Studies of the Mechanistic Diversity of Sodium Cyanoborohydride Reduction of Tosylhydrazones

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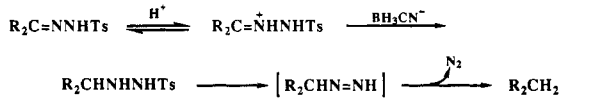
Reduction of tosylhydrazone derivatives of ketones and aldehydes with sodium cyanoborohydride in acidic medium is a mild, albeit versatile, deoxygenation reaction. The reaction mechanism has been proposed to proceed via either a direct hydride attack route or a tautomerization-then-reduction route. By using a mild reduction procedure ($NaBH_3CN$, THF–MeOH, 0 °C), it has been possible to stop the deoxygenation halfway and isolate the nascent tosylhydrazine product. Characterization of the resulting hydrazine to define the origin of the hydrogen being delivered to the former carbonyl carbon has allowed us to unambiguously distinguish betweeen these two possible mechanisms. Studies of reduction of tosylhydrazones derived from conjugated and saturated ketones confirmed earlier speculation that these reductions occur through a direct hydride attack mechanism. The reduction of para-substituted methyl phenyl ketone tosylhydrazones revealed a competition between these two mechanisms. Substrates bearing electron-donating substituents prefer the direct hydride attack pathway, while those with electron-withdrawing substituents favor an initial tautomerization prior to reduction. Sugar and hydroxyl ketone tosylhydrazones are also reduced by competing mechanisms. The mechanistic diversity in those cases may be attributed to the inductive effects compelled by the α substituents and the conformational constraints imposed by the ring structure. The mechanistic insights gained from these studies indicate that the direct hydride attack mechanism is the main reaction pathway due to the propensity of $NaBH_3CN$ to selectively attack the iminium ion. The tautomerization-then-reduction mechanism prevails only when the tautomerization of hydrazone to azohydrazine is facilitated.

The conversion of carbonyl compounds to the corresponding hydrocarbons is one of the key functional group interconversions frequently encountered in the synthesis of complex organic molecules. Since sodium cyanoborohydride is a mild, acid-stable reducing agent[1] with a propensity for selectively attacking iminium ion,[2] the reduction of tosylhydrazone to alkane by the cyanohydridoborate reagent in acidic media has been demonstrated to be a compelling alternative to the Wolff–Kishner and other direct/indirect deoxygenation methods for achieving this transformation.[3] This mild deoxygenation method can also be applied to reduce tosylhydrazones derived from α,β-unsaturated ketones.[4] Depending on the nature of the olefinic tosylhydrazone, both saturated alkane and/or alkene with double-bond migration to the site originally bearing the carbonyl group may be formed.[4a] The mechanistic course of this reduction is generally believed to proceed in the same fashion as the well-established sodium borohydride–acetic acid reduction of tosylhydrazones.[5] As delineated in eq 1, it is initiated by the protonation of



(1)

tosylhydrazone to form an iminium cation followed by hydride reduction of the C=N group to generate a tosylhydrazine derivative.[2-5] Subsequent elimination of *p*-toluenesulfinic acid gives rise to a diazene intermediate,[6] which then decomposes by releasing N_2 to afford the corresponding reduced hydrocarbon. Support for this proposition was provided by the studies of the reduction of α,β-unsaturated tosylhydrazones with $NaBD_3CN$ in which the deuterium was found exclusively at the original carbonyl carbon.[4]

The reduction of a saturated tosylhydrazone by $NaBD_3CN$ also led to the formation of a singly deuterated hydrocarbon, and, as expected, a dideuterium-labeled alkane was obtained if the reduction was carried out with $NaBD_3CN$ and a deuterated acid catalyst.[7] Although the pathway of eq 1 has been used to interpret these labeling results,[8] the actual mechanism of the reduction of saturated tosylhydrazones is still ambiguous. One should keep in mind that the original imine group is fully reduced to a methylene moiety under the reduction conditions (DMF–sulfolane, 105–110 °C). According to the mechanism of eq 1, of the two hydrogen atoms of the CH_2 formed, one originates from the reducing hydride and the second from the NH of the tosylhydrazone or from the water during the workup of the reaction mixture. Since the corresponding methylene hydrogens are chemically equivalent, unless the nascent hydrazine intermediate can be apprehended, it is virtually impossible to ascertain whether the deuterium incorporated in the singly labeled product is derived directly from the deuteride reducing agent. Fortunately, a modified procedure ($NaBH_3CN$, MeOH–THF, 0 °C) which stops the reduction at the hydrazine stage is known[9] and was adopted in our recent

(1) Kreevoy, M. M.; Hutchins, J. E. C. *J. Am. Chem. Soc.* **1969**, *91*, 4329.

(2) (a) Borch, R. F.; Durst, H. D. *J. Am. Chem. Soc.* **1969**, *91*, 3996. (b) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *Ibid.* **1971**, *93*, 2897. (c) Borch, R. F.; Hassid, A. I. *J. Org. Chem.* **1972**, *37*, 1673.

(3) (a) Hutchins, R. O.; Natale, N. R. *Org. Prep. Proced. Int.* **1979**, *11*, 203. (b) Hutchins, R. O.; Maryanoff, B. E.; Milewski, C. A. *J. Am. Chem. Soc.* **1971**, *93*, 1793. (c) Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E. *Ibid.* **1973**, *95*, 3662. (d) Lane, C. F. *Aldrichemica Acta* **1975**, *8*, 3.

(4) (a) Taylor, E. J.; Djerassi, C. *J. Am. Chem. Soc.* **1976**, *98*, 2275. (b) Hutchins, R. O.; Kacher, M.; Rua, L. *J. Org. Chem.* **1975**, *40*, 923. (c) Lane, C. F. *Synthesis* **1975**, 135.

(5) (a) Hutchins, R. O.; Natale, N. R. *J. Org. Chem.* **1978**, *43*, 2299. (b) Fischer, M.; Pelah, Z.; Williams, D. H.; Djerassi, C. *Chem. Ber.* **1965**, *98*, 3236. (c) Caglioti, L. *Tetrahedron* **1966**, *22*, 487. (d) Caglioti, L.; Grasselli, P. *Chem. Ind. (London)* **1964**, 153.

(6) (a) Tsuji, T.; Kosower, E. M. *J. Am. Chem. Soc.* **1971**, *93*, 1992. (b) Tsuji, T.; Kosower, E. M. *Ibid.* **1971**, *93*, 1992. (c) Kosower, E. M. *Acc. Chem. Res.* **1971**, *4*, 193. (d) McKenna, C. E.; Traylor, T. G. *J. Am. Chem. Soc.* **1971**, *93*, 2313.

(7) Klein, H.; Midgley, I.; Djerassi, C., unpublished results cited in ref 4a.

(8) The same mechanism has been used to explain the reduction of saturated tosylhydrazones with other boran/boron hydride reagents, such as: (a) Fleet, G. W. J.; Harding, P. J. C.; Whitcombe, M. J. *Tetrahedron Lett.* **1980**, 4031. (b) Kabalka, G. W.; Yang, D. T. C.; Chandler, J. H.; Baker, J. D., Jr. *Synthesis* **1977**, 124. (c) Kabalka, G. W.; Baker, J. D., Jr.; Neal, G. W. *J. Org. Chem.* **1977**, *42*, 512. (d) Kabalka, G. W.; Yang, D. T. C.; Baker, J. D., Jr. *Ibid.* **1977**, *41*, 574. (e) Kabalka, G. W.; Hutchins, R. O.; Natale, N. R.; Yang, D. T. C.; Broach, V. *Org. Synth.* **1980**, *59*, 42.

(9) Nair, V.; Sinhababu, A. K. *J. Org. Chem.* **1978**, *26*, 5013.

0022-3263/89/1954-4175$01.50/0

study of the reduction of sugar tosylhydrazones. To our surprise, by examining the isolated hydrazine products, we have found that the hydrogen atom being delivered to the imino carbon is not derived from the boron reducing agent, but rather is from the acidic source (HCl).[10] Thus, an alternative mechanism is conceivable starting with an acid-catalyzed hydrazone–azohydrazine tautomerization step which permits the solvent hydrogen to be incorporated at the original carbonyl carbon. Such acid- or base-catalyzed tautomerization between hydrazone and the corresponding azo species is well precedented.[11] As shown in eq 2, subsequent reduction of the transient azohydrazine species furnishes the end product with the observed labeling pattern.

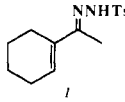
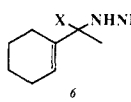
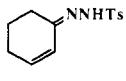
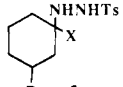
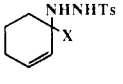
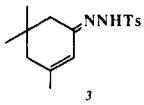
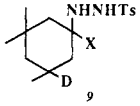
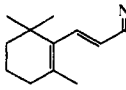
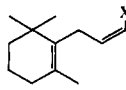
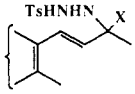
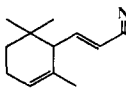
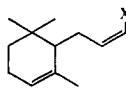
$$R_2C{=}NNHTs \overset{H^+}{\rightleftharpoons} R_2CHN{=}NTs \xrightarrow{BH_3CN^-} R_2CHNHNHTs \longrightarrow R_2CH_2 \qquad (2)$$

The apparent mechanistic discrepancy between the latter observation[10] and the earlier work performed by Djerassi and his co-workers[4,7] is intriguing. It is probable that the reduction of tosylhydrazones takes place readily in polar and aprotic solvents (DMF–sulfolane) at high temperature (eq 1) due to the propensity of the hydride species to selectively attack the iminium cation under these conditions.[2] When the reaction is conducted in polar but protic solvents (THF–MeOH) at low temperature, the reduction step may occur only after an initial tautomerization[11] to generate a more reactive azo intermediate which will then be reduced by hydride addition (eq 2). The choice of which mechanism occurs may thus be determined by the medium and temperature. However, it is also possible that such mechanistic alternation may simply be attributed to the varied nature of substrates employed in these two studies. In an attempt to further probe this reduction mechanism, we have conducted a systematic study to examine the impact of the nature of the substrate and the effects of the substitution, both electronic and steric, on the course of this reaction. Summarized herein are the results of these studies and their implications on the diversity of the reaction pathways.

Results and Discussion

The reduction was conducted at 0 °C as described before with excess of the reducing agent in THF/MeOH (1:1 by volume).[9,10] The acidity of the reaction mixture was adjusted by the addition of methanolic HCl solution to keep the methyl orange indicator at the red-yellow transition point. Since the cyanoborohydride reagent is labile at low pH[1,2] and formation of undesired elimination products (Bamford–Stevens products)[12] prevails at high pH, the acidity of the reaction needs to be carefully monitored. Automatic titration by a pH controller is the method of choice; however, visual discernment and manual adjustment is a convenient and satisfactory alternative. The conditions described here are mild enough that the proximate tosylhydrazine intermediate can be isolated. Characterization of the resulting tosylhydrazine has allowed us to unambiguously define the origin of the hydrogen being delivered to the imino carbon. The deuterium content was estimated mainly based on the NMR integration of the C*H*N signal of each labeled hydrazine product.

Table I. Reduction of Tosylhydrazones of Conjugated Ketones

substrate	product	X = D	X = H
 1	 6	91%	9%
 2	 7  8	100%	0%
 3	 9	100%	0%
 4	 10  12	100%	0%
 5	 11	100%	0%

Tosylhydrazones of Conjugated Ketones. As pointed out earlier, the mechanism delineated in eq 1 was based on the results obtained from the reduction of α,β-unsaturated tosylhydrazones in DMF–sulfolane at 110 °C.[4,7] The mechanism of eq 2, on the other hand, was based on the insights gained from the reduction of sugar tosylhydrazones in THF–MeOH at 0 °C.[10] In order to clarify the mechanistic ambiguity generated by these two independent studies, a direct comparison of the effect of the two distinct reduction conditions on substrates of the same type is required. Thus, a series of tosylhydrazones derived from conjugated ketones was prepared and tested under the mild reduction conditions described.

As shown in Table I, $NaBD_3CN$ reduction of the tosylhydrazone **1** produced **6** as the sole product. The deuterium labeling of **6** clearly shows that the initial hydride attack occurs at the imino carbon. When the conformationally fixed transoid α,β-unsaturated tosylhydrazones **2** and **3** were reduced with $NaBD_3CN$, mixtures of hydrocarbons consisting of alkenes and alkanes (compounds **7–9**) were obtained. Based on the labeling patterns of the products, the saturated alkane formation observed in these cases must proceed via a pathway involving a Michael-type hydride addition to the β-carbon of the protonated conjugated tosylhydrazone.[2,3c,13] This is followed by the isomerization of the resulting alkenylhydrazine to the saturated tosylhydrazone which undergoes a second cycle of reprotonation and reduction to produce the saturated hydrocarbon (eq 3). A similar double reduction has been noted by Taylor and Djerassi in the reduction of α,β-unsaturated steroidal tosylhydrazones.[4a] The hydrogen incorporated at the original carbonyl site in **7–9** is clearly derived directly from the hydride reducing agent.

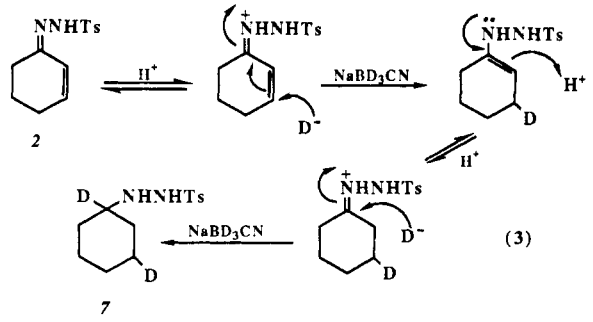
When the tosylhydrazones of α and β-ionone (**4** and **5**) were reduced by $NaBD_3CN$, alkanes where the double

(10) Han, O.; Shih, Y.; Liu, L.-d.; Liu, H. W. *J. Org. Chem.* **1988**, *53*, 2105.

