose (*p*-Tolylsulfonyl)hydrazone (9). This compound was prepared from 2-*O*-acetyl-1,5-anhydro-4-*O*-benzoyl-3-[2-(*p*-tolylsulfonyl)-hydrazino]-L-*lyxo*-pentitol (**8**)[8] based on the method described in the general procedures. The product was purified by flash chromatography (10% EtOAc/benzene). The yield was 96%: ^1H NMR ($CDCl_3$) δ 9.35 (1 H, br s, NH), 8.04 (2 H, d, J = 7.3, ortho H's), 7.65 (1 H, t, J = 7.1, para H), 7.52 (2 H, dd, J = 7.3, 7.1, meta H's), 7.43, 6.88 (2 H each, d, J = 8.2, Ts H's), 5.65 (1 H, dd, J = 10.8, 6.2, 2-H), 5.26 (1 H, br s, 4-H), 4.28 (1 H, dd, J = 10.8, 6.2, 1-H), 4.15 (1 H, d, J = 13.0, 5-H), 3.72 (1 H, dd, J = 13.0, 1.6, 5-H), 3.65 (1 H, t, J = 10.8, 1-H), 2.30 (3 H, s, Ts-Me), 2.12 (3 H, s, CH_3C=O); ^{13}C NMR ($CDCl_3$) δ 172.0 (CH_3C=O), 164.8 (PhC=O), 146.9 (C-3), 143.8, 133.6, 130.0, 129.4, 129.2, 128.5, 128.1 (Ar C's), 70.3, 69.9, 66.6, 66.5 (C-1, 2, 4, 5), 21.6 (Ts-Me), 20.5 (CH_3C=O); high-resolution FAB-MS calcd for $C_{21}H_{23}N_2O_7S$ $(M + H)^+$ 447.1226, found 447.1222.

***trans*-2-Acetoxy-6-(benzoyloxy)cyclohexanone (*p*-Tolylsulfonyl)hydrazone (11).** This compound was prepared from (1*S*,2*S*,6*S*)-2-acetoxy-6-(benzoyloxy)-1-[2-(*p*-tolylsulfonyl)-hydrazino]cyclohexane (**10**)[8] based on the method described in the general procedures. The product was purified by flash chromatography (10% EtOAc/benzene). The yield was 92%: mp 111–112 °C; ^1H NMR ($CDCl_3$) δ 9.10 (1 H, s, NH), 8.04–6.76 (9 H, m, Ar and Ts H's), 5.48 (2 H, m, 2-, 6-H's), 2.27 (3 H, s, Ts-Me), 2.09 (3 H, s, CH_3C=O), 2.05–1.88 (6 H, m, 3-, 4-, 5-H's). Anal. Calcd for $C_{22}H_{24}N_2O_6S$: C, 59.45; H, 5.44; N, 6.30; S, 7.21. Found: C, 59.50; H, 5.50; N, 6.29; S, 7.16.

Cyclohexyl *p*-Tolyl Sulfone (23). Via the method described in the general procedures, this compound was obtained from [2-(*p*-tolylsulfonyl)hydrazino]cyclohexane (**21**)[8] in 93% yield. The reaction was complete in a few minutes, and the product was purified by flash chromatography (5% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ 7.59, 7.30 (2 H each, d, J = 8.3, Ts H's), 4.31 (1 H, m, CHS), 2.41 (3 H, s, Ts-Me), 2.01–1.96 (1 H, m, ring H), 1.78–1.68 (3 H, m, ring H's), 1.62–1.19 (6 H, m, ring H's); ^{13}C NMR ($CDCl_3$) δ 142.9, 142.4, 129.6, 125.1 (Ar C's), 77.8 (C-S), 33.7, 33.6, 25.2, 23.9 (ring C's), 21.5 (Ts-Me); high-resolution FAB-MS calcd for $C_{13}H_{19}O_2S$ $(M + H)^+$ 239.1106, found 239.1120.

Isopropyl *p*-Tolyl Sulfone (24). This compound was obtained from 2-[2-(*p*-tolylsulfonyl)hydrazino]propane (**22**).[8] The reaction was complete in a few minutes, and compound **24** was isolated in 50% yield after repeated preparative TLC purification (5% hexane/$CHCl_3$). The low overall yield may be attributed to the volatility of other possible products, such as isopropyl iodide, that might have been evaporated during the workup: ^1H NMR ($CDCl_3$) δ 7.58, 7.31 (2 H each, d, J = 8.2, Ts H's), 4.58 (1 H, hep, J = 6.2, CHS), 2.41 (3 H, s, Ts-Me), 1.36, 1.23 (3 H each, d, J = 6.2, Me's); ^{13}C NMR ($CDCl_3$) δ 143.4, 129.6, 129.5, 128.1, 125.1 (Ar C's), 72.7 (C-S), 24.0 (Me), 23.8 (Me), 21.5 (Ts-Me); high-resolution FAB-MS calcd for $C_{10}H_{15}O_2S$ $(M + H)^+$ 199.0793, found 199.0783.