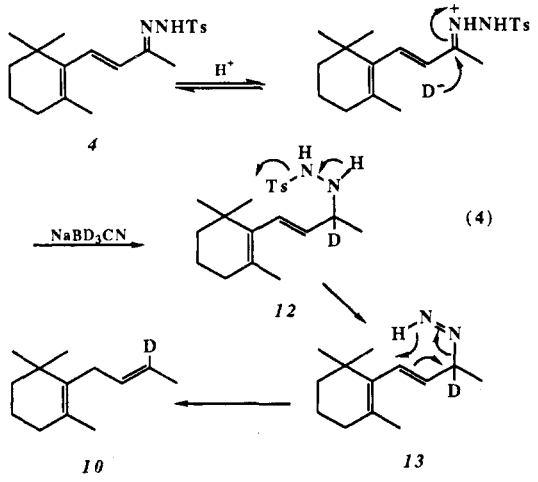
(11) (a) Buckingham, J. *Quart. Rev.* **1969**, *23*, 37, and references cited therein. (b) Simon, H.; Kraus, A. In *Synthetic Methods for Carbohydrates*, ACS Symposium Series, El Khadem, H. S., Ed.; American Chemical Society: Washington, DC, 1976; Vol. 39, p 188.

(12) (a) Bamford, W. R.; Stevens, T. S. *J. Chem. Soc.* **1952**, 4735. (b) Shapiro, R. H. *Org. React. N.Y.* **1976**, *23*, 405, and references cited therein.

(13) Reduction of α,β-unsaturated systems by hydride addition in a 1,4-fashion has also been noted for $NaBH_4$ (Brown, H. C.; Hess, H. M. *J. Org. Chem.* **1969**, *34*, 2206) and $LiAlH_4$ (Elphimoff-Felkin, I.; Verrier, M. *Tetrahedron Lett.* **1968**, 1515).



bond had migrated to the position formerly occupied by the carbonyl moiety were isolated as the major products (**10** and **11**, respectively). Only a trace amount of the hydrazine derivative (such as **12**) was found in the reaction mixture. The observed alkene migration has been suggested to proceed through a diazene intermediate **13**, which deposits a hydride via a 1,5-shift as illustrated in eq 4.[4b,5a] As expected, the deuterium found in **10–12** is again located exclusively at the original carbonyl carbon.

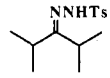
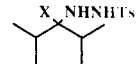
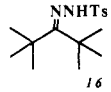
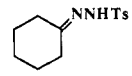
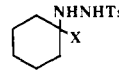
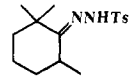
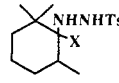
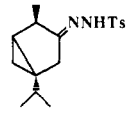
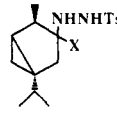
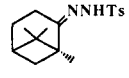


On the basis of these results, it is evident that cyanoborohydride reduction of α,β-unsaturated tosylhydrazones proceeds via the same course (eq 1) regardless of the modification of the reaction conditions. Therefore, the earlier conjecture[10] that the reduction mechanism is determined by the medium and temperature should be amended.

Tosylhydrazones of Saturated Ketones. To further explore the scope and limitations of the direct hydride attack mechanism (eq 1), attention was then directed to the study of the cyanoborohydride reduction of tosylhydrazones of saturated ketones. It is noteworthy that the fundamental distinction between the mechanisms shown in eq 1 and 2 is the actual mode of the reduction of the imine group of the tosylhydrazones. Namely, in eq 1, the C=N moiety is reduced via a direct hydride addition, while in eq 2, the C=N function is saturated through a hydrazone–azohydrazine tautomerization, and the actual reduction occurs on the azo group. It is expected that varying degrees of substitution around the imino carbon may impose steric constraints of different magnitudes toward nucleophilic attack. If present to a high degree, such steric interaction may affect the path of hydride delivery during reduction and alter the reaction course. Thus, a variety of tosylhydrazones (**14–20**) prepared from both simple and hindered ketones were examined under the mild conditions described above.

Unfortunately, the major products isolated from the reduction of this series of tosylhydrazones, especially compounds bearing more than two substituents α to the imino carbon, were the corresponding fully reduced simple alkanes whose structures are bereft of mechanistic information. This problem was circumvented by carefully controlling the reaction pH, keeping the reaction mixture cool during the reaction and workup, and washing the silica gel column with Et_3N prior to chromatographic purification to increase the yield of the minor, albeit desired, hydrazine product. Although the improvement was only modest, adopting these measures has allowed sufficient hydrazine product to be isolated in each case for NMR analysis.

Table II. Reduction of Tosylhydrazones of Saturated Ketones

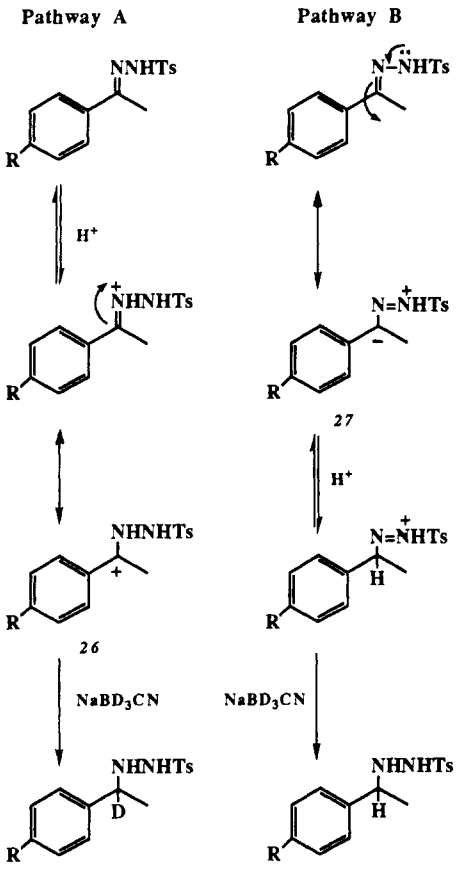
substrate	product	X = D	X = H
 14	 21	100%	0%
 15	 22	100%	0%
 16	NR		
 17	 23	94%	6%
 18	 24	100%	0%
 19	 25	96%	4%
 20	NR		

Presented in Table II are the results of reduction of this series of saturated tosylhydrazones with $NaBD_3CN$. The outcomes are surprisingly uniform despite the structural variations of the tosylhydrazones used. Namely, the deuterium atom incorporated at the former carbonyl carbon of every tosylhydrazine characterized (**21–25**) was derived exclusively from the deuteride reducing agent.[14] These results indicate that the reduction of tosylhydrazones of saturated ketones is akin to the reduction of α,β-unsaturated tosylhydrazones, and must proceed via a direct hydride addition to the imino carbon of the substrate (eq 1). This conclusion was further supported by the reductions of the tosylhydrazones of di-*tert*-butyl ketone **16**[15] and *d*-camphor **20** in which no reactions were discernible. Apparently, hydride attack on the imino carbon with concomitant formation of tetrahedron geom-

(14) Compounds **24** and **25**, derived from the reduction of tosylhydrazones of 2,2,6-trimethylcyclohexanone **18** and thujone **19**, respectively, were both mixtures of two stereoisomers, which were found to be labile to repeated chromatographic separations. However, the coexistence of two stereoisomers in each sample imposed no complication to the NMR analysis, since the corresponding hydrazine methine (C*H*N) resonance was well resolved.

(15) This compound was prepared from trimethylacetonitrile according to Hartzler's procedure (Hartzler, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 4527).

Scheme I



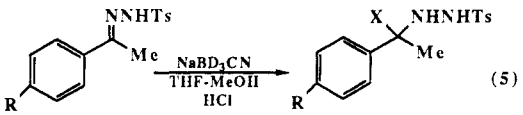
etry was impeded considerably by the steric interaction between the developing hydrazine and the proximate bulky substituents. Similar marked rate decreases have also been noted in the reduction of these two compounds under the conventional reduction conditions (DMF–sulfolane, 105–110 °C).[3c] Thus, reduction of simple ketone tosylhydrazones appears to be following only the direct hydride addition mechanism. If the bulkiness of the α-substituent is great enough to prevent the hydride attack necessary for the formation of the hydrazine, no reaction will take place.

Tosylhydrazones of Aryl Ketones. Another aspect distinguishing the mechanisms of eq 1 and 2 is the differing nature of charge delocalization at the imino carbon during the transition of this reduction. As shown in Scheme I, initial protonation of the C=N bond (pathway A) promotes the polarization of the iminium moiety, which makes the azomethine carbon positively charged (**26**) and, consequently, vulnerable to nucleophilic attack. Following this route, the hydrogen atom incorporated at the original carbonyl carbon should be derived from the hydride reducing reagent. However, a hydrazone is a nitrogen analogue of enamines. A hydrazone structure is similar to those of vinyl ethers, vinyl sulfides, *N*-vinylcarboxamides, and *N*-vinylsulfonamides, which all behave as 1,3-dipolar species.[16] The conjugation of the C=N bond with an adjacent nitrogen atom facilitates the delocalization of the nonbonding electrons on the nitrogen to the olefinic β-carbon and thus renders the azomethine carbon negatively charged (**27**). Such hydrazone–azohydrazine tautomerization is known to be catalyzed by acid[11] and subsequent reduction removes azohydrazine from the equilibrium, driving the tautomerization to completion. This mechanism will lead to solvent proton incorporation at the former carbonyl carbon (pathway B).

Table III. Reduction of Tosylhydrazones of Aryl Ketones

substrate	R	product	X = D	X = H
28	NH_2	36	95%	5%
29	OMe	37	90%	10%
30	H	38	83%	17%
31	Cl	39	80%	20%
32	CO_2Et	40	67%	33%
33	CF_3	41	70%	30%
34	CN	42	43%	57%
35	NO_2	43	24%	76%

In order to characterize the electronic nature of the transition state and to assess its effect on the regulation of these reaction mechanisms, a series of reductions of tosylhydrazones prepared from aryl ketones were conducted. These compounds (**28–35**) are all of methyl phenyl ketone origin, and each bears a different substituent with well defined electronic properties at the para position so that the reaction's sensitivity toward charge development can be probed (eq 5). Although the aryl carbonyl derivatives have been reported to be quite resistant to reduction by cyanoborohydride in DMF–sulfolane even at elevated temperatures due to the low electrophilicity at the imino carbon,[3c] they were swiftly reduced with high yields under the reaction conditions used (THF–MeOH, 0 °C).[17]



(5)

The results of reduction with $NaBD_3CN$ are summarized in Table III. It is noteworthy that the labeling patterns are remarkably different from those observed for the reduction of saturated and α,β-unsaturated tosylhydrazones under identical conditions. As noted in Table III, the unlabeled hydrazine, in most cases, was isolated concurrently with the labeled hydrazine. The ratio of the unlabeled and labeled species of each product (**36–43**) varies considerably with the electronic properties of the para substituent.[18] This ratio increases slowly, with a low value for an electron-releasing substituent (R = NH_2), a moderate value with R = CO_2Et and CF_3, and then escalates more rapidly to higher values when R = CN and NO_2 are used.

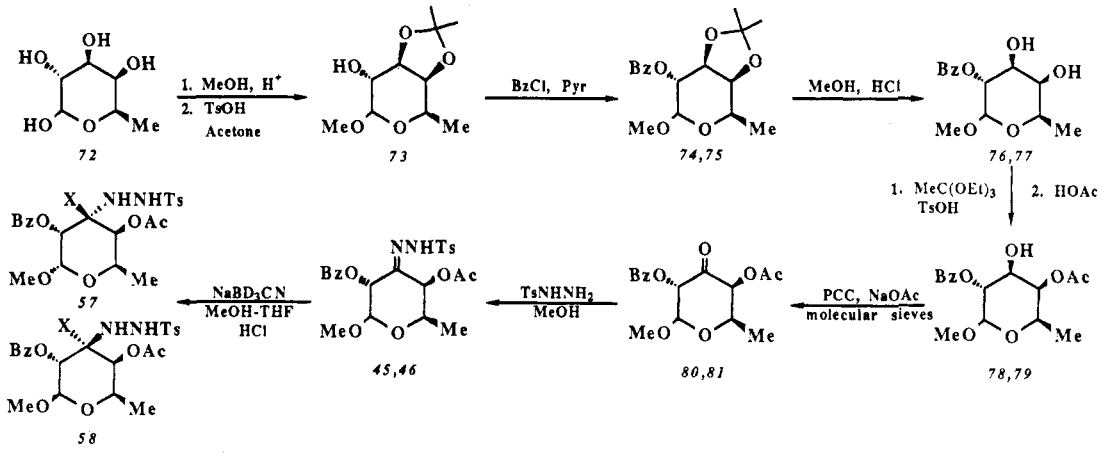
Since the reduction is essentially irreversible and the reactions were always run to completion, examining the ratio of the normal and labeled species of each hydrazine product provides a convenient means to quantitatively estimate the preference of the reaction flux to advance via these two alternate routes (pathway A or B) for each hydrazone. These analyses have revealed a close correlation

(16) Some hydrazones are known to behave as 1,3-dipolar compounds in which the azomethine carbon is a center of nucleophilic attack (examples, see: (a) Snider, B. B.; Conn, R. S. E.; Sealfon, S. *J. Org. Chem.* **1979**, *44*, 218. (b) Le Fevre, G. ; Hamelin, J. *Tetrahedron Lett.* **1980**, 878). Cases are also known which have electrophilic substitution occurring at the azomethine carbon (examples, see: (c) Grundemann, E.; Brehme, R.; Nikolajewski, H. E. *J. Prakt. Chem.* **1982**, *324*, 575. (d) Kamitori, Y.; Masuda, R.; Fujitani, T.; Ohara, S.; Yokoyama, T. *J. Org. Chem.* **1988**, *53*, 129. (e) Kamitori, Y.; Hojo, M.; Msuda, R.; Yoshida, T.; Ohara, S.; Yamada, K.; Yoshikawa, N. *Ibid.* **1988**, *53*, 519).

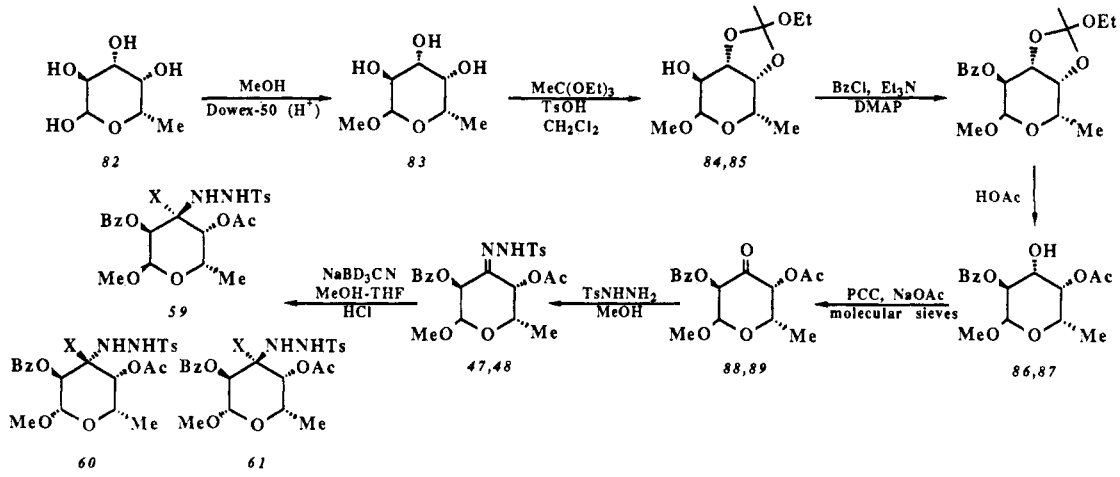
(17) It was reported that addition of mercury(II) complexes is necessary to overcome the reluctance toward $NaBH_3CN$ reduction of some aryl carbonyl tosylhydrazones (Rosini, G.; Medici, A. *Synthesis* **1976**, 530). However, the reduction under the conditions described here was reasonably rapid, no mercury(II) complex was required.

(18) The ratio of the unlabeled and labeled species of each hydrazine product was estimated based on the NMR integration of the *CH*N signal whose assignment was confirmed by 2D-COSY analysis.

Scheme II



Scheme III



between these ratios and the substituent constants σ_p of the respective para-substituents. In fact, a Hammett plot (Figure 1) of the logarithm of the product ratios (log H/D) versus σ_p shows a distinct break, with R = NO_2, CN, CF_3, and CO_2Et on one line (ρ = 2.69) and the other substituents on another line (ρ = 0.79). It is apparent that the substituent effect is smaller for electron-donating and larger for electron-attracting substituents on the phenyl ring. The failure to obtain a linear plot is not unusual. Hammett plots with concave upward curvatures are usually ascribed to competition between two mechanisms with opposite electronic demands, where each one predominates over a different range of σ values.[19] By analogy, the nonlinear correlation of the product ratios and the substituent constants seen in this case unequivocally confirms the presence of two competing mechanisms in this reduction. With electron-withdrawing substituents, the reaction favors an initial tautomerization prior to reduction (pathway B). For electron-supplying substituents, however, the reaction prefers the direct hydride attack route (pathway A). The large positive ρ value of 2.69 found for arylhydrazones bearing strong electron-withdrawing substituents also supports an electron-rich transition state.

Tosylhydrazones of Sugar Derivatives and Hydroxyl Ketones. On the basis of the aforementioned results, the mechanistic diversity of the cyanoborohydride

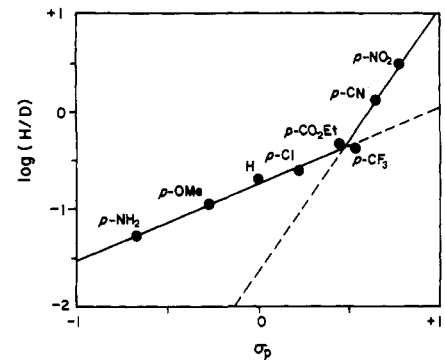
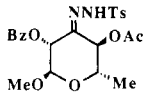
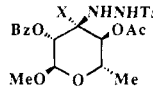
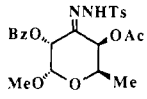
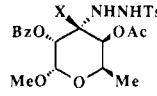
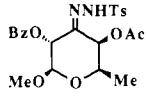
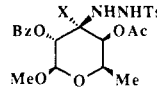
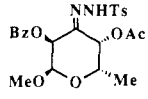
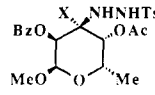
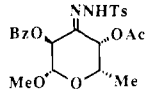
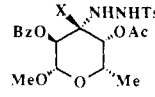
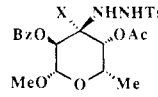
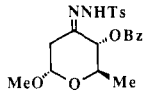
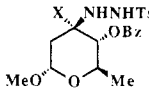
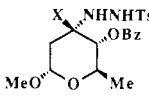
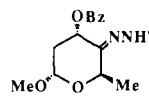
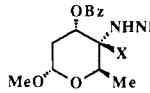
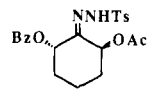
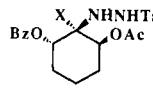
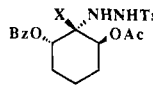
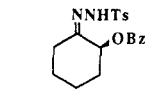
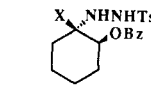
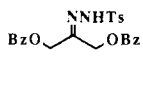
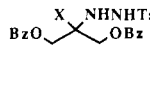
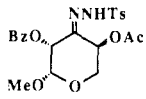
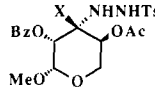
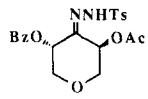
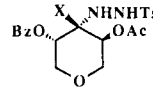
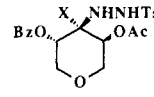


Figure 1. Hammett plot for the reduction of tosylhydrazones of aryl ketones. (H/D) represents the ratio between the unlabeled and labeled species of each hydrazine product.

reduction of tosylhydrazones appears to be directly correlated to the electronic nature of the transition state. It also reveals that the tautomerization-then-reduction mechanism (eq 2) prevails when the delocalization of the transiently developed charge is promoted through inductive stabilization by electron-withdrawing substituents. These findings coincide with our earlier suggestion that when the hydrazone–azohydrazine tautomerization is facilitated, the mechanism shown in eq 2 becomes prominent. However, the reduction of a sugar tosylhydrazone with $NaBD_3CN$ had been shown to proceed solely via the mechanism of eq 2 since the corresponding hydrazine product is devoid of any deuterium incorporation at the former carbonyl carbon.[10] From the examination of the structure of the sugar tosylhydrazone 44 used in our earlier

(19) (a) Schreck, J. O. *J. Chem. Educ.* **1971**, *48*, 103. (b) Hirsch, J. A. *Concepts in Theoretical Organic Chemistry*, Allyn & Bacon, Inc.; Boston, 1974; pp 128–146. (c) Schowen, R. L.; Hopper, C. R.; Bazikian, C. M. *J. Am. Chem. Soc.* **1972**, *94*, 3095. (d) Tashma, R.; Rappoport, Z. *Ibid.* **1977**, *99*, 1845.

Table IV. Reduction of Tosylhydrazones of Sugar Derivatives and Hydroxyl Ketones

substrate	product	X = D	X = H
 44	 56	0%	100%
 45	 57	0%	100%
 46	 58	0%	100%
 47	 59	0%	100%
 48	 60	0%	100%
	 61	0%	100%
 49	 62	42%	58%
	 63	35%	65%
 50	 64	40%	60%
 51	 65	67%	33%
	 66	75%	25%
 52	 67	100%	0%
 53	 68	100%	0%
 54	 69	32%	68%
 55	 70	45%	55%
	 71	45%	55%

study, it is not obvious why the tautomerization-then-reduction mechanism should dominate over the direct hydride attack mechanism. In an attempt to gain more insights into the reduction of this class of molecules, a series of tosylhydrazones of sugar derivatives and hydroxyl ketones **45–55** were synthesized and tested.

Preparation of these model compounds called for the regioselective esterification and oxidation at the designated loci of the polyhydroxyl precursors. As shown in Schemes II and III, the key step shared by the syntheses of the tosylhydrazone derivatives **45–48** involves a selective protection of two vicinal cis diols via orthoester formation. This allows the subsequent esterification (benzoylation) to occur in a well-defined manner. Hydrolysis of the resulting derivatized orthoester via a dioxolenium ion intermediate is another crucial step which gives almost exclusively the hydroxy ester product with the acetyl ester function axial and the hydroxyl group equatorial.[20] Since the precursors used in these syntheses had been carefully chosen, a 1,3-diester was formed as the major, if not the only, product in each case. Subsequent oxidation of the C-3 hydroxyl group with pyridinium chlorochromate[21] and coupling of the nascent keto sugar derivatives with tosylhydrazine was straightforward and gave high yields. Thus, relying on these two stereospecific manipulations, compounds **45**/**46** and **47**/**48** were readily prepared from D-fucose **72** (Scheme II)[22] and L-fucose **82** (Scheme III), respectively.

As summarized in Table IV, reduction of these fully substituted hexopyranoside tosylhydrazones **44–48** with sodium cyanoborodeuteride showed no deuterium incorporation, and thus confirmed our earlier observation that the hydrogen being delivered to the imino carbon in hexopyranose tosylhydrazones is not derived from the boron reducing agent. Reduction of these sugar tosylhydrazones evidently follows the tautomerization-then-reduction route (eq 2), as previously surmised. The common structural feature shared by compounds **44–48** is the array of two ester groups displayed separately on each side of the hydrazone moiety. Recalling the conclusions drawn from the reductions of aryl carbonyl hydrazones, it is likely that the electron-withdrawing effect compelled by the α,α'-diester functionality may stabilize an electron-rich transition state, and thus facilitate the foregoing mechanism for the reduction of these molecules. If this explanation is correct, removal of one of the α-ester groups from the hydrazone substrate would disrupt the generation of transient carbanionic character on the imino carbon and consequently, induce an alteration of the reduction pathway. Thus, compounds **49** and **50** were synthesized to test this contention.

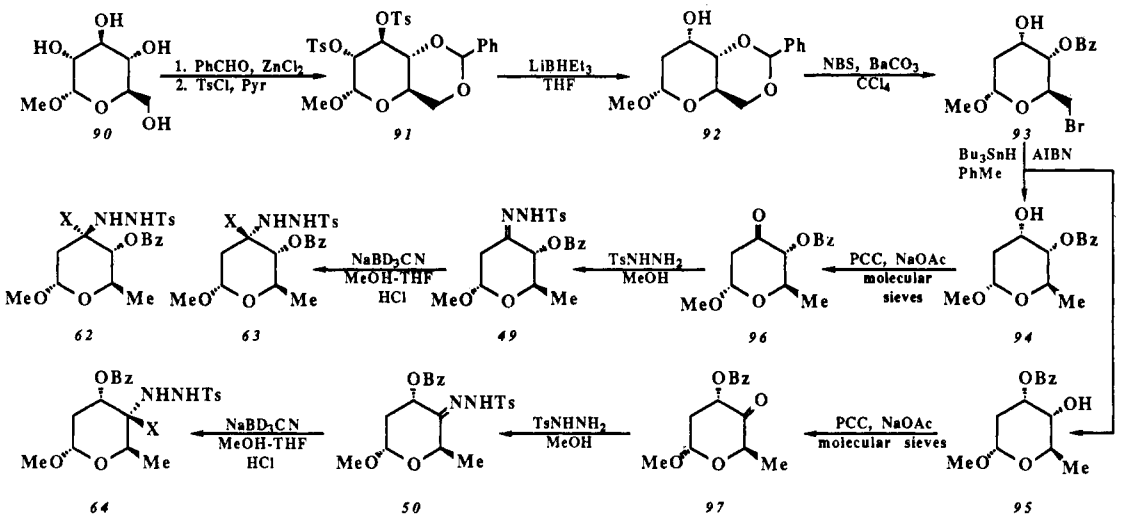
Preparation of the 2,6-dideoxypyranose hydrazones **49** and **50** shared several of the initial steps as depicted in Scheme IV. The C-2 deoxygenation was accomplished by

(20) (a) King, J. F.; Allbutt, A. D. *Can. J. Chem.* **1970**, *48*, 1754. (b) Deslongchamps, P.; Atlani, P.; Frehel, D.; Malaval, A. *Ibid.* **1972**, *50*, 3405.

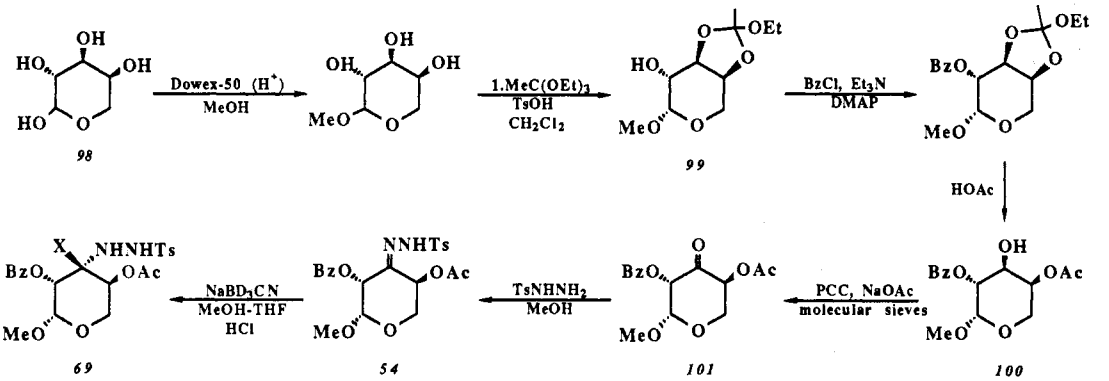
(21) (a) Herscovici, J.; Antonakis, K. *J. Chem. Soc., Chem. Commun.* **1980**, 561. (b) Herscovici, J.; Egron, M.; Antonakis, K. *J. Chem. Soc., Perkin Trans. 1*, **1982**, 1967. (c) Czernecki, S.; Georgoulis, C.; Stevens, C. L.; Vijayakakumaran, K. *Synth. Commun.* **1986**, *16*, 11.

(22) Weigel, T. M.; Liu, H. W. *Tetrahedron Lett.* **1988**, 4221.