4′-Nitroacetophenone (*p*-Tolylsulfonyl)hydrazone (29). This compound was prepared from 4′-nitroacetophenone (*p*-tolylsulfonyl)hydrazine, **25**.[8] It was purified by flash chromatography (25% EtOAc/hexane), and the yield was 95%. Com-

pound **29**: mp 196–198 °C (lit. mp 197–198 °C);[17] ^{1}H NMR (acetone-d_6) δ 9.73 (1 H, br s, NH), 8.22, 7.98 (2 H each, d, J = 8.8, Ar H's), 7.89, 7.40 (2 H each, d, J = 8.3, Ts H's), 2.39 (3 H, s, Ts-Me), 2.32 (3 H, s, Me); ^{13}C NMR (acetone-d_6) δ 149.0 (C=N), 144.8, 144.5, 137.3, 129.8, 130.3, 128.8, 128.0, 124.2 (Ar C's), 21.4 (Ts-Me), 13.9 (Me).

Acetophenone (*p*-Tolylsulfonyl)hydrazone (30) and [α-(*p*-Tolylsulfonyl)ethyl]benzene (31). These two compounds were obtained in 4:1 ratio (**30**/**31**) from acetophenone (*p*-tolylsulfonyl)hydrazine (**26**).[8] They were separated and purified by flash chromatography (20% EtOAc/hexane). The total yield was 90%. Compound **30** (white crystal, R_f = 0.64 developed in 50% EtOAc/hexane): mp 134–136 °C; ^{1}H NMR ($CDCl_3$) δ 7.94 (2 H, d, J = 8.3, Ts H's), 7.87 (1 H, br s, NH), 7.85–7.62 (2 H, m, Ar H's), 7.36–7.21 (5 H, m, Ts and Ar H's), 2.43 (3 H, s, Ts-Me), 2.15 (3 H, s, Me); ^{13}C NMR ($CDCl_3$) δ 152.6 (C=N), 144.2, 137.3, 135.4, 129.6, 128.3, 128.1, 126.3 (Ar C's), 21.6 (Ts-Me), 13.5 (Me); high-resolution FAB-MS calcd for $C_{15}H_{17}N_2O_2S$ $(M + H)^+$ 289.1011, found 289.1002. Anal. Calcd for $C_{15}H_{16}N_2O_2S$: C, 62.48; H, 5.59; N, 5.09; S, 11.12. Found: C, 62.55; H, 5.67; N, 5.05; S, 11.19. Compound **31** (pale yellow solid, R_f = 0.78 developed in 50% EtOAc/hexane): ^{1}H NMR ($CDCl_3$) δ 7.40 (2 H, d, J = 8.3, Ts H's), 7.27–7.10 (7 H, m, Ar H's), 4.20 (1 H, q, J = 7.2, C*H*S), 2.38 (3 H, s, Ts-Me), 1.74 (3 H, d, J = 7.2, Me); ^{13}C NMR ($CDCl_3$) δ 144.5, 142.0, 134.0–127.7 (Ar C's), 66.1 (C-S), 21.6 (Ts-Me), 14.1 (Me); high-resolution FAB-MS calcd for $C_{15}H_{17}O_2S$ $(M + H)^+$ 261.0949, found 261.0933. Anal. Calcd for $C_{15}H_{17}O_2S$: C, 68.93; 68.93; H, 6.56; S, 12.27. Found: C, 68.83; H, 6.55; S, 12.34.