Scheme IV



Scheme V



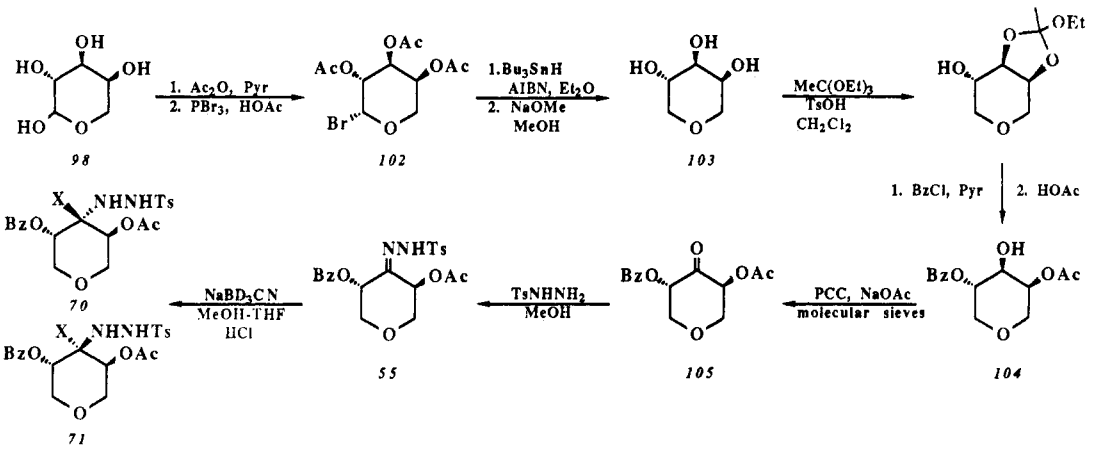
lithium triethylborohydride reduction of the ditosylate species **91**. This reductive cleavage is believed to proceed via the corresponding 3-monotosylate and then an α-D-*allo*-2,3-epoxide intermediate.[23] *N*-Bromosuccinimide-induced cleavage of the benzylidene group in **92**[24] followed by dehalogenation of **93** with tin hydride[25] generated two products, **94** and **95**, due to the intramolecular benzoyl migration. The extent of such neighboring group participation was found to be directly proportional to the reaction temperature. This migration was also discernible in the debenzylidene step when the reaction was conducted under reflux. The final steps of these syntheses included an oxidation and the tosylhydrazone formation. As revealed in Table IV, reduction of **49** and **50** with $NaBD_3CN$ indeed showed deuterium incorporation of 35–42% at the former carbonyl carbon in the hydrazine products **62–64**. These results clearly demonstrate the vital role played by the ester group on regulating the reduction mechanism, and further support the notion that the inductive effect imposed by the ester group is accountable for the mechanistic dominance of the tautomerization-then-reduction pathway.

In an attempt to assess the impact of the inductive effect on the reduction mechanism in general, the same analysis was performed on the carbocyclic and acyclic α,α′-diester tosylhydrazones **51–53**. Preparation of **52** and **53** was forthright and is detailed in the Experimental Section. The cyclohexanone 1,3-diester tosylhydrazone **51** was prepared from cyclohexane-1,2,3-triol[26] based on the same strategy employed in the synthesis of **45–48**. Attempts to prepare this compound by a regiospecific oxidation of the triol with bromine and sodium carbonate in water to generate the corresponding 1,3-dihydroxyl ketone[27] precursor were futile.

The outcomes of $NaBD_3CN$ reduction of these compounds are summarized in Table IV. It was found that the deuterium content of the hydrazine product derived from **51** was 67–75% and that from **52** was quantitative. Apparently, reduction of these carbocyclic tosylhydrazone analogues does not abide by the same reaction course adopted by their pyranoside counterparts **44–50** despite the fact that they all possess the same structural feature, having ester groups α to the imino carbon. Complete deuterium labeling on the tosylhydrazine product was also found for the reduction of **53**, which is the simplest acyclic α,α′-diester tosylhydrazone. These results clearly show that the inductive effect imposed by an α-ester group alone would not be sufficient to slant the reaction mechanism overwhelmingly for the tautomerization-then-reduction route. The cyclic skeleton, especially the pyranose ring structure, seems to be another weighty factor determining the mechanistic diversity. Therefore, the effect of substitution at other loci of the pyranose substrate on the

(23) Baer, H. H.; Hanna, H. R. *Carbohydr. Res.* **1982**, *110*, 19.
(24) Hannesian, S.; Plessas, N. R. *J. Org. Chem.* **1969**, *34*, 1053.
(25) Arita, H.; Ueda, N.; Matsushima, Y. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 567.
(26) The 1,2,3-cyclohexanetriol was purchased from American Tokyo Kasei, Inc. The stereochemistry of this commercial product was not specified. However, based on our results, the relative configurations between these hydroxyl moieties are 1,2-cis and 2,3-trans.
(27) Posternak, T.; Ravenna, F. *Helv. Chim. Acid* **1947**, *30*, 441.

Scheme VI



reduction mechanism was probed.

As shown in Scheme V, preparation of model compound **54** from L-arabinose **98** was analogous to that used for compounds **45–48**. Preparation of another model compound **55** was initiated by C-1 deoxygenation, which was effected through a sequence of acetylation, bromination, hydride reduction, and alkaline hydrolysis.[28] From this 1,5-anhydro-D-arabinitol intermediate **103**, ethoxyethylidene protection followed by benzoylation, hydrolysis, oxidation, and tosylhydrazone coupling led to the formation of **55** (Scheme VI). Interestingly, the mechanistic monopoly of the tautomerization-then-reduction pathway subsided as the substituents crucial for stabilizing the ring conformation were expelled. For example, the extent of deuterium incorporation became prominent (32%) for the reduction of **54** whose C-5 methyl group is missing. This result implied that one third of the reaction flux was now proceeding through the direct hydride attack pathway (eq 1). Such mechanistic divergency was even more predominant when both the C-1 methoxyl and C-5 methyl group were removed from the pyranose tosylhydrazone structure. This is well exemplified by the reduction of **55** to **70** and **71** in which the tautomerization-then-reduction mechanism becomes less significant and the direct hydride attack mechanism now accounts for 45% of the total reaction flux.

No special insight is required to perceive that the ring structure plays a decisive role in controlling the direction of the reaction flux. However, the exact mode of this regulation is not obvious. It is probable that the alleviation of the deformation compelled by a sp^2 center on the pyranose ring structure via tautomerization of the hydrazone to the corresponding azohydrazine prior to reduction provides, at least, a portion of the driving force for the mechanistic bias. This effect, in conjugation with the inductive effect of the α-ester group, may be responsible for the dominance of the tautomerization-then-reduction mechanism found in the reduction of sugar tosylhydrazones.[29]

(28) (a) Gray, G. R.; Barker, R *J. Org. Chem.* **1967**, *32*, 2764. (b) Kocienski, P.; Pant, C. *Carbohydr. Res.* **1982**, *110*, 330.

(29) Given the fact that the addition of hydrogen to the imino carbon may occur by two distinct pathways, it was surprising to note that the stereochemical outcome of this incorporation is virtually identical for these two mechanisms. For example, the reduction products of compounds **49** and **51** exhibit very similar H/D ratio for each diastereomer in the products. A review of Table V also shows that the added hydrogen at the imino carbon is generally introduced trans to the anomeric methoxyl group of the pyranose substrate. Thus, the stereoselectivity of the hydrogen addition step seems to be independent of both structure and mechanism. The controlling factors are not immediately clear. Experiments designed to elucidate the mechanistic basis of such a stereospecificity are in progress.

Conclusions

The results summarized in this paper provide a detailed account of the reaction mechanism of the reduction of tosylhydrazone by $NaBH_3CN$, a mild albeit versatile deoxygenation method. The experiments described above unequivocally demonstrated the existence of two possible mechanisms for this reduction. Although the ratios of the unlabeled and labeled species of each hydrazine product may not be accurate enough to truly reflect the partition ratios of the reaction reflux between these two mechanisms, these data are, at least, qualitatively informative. Namely, the direct hydride attack mechanism (eq 1) is the main reaction pathway in most cases, due to the propensity of $NaBH_3CN$ to selectively attack the iminium ion. However, the tautomerization-then-reduction mechanism (eq 2) becomes prominent if the tautomerization of hydrazone to azohydrazine is facilitated by inductive effects and/or conformational constraints. Thus, the mechanistic diversity of this reduction depends on the intrinsic properties of the tosylhydrazone structure, not on the reduction conditions as previously surmised.

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, sodium 2,2-dimethyl-2-silapentane-5-sulfonate, 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 into the staining solutions of vanillin/ethanol/H_2SO_4 (1:98:1) or phosphomolybdic acid (7% EtOH solution) and then heating. Solvents, unless otherwise specified, were reagent grade and distilled once prior to use.

General Procedures. (a) Hydrazone Formation. To a well-agitated solution of *p*-toluenesulfonhydrazide in 3–4 mL of ethanol is added an equal molar amount of ketone. The reaction mixture is refluxed for 0.5–2 h during which time the resulting hydrazone may precipitate. The crystalline product is collected by filtration and washed thoroughly with cold ether. For the reaction in which no precipitate is formed after refluxing, the solvent is evaporated and the crude product is purified by flash chromatography if necessary. For more labile ketones, such as most sugar and polyhydroxyl ketones, the tosylhydrazone formation is conducted in methylene chloride at room temperature.

(b) Tosylhydrazone Reduction. To a stirred mixture of tosylhydrazone (150 mg) and a trace amount of methyl orange in a solution of 1:1 THF–MeOH (4 mL) under nitrogen is 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 is just changed to yellow. The acidity of this reaction could also be monitored and adjusted by a pH controller; however, visual discernment of the color of the reaction and dropwise addition of acid via syringe to keep the proper acidity gave practically the same results. Additional amounts of acid and reducing agent are added in two to three portions over the next 3–6 h until the reaction is complete. The total amount of $NaBH_3CN$ added is 3–4 molar equiv of that of the tosylhydrazone. The yields of saturated hydrazines are enhanced by performing the reaction at 0 °C rather than room temperature. Workup consists of neutralization with saturated sodium bicarbonate and extraction with methylene chloride. The combined organic extracts are washed with brine, dried over anhydrous sodium sulfate, and evaporated. Most of the aromatic ketone tosylhydrazones can be recrystallized from EtOAc/hexane while others are purified by flash chromatography on silica gel. Lowering the reaction temperature and avoiding the acid wash in the workup are crucial to minimize the formation of fully reduced hydrocarbons. No attempt was made to optimize the yield. Each hydrazine obtained was characterized by the combination of 2D-COSY, NOE difference ^1H NMR, and ^{13}C NMR analyses.

Preparation of compounds **1–43**, **51–53**, and **65–68** were based on the route procedures described above. The spectroscopic and analytical data of these compounds, made available to the editor, were all satisfactory.

Methyl 6-Deoxy-3,4-*O*-isopropylidene-D-galactopyranoside (73). This compound was synthesized from 6-deoxy-D-galactopyranoside **72**, which was derived from galactose following a published procedure.[22] The crude methyl 6-deoxy-D-galactopyranoside (1.36 g, 7.64 mmol), prepared via acidic methanolysis (Dowex-50(H^+)/MeOH) of 6-deoxy-D-galactopyranose **72**, was dissolved in 50 mL of freshly distilled acetone. A catalytic amount of *p*-toluenesulfonic acid was added so that the pH of the reaction solution was acidic. The reaction was stirred at room temperature for 40 h. The solution was then neutralized with solid $NaHCO_3$, filtered through Celite, and concentrated. The product was purified as a mixture of C-1 α and β isomers by flash chromatography (2% MeOH/CH_2Cl_2). NMR analysis revealed that the ratio between the α and β anomers was 6:1. ^1H NMR ($CDCl_3$) of the α anomer: δ 4.45 (1 H, d, J = 3.6, 1-H), 3.96–3.82 (4 H, m, 2-H, 3-H, 4-H, 5-H), 3.19 (3 H, s, OMe), 1.28 (3 H, s, Me), 1.11 (3 H, s, Me), 1.10 (3 H, d, J = 7.4, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer: δ 108.8 (ketalic C), 99.0 (C-1), 76.1 (C-4)*, 75.6 (C-3)*, 69.4 (C-2), 63.3 (C-5), 55.1 (OMe), 27.8 (Me), 25.9 (Me), 16.1 (C-6). ^1H NMR ($CDCl_3$) of the β anomer: δ 5.12 (1 H, d, J = 6.5, 1-H), 3.96–3.82 (4 H, m, 2-H, 3-H, 4-H, 5-H), 3.29 (3 H, s, OMe), 1.28 (3 H, s, Me), 1.17 (3 H, d, J = 6.5, 5-Me), 1.11 (3 H, s, Me). ^{13}C NMR ($CDCl_3$) of the β anomer: δ 109.4 (ketalic C), 103.2 (C-1), 79.0 (C-4)*, 77.6 (C-3)*, 73.1 (C-2), 68.7 (C-5), 56.4 (OMe), 27.9 (Me), 26.1 (Me), 16.3 (C-6).

Methyl 2-*O*-Benzoyl-6-deoxy-3,4-*O*-isopropylidene-α-D-galactopyranoside (74) and Methyl 2-*O*-Benzoyl-6-deoxy-3,4-*O*-isopropylidene-β-D-galactopyranoside (75). To a solution of **73** (821 mg, 3.8 mmol) in 8 mL of dry pyridine was added benzoyl chloride (0.53 mL, 4.56 mmol). The reaction was stirred for 90 min at room temperature and then quenched with a few drops of methanol. The pyridine was removed in the presence of benzene in vacuo, and this process was repeated five times. The α (**74**) and β (**75**) anomers of this product were separated by flash chromatography (15% EtOAc/hexane) with a total yield of 97%. ^1H NMR ($CDCl_3$) of the α anomer **74**: δ 8.36–8.03 (2 H, m, Ar H's), 7.56–7.36 (3 H, m, Ar H's), 5.12 (1 H, dd, J = 8.2, 3.5, 2-H), 4.91 (1 H, d, J = 3.5, 1-H), 4.50–4.08 (3 H, m, 3-H, 4-H, 5-H), 3.34 (3 H, s, OMe), 1.55 (3 H, s, Me), 1.39 (3 H, d, J = 6.6, 5-Me), 1.35 (3 H, s, Me). ^{13}C NMR ($CDCl_3$) of the α anomer **74**: δ 166.2 (Ph*C*=O), 133.2, 130.1, 130.0, 128.3 (Ar C's), 109.4 (ketalic C), 97.4 (C-1), 76.3 (C-4), 73.6 (C-2)*, 72.6 (C-3)*, 63.1 (C-5), 55.6 (OMe), 28.1 (Me), 26.5 (Me), 16.3 (C-6). ^1H NMR ($CDCl_3$) of the β anomer **75**: δ 8.36–8.03 (2 H, m, Ar H's), 7.56–7.36 (3 H, m, Ar H's), 5.23 (1 H, d, J = 9.0, 1-H), 5.17–5.10 (1 H, m, 2-H), 4.50–4.08 (3 H, m, 3-H, 4-H, 5-H), 3.44 (3 H, s, OMe), 1.61 (3 H, s, Me), 1.45 (3 H, d, J = 6.6, 5-Me), 1.35 (3 H, s, Me). ^{13}C NMR ($CDCl_3$) of the β anomer **75**: δ 165.5 (Ph*C*=O), 133.6, 129.9, 129.8, 128.4 (Ar C's), 110.3 (ketalic C), 101.4 (C-1), 77.3 (C-4), 76.6 (C-2), 73.6 (C-3), 69.0 (C-5), 56.6 (OMe), 27.8 (Me), 26.5 (Me), 16.6 (C-6).

Methyl 2-*O*-Benzoyl-6-deoxy-α-D-galactopyranoside (76) and Methyl 2-*O*-Benzoyl-6-deoxy-β-D-galactopyranoside (77). To a solution of **74** (125.9 mg, 0.39 mmol) in 5 mL of freshly distilled methanol was slowly added concentrated HCl (62.5 μL) so that the final concentration of acid in the solution was 0.15 N. The reaction was stirred for 45 min at room temperature. The solution was neutralized with solid $NaHCO_3$, filtered through Celite, and concentrated. Only one spot was revealed on TLC in several different solvent systems; therefore, the product was used in subseuqent reactions without further purification. The same procedure was also employed to convert the β anomer **75** to **77**. ^1H NMR ($CDCl_3$) of the α anomer **76**: δ 8.09–7.93 (2 H, m, Ar H's), 7.57–7.38 (3 H, m, Ar H's), 5.26–5.19 (1 H, m, 2-H), 4.94 (1 H, d, J = 3.4, 1-H), 4.15–3.82 (3 H, m, 3-H, 4-H, 5-H), 3.35 (3 H, s, OMe), 1.29 (3 H, d, J = 6.6, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **76**: δ 167.0 (Ph*C*=O), 133.1, 129.8, 128.4, 128.3 (Ar C's), 97.5 (C-1), 72.4 (C-4)*, 71.9 (C-2)*, 68.4 (C-3), 65.7 (C-5), 55.3 (OMe), 16.1 (C-6). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.39; H, 6.32. ^1H NMR ($CDCl_3$) of the β anomer **77**: δ 8.13–8.08 (2 H, m, Ar H's), 7.61–7.32 (3 H, m, Ar H's), 5.42 (1 H, m, 2-H), 4.24 (1 H, d, J = 7.6, 1-H), 3.93–3.68 (3 H, m, 3-H, 4-H, 5-H), 3.60 (3 H, s, OMe), 1.28 (3 H, d, J = 6.4, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **77**: δ 166.7 (Ph*C*=O), 133.2, 130.0, 129.5, 128.4 (Ar C's), 102.0 (C-1), 73.6 (C-2), 71.5 (C-3), 70.8 (C-4), 69.5 (C-5), 56.8 (OMe), 16.2 (C-6). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.48; H, 6.40.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-D-galactopyranoside (78) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-β-D-galactopyranoside (79). To a suspension of compound **76** (149.5 mg, 0.53 mmol) in 25 mL of methylene chloride was added triethyl orthoacetate (970 μL, 5.29 mmol) and a catalytic amount of *p*-toluenesulfonic acid. After 12 h of stirring at room temperature the methylene chloride was evaporated in vacuo. The residual oil was then dissolved in 80% acetic acid (5 mL) to give a clear solution, and the reaction was allowed to proceed at room temperature for 15 min. The resulting mixture was extracted with methylene chloride, and the organic fractions were combined, washed twice with cold water and once with saturated sodium bicarbonate solution, and dried over anhydrous sodium sulfate prior to concentration. The residue was chromatographed on a silica gel column eluting with 1% MeOH/CH_2Cl_2 to provide 134 mg of the desired compound in pure form. The overall yield of these two steps was 48% (starting from compound **76**). This reaction and purification sequence was also carried out with the β anomer **77**. ^1H NMR ($CDCl_3$) of the α anomer **78**: δ 8.03 (2 H, d, J = 8.4, ortho H's), 7.50 (1 H, t, J = 7.5, para H), 7.39 (2 H, dd, J = 8.4, 7.5, meta H's), 5.25 (1 H, m, 4-H), 5.19 (1 H, dd, J = 10.4, 3.6, 2-H), 4.98 (1 H, d, J = 3.6, 1-H), 4.31 (1 H, m, 3-H), 4.05 (1 H, m, 5-H), 3.34 (3 H, s, OMe), 2.15 (3 H, s, CH_3C=O), 1.14 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **78**: δ 171.4 (CH_3C=O), 166.8 (Ph*C*=O), 133.3, 129.9, 129.6, 128.4 (Ar C's), 97.6 (C-1), 73.8 (C-4), 72.0 (C-2), 67.0 (C-3), 64.6 (C-5), 55.5 (OMe), 20.8 (CH_3C=O), 16.2 (C-6). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 58.99; H, 6.29. ^1H NMR ($CDCl_3$) of the β anomer **79**: δ 8.04–8.01 (2 H, d, J = 8.4, ortho H's), 7.56 (1 H, t, J = 7.2, para H), 7.44 (2 H, dd, J = 8.4, 7.2, meta H's), 5.23 (1 H, b s, 4-H), 5.20 (1 H, dd, J = 10.0, 7.9, 2-H), 4.48 (1 H, d, J = 7.9, 1-H), 3.98 (1 H, m, 3-H), 3.83 (1 H, m, 5-H), 3.50 (3 H, s, OMe), 2.20 (3 H, s, CH_3C=O), 1.25 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **79**: δ 171.3 (CH_3C=O), 166.9 (Ph*C*=O), 133.4, 129.9, 129.6, 128.4 (Ar C's), 101.8 (C-1), 73.6 (C-4)*, 73.0 (C-2)*, 71.8 (C-3), 69.4 (C-5), 57.0 (OMe), 20.8 (CH_3C=O), 16.4 (C-6). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.35; H, 6.18.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-D-*xylo*-hexopyranosid-3-ulose (80) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-β-D-*xylo*-hexopyranosid-3-ulose (81). Pyridinium chlorochromate (90.1 mg, 0.42 mmol) and sodium acetate (85.5 mg, 1.04 mmol) were dissolved in 20 mL of dry methylene chloride. Activated, powdered 3-Å molecular sieves (104 mg) were added to the mixture, and it was cooled to 0 °C. To this solution under nitrogen was added **78** (33.8 mg, 0.10 mmol), which was

dissolved in methylene chloride (5 mL). The reaction was stirred under nitrogen and allowed to warm up to room temperature over 3 h. The solution turned from bright orange to brown. The reaction mixture was diluted with 20 mL of anhydrous ether and was stirred for an additional 1 h. It was filtered through silica gel, which was then washed extensively with ether. The combined filtrates were concentrated to give the desired product **80** in almost pure form. The yield was 89%. This reaction was also carried out with the β anomer **79**. ^{1}H NMR ($CDCl_3$) of the α anomer **80**: δ 8.09 (2 H, d, J = 8.4, ortho H's), 7.57 (1 H, t, J = 7.5, para H), 7.43 (2 H, dd, J = 8.4, 7.5, meta H's), 5.88 (1 H, d, J = 4.2, 2-H), 5.24 (1 H, d, J = 4.2, 1-H), 5.17 (1 H, d, J = 1.8, 4-H), 4.31 (1 H, m, 5-H), 3.44 (3 H, s, OMe), 2.21 (3 H, s, CH_3C=O), 1.24 (3 H, d, J = 6.4, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **80**: δ 194.2 (C-3), 169.5 (CH_3C=O), 165.3 (PhC=O), 133.7, 130.1, 130.0, 128.5 (Ar C's), 100.5 (C-1), 78.3 (C-4), 74.3 (C-2), 67.9 (C-5), 55.8 (OMe), 20.6 (CH_3C=O), 15.6 (C-6). Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.86; H, 5.78. ^{1}H NMR ($CDCl_3$) of the β anomer **81**: δ 8.08 (2 H, d, J = 8.4, ortho H's), 7.56 (1 H, t, J = 7.3, para H), 7.44 (2 H, dd, J = 8.4, 7.3, meta H's), 5.62 (1 H, d, J = 7.8, 2-H), 5.16 (1 H, b s, 4-H), 4.69 (1 H, d, J = 7.8, 1-H), 3.90 (1 H, m, 5-H), 3.59 (3 H, s, OMe), 2.22 (3 H, s, CH_3C=O), 1.37 (3 H, d, J = 6.4, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **81**: δ 195.7 (C-3), 169.6 (CH_3C=O), 165.0 (PhC=O), 133.6, 130.0, 129.9, 128.5 (Ar C's), 102.9 (C-1), 76.9 (C-4), 70.6 (C-2), 66.8 (C-5), 57.3 (OMe), 20.6 (CH_3C=O), 15.8 (C-6). Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.41; H, 5.71.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-D-*xylo*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (45) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-β-D-*xylo*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (46). To a solution of **80** (30.1 mg, 93.5 μmol) in 15 mL of freshly distilled methanol was added *p*-toluenesulfonhydrazide (20.9 mg, 112 μmol). The reaction was stirred under nitrogen at room temperature for 12 h. Ether (15 mL) was added, and the mixture was stirred an additional 30 min. The solvent was evaporated in vacuo, and the product **45** was purified by flash chromatography (CH_2Cl_2). The yield was 82%. The same procedure was also used to convert the β anomer **81** to **46**. ^{1}H NMR ($CDCl_3$) of the α anomer **45**: δ 9.24 (1 H, s, NH), 8.05, 6.79 (2 H each, d, J = 8.2, Ts H's), 7.84–7.42 (5 H, m, Ar H's), 5.59 (1 H, d, J = 3.8, 2-H), 5.10 (1 H, d, J = 1.8, 4-H), 4.97 (1 H, d, J = 3.8, 1-H), 4.24 (1 H, m, 5-H), 3.43 (3 H, s, OMe), 2.25 (3 H, s, Ts-Me), 2.12 (3 H, s, CH_3C=O), 1.29 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **45**: δ 172.2 (CH_3C=O), 165.1 (PhC=O), 143.6 (C-3), 145.6, 133.5, 130.2, 129.3, 129.1, 128.4, 128.3, 128.1 (Ar C's), 99.0 (C-1), 68.5 (C-4)*, 68.4 (C-2)*, 64.6 (C-5), 55.6 (OMe), 21.6 (Ts-Me), 20.4 (CH_3C=O), 15.5 (C-6). ^{1}H NMR ($CDCl_3$) of the β anomer **46**: δ 9.33 (1 H, s, NH), 8.06, 6.82 (2 H each, d, J = 8.0, Ts H's), 7.85–7.25 (5 H, m, Ar H's), 5.40 (1 H, d, J = 8.1, 2-H), 5.06 (1 H, d, J = 1.5, 4-H), 4.67 (1 H, d, J = 8.1, 1-H), 3.88 (1 H, m, 5-H), 3.54 (3 H, s, OMe), 2.29 (3 H, s, Ts-Me), 2.13 (3 H, s; CH_3C=O), 1.37 (3 H, d, J = 6.4, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **46**: δ 172.4 (CH_3C=O), 164.9 (PhC=O), 143.6 (C-3), 146.7, 133.6, 130.1, 129.5, 129.2, 128.4, 128.1, 128.0 (Ar C's), 102.7 (C-1), 70.5 (C-4)*, 69.8 (C-2)*, 68.1 (C-5), 57.1 (OMe), 21.6 (Ts-Me), 20.4 (CH_3C=O), 15.8 (C-6). High-resolution FAB-MS: calcd for $C_{23}H_{27}N_2O_8S$ (M + H)$^+$ 491.1488, found 491.1465.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-gulopyranoside (57) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-β-D-galactopyranoside (58). The reduction reaction was performed on **45** using the general procedure described earlier. The product was purified by flash chromatography (0.5% MeOH/CH_2Cl_2) with a yield of 79%. This reaction was also carried out on the β anomer **46**. ^{1}H NMR ($CDCl_3$) of the α anomer **57**: δ 8.03, 7.22 (2 H each, d, J = 8.3, Ts H's), 7.75 (2 H, d, J = 8.2, ortho H's), 7.62 (1 H, t, J = 7.6, para H), 7.49 (2 H, dd, J = 8.2, 7.6, meta H's), 6.16 (1 H, s, NH), 5.22 (1 H, dd, J = 4.6, 3.7, 2-H), 4.86 (1 H, d, J = 3.7, 1-H), 4.78 (1 H, b d, J = 2.6, 4-H), 4.13 (1 H, b q, J = 6.6, 5-H), 3.35 (3 H, s, OMe), 3.17 (1 H, dd, J = 4.6, 2.6, 3-H), 2.39 (3 H, s, Ts-Me), 2.07 (3 H, s, CH_3C=O), 1.06 (3 H, d, J = 6.6, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **57**: δ 169.7 (CH_3C=O), 165.2 (PhC=O), 144.2, 134.9, 133.7, 129.8, 129.6, 129.3, 128.7, 128.3 (Ar-C's), 97.6 (C-1), 71.8 (C-4), 67.8 (C-2), 61.2 (C-5), 59.7 (C-3), 55.8 (OMe), 21.6 (Ts-Me), 20.8 (CH_3C=O), 15.6 (C-6). ^{1}H NMR ($CDCl_3$) of the β anomer **58**: δ 8.10, 6.81 (2 H, each, d, J = 8.2, Ts H's), 7.77–7.31 (5 H, m, Ar H's), 6.47 (1 H, s, NH), 5.17 (1 H, b d, J = 2.4, 4-H), 4.90 (1 H, dd, J = 8.1, 7.7, 2-H), 4.54 (1 H, d, J = 7.7, 1-H), 3.81 (1 H, b q, J = 6.5, 5-H), 3.48 (3 H, s, OMe), 3.38 (1 H, dd, J = 8.1, 2.4, 3-H), 2.26 (3 H, s, Ts-Me), 2.14 (3 H, s, CH_3C=O), 1.26 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **58**: δ 172.3 (CH_3C=O), 166.3 (PhC=O), 143.7, 133.5, 130.0, 129.9, 129.8, 129.3, 128.6, 128.0 (Ar C's), 102.2 (C-1), 70.6 (C-4)*, 69.9 (C-2)*, 69.0 (C-5)*, 63.8 (C-3), 57.1 (OMe), 21.5 (Ts-Me), 21.0 (CH_3C=O), 16.6 (C-6). High-resolution FAB-MS: calcd for $C_{23}H_{29}N_2O_8S$ (M + H)$^+$ 493.1645, found 493.1661.