4′-Methoxyacetophenone (*p*-Tolylsulfonyl)hydrazone (32) and 1-[α-(Tolylsulfonyl)ethyl]-4-methoxybenzene (33). These two compounds were obtained in 3:2 ratio (**32**/**33**) from 4′-methoxyacetophenone (*p*-tolylsulfonyl)hydrazine (**27**).[8] They were separated and purified by flash chromatography (10–20% EtOAc/hexane). The total yield was 81%. Compound **32** (R_f = 0.57 developed in 50% EtOAc/hexane): mp 168–170 °C (lit. mp 169–171 °C);[17] ^{1}H NMR ($CDCl_3$) δ 7.91, 7.30 (2 H each, d, J = 8.3, Ts H's), 7.59, 6.83 (2 H each, d, J = 8.9, Ar H's), 3.80 (3 H, s, OMe), 2.40 (3 H, s, Ts-Me), 2.10 (3 H, s, Me); ^{13}C NMR ($CDCl_3$) δ 160.8 (C=N), 152.6, 144.1, 135.5, 129.8, 129.6, 128.2, 127.8, 113.7 (Ar C's), 55.3 (OMe), 21.6 (Ts-Me), 13.3 (Me). Anal. Calcd for $C_{16}H_{18}N_2O_3S$: C, 60.36; H, 5.70; N, 8.80; S, 10.07. Found: C, 60.30; H, 5.77; N, 8.72; S, 10.12. Compound **33** (yellow solid, R_f = 0.73 developed in 50% EtOAc/hexane): ^{1}H NMR ($CDCl_3$) δ 7.41, 7.18 (2 H each, d, J = 8.2, Ts H's), 7.05, 6.76 (2 H each, d, J = 8.7, Ar H's), 4.15 (1 H, q, J = 7.1, C*H*S), 3.77 (3 H, s, OMe), 2.38 (3 H, s, Ts-Me), 1.69 (3 H, d, J = 7.1, Me); ^{13}C NMR ($CDCl_3$) δ 159.9, 144.4, 134.0, 130.6, 129.3, 129.2, 125.7, 113.8 (Ar C's), 65.4 (C-S), 55.3 (OMe), 21.6 (Ts-Me), 14.2 (Me); high-resolution FAB-MS calcd for $C_{16}H_{19}O_3S$ $(M + H)^+$ 291.1055, found 291.1046. Anal. Calcd for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.11; H, 6.31; S, 11.09.

1-[α-(Tolylsulfonyl)ethyl]-4-aminobenzene (34) and 1-(α-iodoethyl)-4-aminobenzene (35). These two compounds were obtained in 4:1 ratio (**34**/**35**) from 4′-aminoacetphenone (*p*-tolylsulfonyl)hydrazine (**28**).[8] They were separated and purified by flash chromatography (30% ether/hexane) followed by preparative TLC (50% ether/hexane). The total yield was 56%. Compound **34** (R_f = 0.58 developed in ether): ^{1}H NMR ($CDCl_3$) δ 7.43, 7.18 (2 H each, d, J = 8.3, Ts H's), 6.90, 6.53 (2 H each, d, J = 8.5, Ar H's), 4.10 (1 H, q, J = 7.2, C*H*S), 3.69 (1 H, br s, NH), 2.39 (3 H, s, Ts-Me), 1.68 (3 H, d, J = 7.2, Me); high-resolution FAB-MS calcd for $C_{15}H_{18}NO_2S$ $(M + H)^+$ 276.1058, found 276.1046. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09; S, 11.64. Found: C, 65.35; H, 6.29; N, 5.15; S, 11.52. Compound **35** (R_f = 0.87 developed in ether): ^{1}H NMR ($CDCl_3$) δ 6.89, 6.26 (2 H each, d, J = 8.5, Ar H's), 4.29 (1 H, q, J = 6.7, C*H*I), 1.38 (3 H, d, J = 6.7, Me); high-resolution FAB-MS calcd for $C_8H_{11}NI$ $(M + H)^+$ 247.9938, found 247.9928.

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Registry No. *galacto*-1, 122948-60-1; *gluco*-1, 122948-75-8; **2**, 4049-59-6; **3**, 122948-61-2; **4**, 113668-66-9; **5**, 113668-65-8; **6**, 122948-62-3; **7**, 122948-63-4; **8**, 122948-64-5; **9**, 122948-65-6; **10**, 122948-66-7; **11**, 122948-67-8; **21**, 1146-49-2; **22**, 91011-12-0; **23**, 67963-06-8; **24**, 51751-71-4; **25**, 122948-68-9; **26**, 60565-67-5; **27**, 122948-69-0; **28**, 122948-70-3; **29**, 41780-82-9; **30**, 4545-21-5; **31**, 24422-77-3; **32**, 32117-52-5; **33**, 122948-71-4; **34**, 122948-72-5; **35**, 122948-73-6; **36**, 56750-58-4; **37**, 67381-20-8; **38**, 122948-74-7; *N*-iodosuccinimide, 516-12-1; tosylhydrazine, 1576-35-8.

(17) Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1973**, *95*, 3662.

Additions and Corrections

Vol. 54, 1989

Harry H. Wasserman,* Vincent M. Rotello, David R. Williams, and John W. Benbow. Synthesis of the "Tricarbonyl" Region of FK-506 through an Amidophosphorane.

Page 2785, column 1. Reference 9 was inadvertantly omitted during make-up of the printed version:

(9) Our use of BSA represents a modification of a procedure reported earlier: Cooke, M.; Burman, P. *J. Org. Chem.* **1982**, *47*, 4955. Cooke, M. *J. Org. Chem.* **1982**, *47*, 4963. In the coupling of ylide **3** with acid chloride **4** (outlined in Scheme II) the reaction failed to give the desired keto ylide carboxylate **5** in the absence of BSA.