Methyl 6-Deoxy-3,4-*O*-(1-ethoxyethylidene)-α-L-galactopyranoside (84) and Methyl 6-Deoxy-3,4-*O*-(1-ethoxyethylidene)-β-L-galactopyranoside (85). To a solution of L-fucose **82** (4 g, 24.4 mmol) in methanol was added 1 g of Dowex 50 (H$^+$), and the mixture was refluxed overnight. Filtration and concentration in vacuo provided the crude methyl glycoside.[30] The crude methyl L-fucopyranoside **83** (3.0 g, 16.8 mmol) was redissolved in methylene chloride (30 mL) followed by the sequential addition of triethyl orthoacetate (6.17 mL, 33.6 mmol) and a catalytic amount of *p*-toluenesulfonic acid. After the mixture was stirred overnight at room temperature, the solvent was removed in vacuo and the resulting residue was purified by flash chromatography (20% EtOAc/hexane). This led to the separation of the α (**84**) and β (**85**) anomers with a total yield of 85%. ^{1}H NMR ($CDCl_3$) of the α anomer **84**: δ 4.66 (1 H, d, J = 4.0, 1-H), 4.34 (1 H, t, J = 6.2, 3-H), 4.24–4.19 (1 H, m, 4-H), 4.10–4.05 (1 H, m, 5-H), 3.81–3.76 (1 H, m, 2-H), 3.56–3.49 (2 H, q, J = 6.6, OCH_2CH_3), 3.41 (3 H, s, OMe), 2.64 (1 H, d, J = 5.5, OH), 1.60 (3 H, s, orthoesteric Me), 1.27 (3 H, d, J = 6.6, 5-Me), 1.15 (3 H, t, J = 6.6, CH_2CH_3). ^{13}C NMR ($CDCl_3$) of the α anomer **84**: δ 121.3 (orthoesteric C), 103.0 (C-1), 79.5, 76.4, 73.5, 68.9 (C-2, 3, 4, 5), 58.6 (OMe), 56.8 (OCH_2CH_3), 23.0 (orthoesteric Me), 16.3 (C-6), 15.4 (OCH_2CH_3). ^{1}H NMR ($CDCl_3$) of the β anomer **85**: δ 4.30–4.10 (2 H, m, 3-H, 4-H), 4.01 (1 H, d, J = 8.2, 1-H), 3.80–3.75 (1 H, m, 5-H), 3.49 (2 H, q, J = 7.0, OCH_2CH_3), 3.46 (3 H, s, OMe), 3.45–3.37 (1 H, m, 2-H), 2.93 (1 H, d, J = 2.6, OH), 1.56 (3 H, s, orthoesteric Me), 1.35 (3 H, d, J = 6.6, 5-Me), 1.10 (3 H, t, J = 7.0, CH_2CH_3).

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-L-galactopyranoside (86) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-β-L-galactopyranoside (87). The orthoester **84** (700 mg, 2.82 mmol) was dissolved in methylene chloride (10 mL) followed by the addition of triethyl amine (684 mg, 6.76 mmol), benzoyl chloride (474 mg, 3.37 mmol), and a catalytic amount of 4-(dimethylamino)pyridine. After being stirred at room temperature overnight the mixture was extracted with chloroform, and the organic extracts were washed with a saturated ammonium chloride solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The resulting residue was then stirred in 5 mL of 80% aqueous acetic acid for 30 min at room temperature. This was followed by extraction with methylene chloride, drying over anhydrous magnesium sulfate, and concentration under reduced pressure. The crude product was purified by flash chromatography (10% EtOAc/hexane) to give **86** in 76% yield. The same procedure was also employed to convert the β anomer **85** to **87**. ^{1}H NMR ($CDCl_3$) of the α anomer **86**: δ 8.01 (2 H, d, J = 8.2, ortho H's), 7.50 (1 H, t, J = 7.7, para H), 7.37 (2 H, dd, J = 8.2, 7.7, meta H's), 5.22 (1 H, b d, J = 3.5, 4-H), 5.17 (1 H, dd, J = 10.4, 3.7, 2-H), 4.97 (1 H, d, J = 3.7, 1-H), 4.30 (1 H, dd, J = 10.4, 3.5, 3-H), 4.03 (1 H, q, J = 6.5, 5-H), 3.32 (3 H, s, OMe), 2.92 (1 H, b s, OH), 2.13 (3 H, s, CH_3C=O), 1.12 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **86**: δ 171.4 (CH_3C=O), 166.7 (PhC=O), 133.3, 129.9, 129.7, 128.4 (Ar C's), 97.6 (C-1), 73.8, 72.0, 66.9, 64.6 (C-2,3,4,5), 55.5 (OMe), 20.8 (CH_3C=O), 16.1 (C-6). ^{1}H NMR ($CDCl_3$) of the β anomer **87**: δ 8.03 (2 H, d, J = 7.0, ortho H's), 7.57 (1 H, t, J = 7.4, para H), 7.43 (2 H, dd, J = 7.4, 7.0, meta H's), 5.25–5.16 (2 H, m, 2-H, 4-H), 4.48 (1 H, d, J = 7.9, 1-H), 3.96 (1 H, dd, J = 10.1, 3.6, 3-H), 3.79 (1 H, q, J = 6.5, 5-H), 3.51 (3 H, s, OMe), 2.97 (1 H, b s, OH), 2.20 (3 H, s, CH_3C=O), 1.26 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **87**: δ 171.4 (CH_3C=O), 166.9 (PhC=O), 133.4, 129.9, 129.6, 128.4 (Ar

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C's), 101.8 (C-1), 73.5, 73.0, 71.7, 69.4 (C-2,3,4,5), 57.0 (OMe), 20.9 (CH_3C=O), 16.4 (C-6). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.43; H, 6.18.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-L-*xylo*-hexopyranosid-3-ulose (88) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-β-L-*xylo*-hexopyranosid-3-ulose (89). Both anomers, **86** and **87**, were oxidized to the corresponding aldoketose **88** and **89** with pyridinium chlorochromate in the same manner as previously described for the preparation of **80**. The product was purified by flash chromatography (10% EtOAc/hexane) and the yields for **88** and **89** were 91% and 89%, respectively. ^{1}H NMR ($CDCl_3$) of the α anomer **88**: δ 8.10 (2 H, d, J = 7.1, ortho H's), 7.58 (1 H, t, J = 7.4, para H), 7.44 (2 H, dd, J = 7.4, 7.1, meta H's), 5.89 (1 H, d, J = 4.2, 2-H), 5.25 (1 H, d, J = 4.2, 1-H), 5.19 (1 H, d, J = 1.5, 4-H), 4.35–4.33 (1 H, b q, J = 6.5, 5-H), 3.44 (3 H, s, OMe), 2.21 (3 H, s, CH_3C=O), 1.30 (3 H, d, J = 6.5, 5-Me). ^{13}C NMR ($CDCl_3$) of the α anomer **88**: δ 194.2 (C-3), 169.5 (CH_3C=O), 165.3 (PhC=O), 133.6, 130.1, 129.9, 128.5 (Ar C's), 100.6 (C-1), 78.3, 74.4, 67.9 (C-2, 4, 5), 55.8 (OMe), 20.6 (CH_3C=O), 15.6 (C-6). ^{1}H NMR ($CDCl_3$) of the β anomer **89**: δ 8.07 (2 H, d, J = 7.0, ortho H's), 7.59 (1 H, t, J = 7.4, para H), 7.44 (2 H, dd, J = 7.4, 7.0, meta H's), 5.63 (1 H, d, J = 7.8, 2-H), 5.17 (1 H, d, J = 1.4, 4-H), 4.69 (1 H, d, J = 7.8, 1-H), 3.89 (1 H, dq, J = 6.5, 1.4, 5-H), 3.60 (1 H, s, OMe), 2.22 (3 H, s, CH_3C=O), 1.38 (3 H, d, J = 6.5, 5-Me). Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.76; H, 5.57.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-α-L-*xylo*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (47) and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-6-deoxy-β-L-*xylo*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (48). These hydrazones were prepared from ketones **88** and **89** using the method described in the general procedures. The product was purified by flash chromatography (20% EtOAc/hexane) with a yield of 74% in each case. ^{1}H NMR ($CDCl_3$) of the α anomer **47**: 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 ($CDCl_3$) of the α anomer **47**: 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. ^{1}H NMR ($CDCl_3$) of the β anomer **48**: δ 9.31 (1 H, s, NH), 8.05 (2 H, d, J = 7.1, ortho H's), 7.65 (1 H, t, J = 7.4, para H), 7.52 (1 H, dd, J = 7.4, 7.1, meta H's), 7.37, 6.82 (2 H each, d, J = 8.1, Ts H's), 5.39 (1 H, d, J = 8.1, 2-H), 5.06 (1 H, d, J = 1.6, 4-H), 4.66 (1 H, d, J = 8.1, 1-H), 3.87 (1 H, dq, J = 6.4, 1.6, 5-H), 3.54 (3 H, s, OMe), 2.29 (3 H, s, Ts-Me), 2.13 (3 H, s, CH_3C=O), 1.37 (3 H, d, J = 6.4, 5-Me). ^{13}C NMR ($CDCl_3$) of the β anomer **48**: δ 172.4 (CH_3C=O), 164.9 (PhC=O), 146.6 (C-3), 143.8, 133.4, 130.1, 129.2, 128.4, 128.0 (Ar C's), 102.7 (C-1), 70.5, 69.8, 68.1 (C-2, 4, 5), 57.1 (OMe), 21.6 (CH_3C=O), 20.4 (Ts-Me), 15.8 (C-6). High-resolution FAB-MS: calcd for $C_{23}H_{27}N_2O_8S$ $(M + H)^+$ 491.1488, found 491.1488. Anal. Calcd for $C_{23}H_{26}N_2O_8S$: C, 56.32; H, 5.34; N, 5.71; S, 6.54. Found: C, 56.12; H, 5.34; N, 5.73; S, 6.48.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)hyrazino]-α-L-gulopyranoside (59), Methyl 4-*O*-Acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)-hydrazino]-β-L-galactopyranoside (60), and Methyl 4-*O*-Acetyl-2-*O*-benzoyl-3,6-dideoxy-3-[2-(*p*-tolylsulfonyl)hyrazino]-β-L-gulopyranoside (61). Reduction of **47** and **48** with $NaBH_3CN$ was conducted based on the method described in the general procedures. Only one product (**59**) was obtained from the reduction of **47**, while two C-3 epimers (**60**:**61**, 4:1) were generated rom the reduction of **48**. Compound **59** was purified by flash chromatography (10% EtOAc/benzene) with a yield of 89%, while **60** and **61** were separable under the same conditions with a 85% yield. ^{1}H NMR ($CDCl_3$) of **59**: δ 8.03 (2 H, d, J = 7.8, ortho H's), 7.61 (1 H, t, J = 7.3, para H), 7.48 (2 H, dd, J = 7.8, 7.3, meta H's), 7.74, 7.21 (2 H, each, d, J = 8.2, Ts H's), 6.21 (1 H, d, J = 1.7, NH), 5.22 (1 H, dd, J = 4.7, 3.8, 2-H), 4.85 (1 H, d, J = 3.8, 1-H), 4.79 (1 H, b d, J = 3.3, 4-H) 4.14 (1 H, b q, J = 6.6, 5-H), 3.35 (3 H, s, OMe), 3.18 (1 H, dd, J = 4.7, 3.3, 3-H), 2.39 (3 H, s, Ts-Me), 2.07 (3 H, s, CH_3C=O), 1.05 (3 H, d, J = 6.6, 5-Me). ^{13}C NMR ($CDCl_3$) of **59**: δ 169.7 (CH_3C=O), 165.5 (PhC=O), 144.1, 135.0, 133.6, 129.8, 129.6, 129.3, 128.7, 128.3 (Ar-C's), 97.6 (C-1), 71.9, 67.7, 61.1, (C-2, 4, 5), 59.7 (C-3), 55.8 (OMe), 21.6 (Ts-Me), 20.8 (CH_3C=O). Anal. Calcd for $C_{23}H_{28}N_2O_8S$: C, 56.09; H, 5.73; N, 5.69; S, 6.51. Found: C, 55.91; H, 5.68; N, 5.66; S, 6.60. ^{1}H NMR ($CDCl_3$) of **60**: δ 8.12–6.83 (9 H, m, Ar and Ts H's), 6.38 (1 H, d, J = 2.7, NH), 5.17 (1 H, d, J = 1.8, 4-H), 4.90 (1 H, dd, J = 7.8, 6.1, 2-H), 4.55 (1 H, d, J = 7.8, 1-H), 3.82 (1 H, b q, J = 6.4, 5-H), 3.50 (3 H, s, OMe), 3.32–3.29 (1 H, m, 3-H), 2.16 (3 H, s, Ts-Me), 1.55 (3 H, s, CH_3C=O), 1.28 (3 H, d, J = 6.4, 5-Me). High-resolution FAB-MS: calcd for $C_{23}H_{29}N_2O_8S$ $(M + H)^+$ 493.1645, found 493.1643. ^{1}H NMR ($CDCl_3$) of **61**: δ 7.98 (2 H, d, J = 7.9, ortho H's), 7.61 (1 H, t, J = 7.4, para H), 7.46 (2 H, dd, J = 7.9, 7.4, meta H's), 7.76, 7.26 (2 H each, d, J = 8.3, Ts H's), 5.81 (1 H, b d, J = 2.2, NH), 5.19 (1 H, dd, J = 7.8, 4.5, 2-H), 4.89 (1 H, dd, J = 4.0, 1.8, 4-H), 4.72 (1 H, d, J = 7.8, 1-H), 4.22 (1 H, b s, NH), 3.99 (1 H, b q, J = 6.6, 5-H), 3.45 (3 H, s, OMe), 3.49–3.44 (1 H, m, 3-H), 2.41 (3 H, s, Ts-Me), 2.09 (3 H, s, CH_3C=O), 1.01 (3 H, d, J = 6.6, 5-Me).

Reduction of **47** and **48** with $NaBD_3CN$ led to no deuterium incorporation in the hydrazine products.

Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (91). A mixture of methyl α-D-glucopyranoside **90** (120 g, 0.62 mol), freshly fused and powdered zinc chloride (90 g, 0.66 mol), and benzaldehyde (300 mL, 2.95 mol) was mechanically stirred for 36 h at room temperature. The viscous albeit homogeneous mixture was poured slowly into 2.5 L of cold water with vigorous stirring, and the mixture was refrigerated overnight. The sticky precipitate was collected, suspended in petroleum ether, and stirred at room temperature for 1 h, so that benzaldehyde could be extracted and then removed. The crude product was filtered, washed twice with 200 mL of petroleum ether and 200 mL of cold water, dried overnight in air, and then in a vacuum oven at 70 °C. The yield was 63%. Without further purification, the methyl 4,6-*O*-benzylidene-α-D-glucopyranoside obtained was dissolved in 700 mL of pyridine, and the solution was chilled in an ice–water bath. To this well-agitated solution was added *p*-toluenesulfonyl chloride (220 g, 1.15 mol) over a period of 15 min. This mixture was allowed to warm to room temperature and kept at 50 °C for 48 h. The resulting yellow solution was poured into ice–water followed by chloroform extraction. The chloroform layer was separated, and the excess pyridine was removed by repeated extraction with saturated cupric sulfate solution. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The desired product was crystallized from ethanol, mp 147–148 °C. The yield was 78%. ^{1}H NMR ($CDCl_3$): δ 7.80 (2 H, d, J = 8.4, Ts H's), 7.61 (2 H, d, J = 7.9, Ts H's), 7.36–7.26 (5 H, m, Ar H's), 6.92 (2 H, d, J = 7.9, Ts H's), 5.28 (1 H, s, acetalic H), 5.08 (1 H, t, J = 9.5, 3-H), 5.02 (1 H, d, J = 3.7, 1-H), 4.40 (1 H, dd, J = 9.5, 3.7, 2-H), 4.23 (1 H, dd, J = 10.3, 4.6, 6-H), 3.83 (1 H, dt, J = 10.3, 9.5, 5-H), 3.64 (1 H, t, J = 10.3, 6-H), 3.49 (1 H, t, J = 9.5, 4-H), 3.38 (3 H, s, OMe), 2.43 (3 H, s, Ts-Me), 2.24 (3 H, s, Ts-Me). ^{13}C NMR ($CDCl_3$) δ 145.4–126.4 (Ar C's), 101.9 (ketalic C), 98.5 (C-1), 79.0 (C-4), 76.5 (C-2)*, 76.0 (C-3)*, 68.6 (C-5), 62.4 (C-6), 56.0 (OMe), 21.7 (Ts-Me), 21.6 (Ts-Me).

Methyl 4,6-*O*-Benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (92). To a solution of the ditosylate **91** (6.0 g, 10.2 mmol) in 30 mL of dry THF was added 60 mL (60.0 mmol) of lithium triethylborohydride (1 M in THF) dropwise with stirring. The reaction mixture was refluxed under nitrogen for 1 h. The excess reducing agent was quenched with ethyl acetate, and the resulting mixture was diluted with saturated ammonium chloride solution followed by chloroform extraction. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated. The product was sufficiently pure and subjected to the next reaction directly without further purification. The yield was 94%. ^{1}H NMR ($CDCl_3$): δ 7.52–7.48, 7.39–7.34 (5 H, m, Ar H's), 5.62 (1 H, s, acetalic H), 4.78 (1 H, d, J = 3.9, 1-H), 4.30 (1 H, dd, J = 10.1, 5.1, 6-H), 4.25–4.17 (1 H, m, 5-H), 4.15–4.11 (1 H, m, 3-H), 3.77 (1 H, t, J = 10.1, 6-H), 3.60 (1 H, dd, J = 9.6, 2.7, 4-H), 3.40 (3 H, s, OMe), 3.00 (1 H, d, J = 6.8, OH), 2.18 (1 H, dd, J = 14.9, 3.1, 2-H), 2.00 (1 H, ddd, J = 14.9, 3.9, 3.5, 2-H). ^{13}C NMR ($CDCl_3$) δ 137.5, 129.1, 128.3, 126.3 (Ar

C's), 102.1 (acetalic C), 98.6 (C-1), 79.7 (C-4), 69.4 (C-5), 65.0 (C-6), 58.2 (C-3), 55.4 (OMe), 35.5 (C-2).

Methyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-α-D-*ribo*-hexopyranoside (93). To a solution of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (**92**) (2 g, 7.52 mmol) in freshly distilled carbon tetrachloride (60 mL) were added *N*-bromosuccinimide (2 g, 11.1 mmol) and barium carbonate (2.2 g, 11.2 mmol). The reaction mixture was heated with stirring at 45 °C for 20 min, during which time the solution turned brick red. Longer reaction time (2 h) and/or higher reaction temperature (refluxing) led to benzoyl migration to form both **93** and the corresponding 3-*O*-benzoyl product in 1:1 ratio. The white precipitate was removed by filtration through Celite, and the majogany filtrate was diluted with chloroform and extracted with water several times. The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo to give a red oil as the crude product. Purification by flash chromatography (10% EtOAc/hexane) afforded the desired product **93** in 60% yield. ^{1}H NMR ($CDCl_3$) δ 7.98 (2 H, d, J = 7.4, ortho H's), 7.49 (1 H, t, J = 7.1, para H), 7.37 (2 H, dd, J = 7.4, 7.1, meta H's), 4.84 (1 H, dd, J = 10.1, 2.8, 4-H), 4.81 (1 H, d, J = 3.3, 1-H), 4.33 (1 H, m, 5-H), 4.24 (1 H, m, 3-H), 3.58 (1 H, dd, J = 11.1, 2.3, 6-H), 3.46 (1 H, dd, J = 11.1, 7.0, 6-H), 3.40 (3 H, s, OMe), 2.15 (1 H, dd, J = 14.8, 3.3, 2-H), 2.03 (1 H, dt, J = 14.8, 3.5, 2-H). ^{13}C NMR ($CDCl_3$) δ 165.4 (C=O), 133.4, 129.8, 129.7, 128.4 (Ar C's), 98.6 (C-1), 72.7 (C-5), 65.3 (C-4), 65.0 (C-3), 55.5 (OMe), 35.0 (C-6), 33.2 (C-2).

Methyl 4-*O*-Benzoyl-2,6-dideoxy-α-D-*ribo*-hexopyranoside (94) and Methyl 3-*O*-Benzoyl-2,6-dideoxy-α-D-*ribo*-hexopyranoside (95). Compound **93** (1.5 g, 4.35 mmol) was dissolved in 40 mL of toluene with stirring under nitrogen. To this solution were added tributyltin hydride (1.9 mL, 7.06 mmol) and a few crystals of azobisisobutyronitrile (AIBN). The resulting mixture was kept in an oil bath at 60 °C for 2 h. The solvent was then evaporated, and the product was extracted with chloroform. The combined organic extracts were dried, concentrated, and purified by flash chromatography (10% EtOAc/benzene). Two products, **94** and **95**, were isolated in a 1:1 ratio with a total yield of 80%. ^{1}H NMR ($CDCl_3$) of **94**: δ 8.01 (2 H, d, J = 7.2, ortho H's), 7.48–7.33 (3 H, m, Ar H's), 4.74 (1 H, d, J = 3.1, 1-H), 4.69 (1 H, dd, J = 10.2, 2.6, 4-H), 4.25–4.22 (1 H, m, 5-H), 4.22–4.18 (1 H, m, 3-H), 3.34 (3 H, s, OMe), 2.07 (1 H, dd, J = 14.8, 2.8, 2-H), 1.95 (1 H, dt, J = 14.8, 3.1, 2-H), 1.22 (3 H, d, J = 6.2, 5-Me). ^{13}C NMR ($CDCl_3$) of **94**: δ 165.8 (PhC=O), 133.1, 130.0, 129.7, 128.4 (Ar C's), 98.6 (C-1), 75.5 (C-4), 65.6 (C-5), 61.3 (C-3), 55.2 (OMe), 35.4 (C-2), 17.7 (C-6). ^{1}H NMR ($CDCl_3$) of **95**: δ 8.01 (2 H, d, J = 7.1, ortho H's), 7.52 (1 H, t, J = 7.4, para H's), 7.39 (2 H, dd, J = 7.4, 7.1, meta H's), 5.36 (1 H, dd, J = 6.6, 3.3, 3-H), 4.66 (1 H, d, J = 4.1, 1-H), 4.04 (1 H, m, 5-H), 3.49–3.42 (1 H, m, 4-H), 3.32 (3 H, s, OMe), 2.22 (1 H, dd, J = 15.2, 3.3, 2-H), 1.99 (1 H, ddd, J = 15.2, 4.1, 3.3, 2-H), 1.29 (3 H, d, J = 6.3, 5-Me). ^{13}C NMR ($CDCl_3$) of **95**: δ 166.9 (PhC=O), 133.3, 130.4, 129.9, 128.4 (Ar C's), 97.0 (C-1), 72.1 (C-4), 70.0 (C-3), 64.2 (C-5), 55.1 (OMe), 33.6 (C-2), 17.8 (C-6).

Methyl 4-*O*-Benzoyl-2,6-dideoxy-α-D-*erythro*-hexopyranosid-3-ulose (96) and Methyl 3-*O*-Benzoyl-2,6-dideoxy-α-D-*erythro*-hexopyranosid-4-ulose (97). To a mixture of pyridinium chlorochromate (1.3 g, 6.03 mmol), powered 3-Å molecular sieves (2 g), and sodium acetate (740 mg, 9.02 mmol) in dry methylene chloride (30 mL) was added compound **94** (400 mg, 1.50 mmol), which was dissolved in methylene chloride. After 2 h of stirring at room temperature, an equal volume of anhydrous ether was poured into this reaction and the resulting mixture was stirred for an additional 30 min. The mixture was then filtered through silica gel, and the filtrate was evaporated to dryness. The yield of **96** was 95%. Compound **95** was similarly converted to **97** in 92% yield. ^{1}H NMR ($CDCl_3$) of **96**: δ 8.04 (2 H, d, J = 7.8, ortho H's), 7.54 (1 H, t, J = 7.3, para H), 7.39 (2 H, dd, J = 7.8, 7.3, meta H's), 5.14 (1 H, d, J = 10.0, 4-H), 5.08 (1 H, d, J = 4.4, 1-H), 4.30–4.22 (1 H, m, 5-H), 3.34 (3 H, s, OMe), 2.85 (1 H, dd, J = 13.8, 4.4, 2-H), 2.64 (1 H, d, J = 13.8, 2-H), 1.39 (3 H, d, J = 6.2, 5-Me). ^{13}C NMR ($CDCl_3$) of **96**: δ 197.3 (C-3), 164.4 (PhC=O), 132.6, 129.1, 128.4, 127.7 (Ar C's), 98.7 (C-1), 78.1 (C-4), 67.0 (C-5), 54.1 (OMe), 45.6 (C-2), 17.9 (C-6). ^{1}H NMR ($CDCl_3$) of **97**: δ 8.07 (2 H, d, J = 7.3, ortho H's), 7.57 (1 H, dd, J = 7.6, 7.3, para H), 7.44 (2 H, dd, J = 7.6,7.3, meta H's), 5.75 (1 H, dd, J = 13.3, 7.0, 3-H), 5.09 (1 H, t, J = 6.7, 1-H), 4.44 (1 H, q, J = 7.0, 5-H), 3.43 (3 H, s, OMe), 2.84 (1 H, ddd, J = 13.8, 7.0, 6.7, 2-H), 2.13 (1 H, ddd, J = 13.8, 13.3, 6.7, 2-H), 1.40 (3 H, d, J = 7.0, 5-Me). ^{13}C NMR ($CDCl_3$) of **97**: δ 197.8 (C-4), 164.5 (PhC=O), 132.6, 129.1, 128.5, 127.7 (Ar C's), 96.7 (C-1), 70.8 (C-3)*, 69.7 (C-5)*, 54.4 (OMe), 32.6 (C-2), 15.0 (C-6). High-resolution FAB-MS: calcd for $C_{14}H_{17}O_5$ $(M + H)^+$ 265.1076, found 265.1063.

Methyl 4-*O*-Benzoyl-2,6-dideoxy-α-D-*erythro*-hexopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (49) and Methyl 3-*O*-Benzoyl-2,6-dideoxy-α-D-*erythro*-hexopyranosid-4-ulose (*p*-Tolylsulfonyl)hydrazone (50). These compounds were prepared according to the hydrazone formation method described in the general procedures. The crude products were purified by flash chromatography (20% EtOAc/hexane). The yields of **49** and **50** were 90% and 88%, respectively. ^{1}H NMR ($CDCl_3$) of **49**: δ 8.06, 6.90 (2 H each, d, J = 8.1, Ts H's), 7.54–7.40 (5 H, m, Ar H's), 5.10 (1 H, d, J = 9.5, 4-H), 4.85 (1 H, d, J = 3.8, 1-H), 4.11 (1 H, m, 5-H), 3.28 (3 H, s, OMe), 2.92 (1 H, d, J = 14.9, 2-H), 2.41–2.31 (1 H, m, 2-H), 2.31 (3 H, s, Ts-Me), 1.29 (3 H, d, J = 6.2, 5-Me). ^{13}C NMR ($CDCl_3$) of **49**: δ 165.3 (PhC=O), 150.2 (C-3), 143.7, 134.6, 133.4, 130.0, 129.5, 129.1, 128.5, 128.2 (Ar C's, Ts C's), 97.6 (C-1), 74.0 (C-4), 67.4 (C-5), 54.7 (OMe), 32.7 (C-2), 21.6 (Ts-Me), 18.2 (C-6). High-resolution FAB-MS: calcd for $C_{21}H_{25}N_2O_6S$ $(M + H)^+$ 433.1433, found 433.1436. ^{1}H NMR ($CDCl_3$) of **50**: δ 9.76 (1 H, s, NH), 8.01 (2 H, d, J = 7.8, ortho H's), 7.60 (1 H, t, J = 7.5, para H), 7.49 (2 H, dd, J = 7.8, 7.5, meta H's), 7.82, 7.22 (2 H each, d, J = 8.1, Ts H's), 5.57 (1 H, t, J = 2.0, 3-H), 4.83 (1 H, b s, 1-H), 4.52 (1 H, q, J = 6.3, 5-H), 3.44 (3 H, s, OMe), 2.34 (3 H, s, Ts-Me), 2.27 (2 H, d, J = 2.0, 2-H's), 1.23 (3 H, d, J = 6.3, 5-Me). ^{13}C NMR ($CDCl_3$) of **50**: δ 167.3 (PhC=O), 150.8 (C-4), 143.8–128.3 (Ar C's), 96.8 (C-1), 62.6 (2 C's, C-3, C-5), 55.4 (OMe), 34.8 (C-2), 21.5 (Ts-Me), 15.5 (C-6). High-resolution FAB-MS: calcd for $C_{21}H_{25}N_2O_6S$ $(M + H)^+$ 433.1433, found 433.1407. Anal. Calcd for $C_{21}H_{24}N_2O_6S$: C, 58.32; H, 5.59; N, 6.48; S, 7.41. Found: C, 58.33; H, 5.64; N, 6.55; S, 7.43.

Methyl 4-*O*-Benzoyl-2,3,6-trideoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-*arabino*-hexopyranoside (62), Methyl 4-*O*-Benzoyl-2,3,6-trideoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-*ribo*-hexopyranoside (63), and Methyl 3-*O*-Benzoyl-2,4,6-trideoxy-4-[2-(*p*-tolylsulfonyl)hydrazino]-α-D-*ribo*-hexopyranoside (64). Reduction of **49** and **50** with $NaBH_3CN$ was conducted based on the method described in the general procedures. Only one product (**64**) was obtained from the reduction of **50**, while two epimers (**62**:**63**, 1:1) at C-3 were generated from the reduction of **49**. Compound **64** was purified by flash chromatography (10% EtOAc/benzene) with a yield of 80%, while **62** and **63** were separable under the same conditions with a 85% yield. ^{1}H NMR ($CDCl_3$) of **62**: δ 8.00 (2 H, d, J = 7.8, ortho H's), 7.60 (1 H, t, J = 7.4, para H), 7.46 (2 H, dd, J = 7.8, 7.4, meta H's), 7.74, 7.22 (2 H each, d, J = 8.2, Ts H's), 6.62 (1 H, s, NH), 4.72 (1 H, d, J = 2.9, 1-H), 4.66 (1 H, t, J = 9.7, 4-H), 3.93 (1 H, dq, J = 9.7, 6.1, 5-H), 3.68 (1 H, b s, NH), 3.33 (3 H, s, OMe), 3.21 (1 H, ddd, J = 12.1, 9.7, 4.8, 3-H), 2.37 (3 H, s, Ts-Me), 1.94 (1 H, m, 2-H), 1.81 (1 H, m, 2-H), 1.18 (3 H, d, J = 6.1, 5-Me). ^{13}C NMR ($CDCl_3$) of **62**: δ 167.3 (PhC=O), 143.7–128.0 (Ar C's), 98.1 (C-1), 75.3 (C-4), 65.1 (C-5), 55.7 (OMe), 54.7 (C-3), 33.1 (C-2), 21.5 (Ts-Me), 18.0 (C-6). For the deuterated **62** obtained from $NaBD_3CN$ reduction of **49**: ^{1}H NMR spectrum is identical with that of the unlabeled compound, except the intensity of δ 3.21 is diminished and the splitting pattern of δ 4.66 changed. The deuterium content was estimated to be 42%. ^{1}H NMR ($CDCl_3$) of **63**: δ 8.00 (2 H, d, J = 7.6, ortho H's), 7.62 (3 H, m, para H, Ts H's), 7.46 (2 H, dd, J = 7.9, 7.6, meta H's), 7.08 (2 H, d, J = 8.0, Ts H's), 6.14 (1 H, s, NH), 4.82 (1 H, dd, J = 9.2, 4.1, 4-H), 4.68 (1 H, m, 1-H), 4.34 (1 H, b m, NH), 4.10 (1 H, dt, J = 9.2, 6.4, 5-H), 3.37–3.34 (1 H, m, 3-H), 3.33 (3 H, s, OMe), 2.34 (3 H, s, Ts-Me), 2.03–1.97 (1 H, m, 2-H), 1.85–1.81 (1 H, m, 2-H), 1.20 (3 H, d, J = 6.4, 5-Me). ^{13}C NMR ($CDCl_3$) of **63**: δ 165.5 (PhC=O), 143.7–128.1 (Ar C's), 97.9 (C-1), 74.3 (C-4), 62.8 (C-5), 55.4 (OMe), 54.7 (C-3), 31.8 (C-2), 21.6 (Ts-Me), 17.9 (5-Me). For the deuterated **63** obtained from $NaBD_3CN$ reduction of **49**: ^{1}H NMR spectrum is identical with that of the unlabeled compound, except the intensity of δ 3.37–3.34 is diminished and the splitting pattern of δ 4.82 changed. The deuterium content was estimated to be 35%. ^{1}H NMR ($CDCl_3$) of

64: δ 8.03 (2 H, d, J = 7.8, ortho H's), 7.55 (1 H, t, J = 7.3, para H), 7.42 (2 H, dd, J = 7.8, 7.3, meta H's), 7.81, 7.27 (2 H each, d, J = 8.2, Ts H's), 6.16 (1 H, b s, NH), 5.20 (1 H, b d, J = 3.4, 3-H), 4.64 (1 H, d, J = 3.7, 1-H), 4.35 (1 H, b q, J = 6.8, 5-H), 3.90 (1 H, b s, NH), 3.30 (3 H, s, OMe), 2.80 (1 H, b s, 4-H), 2.37 (3 H, s, Ts-Me), 2.02 (1 H, dt, J = 15.3, 4.3, 2-H), 1.88 (1 H, b d, J = 15.3, 2-H), 1.20 (3 H, d, J = 6.8, 5-Me). ^{13}C NMR ($CDCl_3$) of **64**: δ 165.6 (PhC=O), 144.2–128.3 (Ar C's), 97.5 (C-1), 67.2 (C-3), 61.4 (C-5), 59.7 (C-4), 55.2 (OMe), 28.6 (C-2), 21.5 (Ts-Me), 16.8 (C-6). High-resolution FAB-MS: calcd for $C_{21}H_{27}N_2O_6S$ (M + H)$^+$ 435.1590, found 435.11585. For the deuterated **64** obtained from $NaBD_3CN$ reduction of **50**: ^{1}H NMR spectrum is identical with that of the unlabeled compound, except the intensity of δ 2.80 is diminished and the splitting pattern of δ 5.20 changed. The deuterium content was estimated to be 40%.

Methyl 3,4-*O*-(1-Ethoxyethylidene)-α-L-arabinopyranoside (99). Via the same procedure used in the synthesis of **84**, this compound was prepared from methyl α-L-arabinopyranoside, which was in turn derived from arabinose **98** via methanolysis. The crude product was purified by flash chromatography (on Et_3N pretreated silica gel, 20% EtOAc/hexane). The yield was 85%. ^{1}H NMR ($CDCl_3$) δ 4.69 (1 H, d, J = 3.7, 1-H), 4.40–4.38 (1 H, m, 4-H), 4.32 (1 H, dd, J = 6.4, 6.2, 3-H), 3.90–3.87 (2 H, m, 5-H's), 3.78–3.75 (1 H, m, 2-H), 3.55 (2 H, q, J = 7.0, OCH_2CH_3), 3.43 (3 H, s, OMe), 2.44 (1 H, d, J = 6.3, OH), 1.16 (3 H, t, J = 7.0, OCH_2CH_3). ^{13}C NMR ($CDCl_3$) δ 168.0 (orthoesteric C), 98.0 (C-1), 73.2, 69.2, 59.5 (C-2, 3, 4), 59.0 (C-5), 58.5 (OCH_2CH_3), 55.6 (OMe), 22.4 (orthoesteric Me), 15.4 (OCH_2CH_3).

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-α-L-arabinopyranoside (100). This compound was prepared based on the same strategy used in the synthesis of **86**. Compound **100** was obtained after flash chromatography (20% EtOAc/hexane) purification in 83% yield. ^{1}H NMR ($CDCl_3$) δ 7.96 (2 H, d, J = 7.4, ortho H's), 7.44 (1 H, t, J = 7.2, para H), 7.31 (2 H, dd, J = 7.4, 7.2, meta H's), 5.18 (1 H, dd, J = 10.2, 3.5, 2-H), 5.08 (1 H, d, J = 1.7, 4-H), 4.93 (1 H, d, J = 3.5, 1-H), 4.21 (1 H, b d, J = 10.2, 3-H), 3.75 (1 H, d, J = 12.5, 5-H$_e$), 3.64 (1 H, dd, J = 12.5, 1.7, 5-H$_a$), 3.31 (1 H, b s, OH), 3.26 (3 H, s, OMe), 2.03 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 171.1 (CH_3C=O), 166.6 (PhC=O), 133.2, 129.8, 129.6, 128.3 (Ar C's), 97.8 (C-1), 72.1, 72.0, 66.0 (C-2,3,4), 60.2 (C-5), 55.5 (OMe), 21.0 (CH_3C=O). Anal. Calcd for $C_{15}H_{18}O_7$: C, 58.06; H, 5.85. Found: C, 58.20; H, 5.84.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-α-L-*threo*-pentopyranosid-3-ulose (101). Oxidation of **100** was achieved by the same method used in the synthesis of **80** with pyridinium chlorochromate. The product was filtered through a silica gel column with ether, and the yield was 98%. ^{1}H NMR ($CDCl_3$) δ 8.04 (2 H, d, J = 7.7, ortho H's), 7.51 (1 H, t, J = 7.4, para H), 7.31 (2 H, dd, J = 7.7, 7.4, meta H's), 5.87 (1 H, d, J = 4.0, 2-H), 5.24 (1 H, d, J = 4.0, 1-H), 5.11 (1 H, s, 4-H), 4.08–3.97 (2 H, AB q, J = 13.2, 5-H's), 3.37 (3 H, s, OMe), 2.10 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 193.5 (C-3), 169.4 (CH_3C=O), 165.1 (PhC=O), 133.6, 130.0, 128.8, 128.5 (Ar C's), 101.4 (C-1), 76.4, 74.9 (C-2,4), 63.2 (C-5), 55.7 (OMe), 20.7 (CH_3C=O).

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-α-L-*threo*-pentopyranosid-3-ulose (*p*-Tolylsulfonyl)hydrazone (54). Hydrazone formation was accomplished according to the standard method described in the general procedures. Compound **54** was purified by flash chromatography (25% EtOAc/hexane) with a yield of 95%. ^{1}H NMR ($CDCl_3$) δ 9.33 (1 H, s, NH), 8.08–7.50 (5 H, m, Ar H's), 7.45, 6.81 (2 H each, d, J = 8.1, Ts H's), 5.63 (1 H, d, J = 3.5, 2-H), 5.25 (1 H, d, J = 1.9, 4-H), 5.02 (1 H, d, J = 3.5, 1-H), 4.10 (1 H, dd, J = 13.1, 1.9, 5-H), 3.85 (1 H, d, J = 13.1, 5-H), 3.46 (3 H, s, OMe), 2.27 (3 H, s, Ts-Me), 2.12 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 172.0 (CH_3C=O), 165.1 (PhC=O), 144.5 (C-3), 143.5–128.1 (Ar C's), 99.6 (C-1), 68.7, 66.3 (C-2, 4), 60.7 (C-5), 55.7 (OMe), 21.5 (Ts-Me), 20.5 (CH_3C=O). Anal. Calcd for $C_{22}H_{24}N_2O_8S$: C, 55.45; H, 5.08; N, 5.88; S, 6.73. Found: C, 55.35; H, 5.06; N, 5.82; S, 6.81.

Methyl 4-*O*-Acetyl-2-*O*-benzoyl-3-deoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-α-L-*lyxo*-pentopyranoside (69). The reduction described in the general procedures was used to reduce compound **54**. After purification by flash chromatography (5% EtOAc/benzene) the desired product **69** was isolated in 34% yield. ^{1}H NMR ($CDCl_3$) δ 8.04 (2 H, d, J = 7.4, ortho H's), 7.62 (1 H, t, J = 7.2, para H), 7.48 (2 H, dd, J = 7.4, 7.2, meta H's), 7.74, 7.23 (2 H each, d, J = 8.1, Ts H's), 6.32 (1 H, d, J = 2.0, NH), 5.35 (1 H, dd, J = 4.2, 3.2, 2-H), 4.79–4.75 (1 H, m, 4-H), 4.71 (1 H, d, J = 3.2, 1-H), 4.42 (1 H, b d, J = 6.5, NH), 3.97 (1 H, dd, J = 12.8, 2.5, 5-H), 3.50 (1 H, dd, J = 12.8, 4.2, 5-H), 3.32 (3 H, s, OMe), 3.30 (1 H, m, 3-H), 2.39 (3 H, s, Ts-Me), 2.07 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 170.0 (CH_3C=O), 165.9 (PhC=O), 144.1–128.2 (Ar C's), 98.3 (C-1), 69.3, 68.2 (C-2,4), 60.4 (C-5), 56.3 (OMe), 44.2 (C-3), 21.6 (Ts-Me), 21.0 (CH_3C=O). High-resolution FAB-MS: calcd for $C_{22}H_{27}N_2O_8S$ (M + H)$^+$ 479.1488, found 479.1469. Anal. Calcd for $C_{22}H_{26}N_2O_8S$: C, 55.22; H, 5.48; N, 5.85; S, 6.70. Found: C, 55.24; H, 5.53; N, 5.80; S, 6.76.

When $NaBD_3CN$ was used as the reducing agent, the intensity of δ 3.30 diminished and the splitting pattern of δ 5.35 simplified. The deuterium content was estimated to be 32%.

2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl Bromide (102). Arabinose **98** (4.0 g, 27.0 mmol) was stirred in a solution of acetic anhydride (12.5 mL, 133 mmol) and pyridine (50 mL) at room temperature overnight. The reaction was quenched with water, and the resulting mixture was extracted with methylene chloride. The combined organic extracts were evaporated, and excess pyridine was removed in the presence of benzene in vacuo. The crude tetraacetyl arabinoside syrup (4.0 g, 12.6 mmol) was then dissolved in 70 mL of acetic acid followed by the dropwise addition of phosphorus tribromide (11.5 mL, 121 mmol). After stirring at room temperature for 4 h the mixture was diluted with methylene chloride, poured into ice–water, and extracted with more methylene chloride. The organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuo to a white solid. The overall yield of these two steps was 82%. ^{1}H NMR ($CDCl_3$) δ 6.67 (1 H, d, J = 3.7, 1-H), 5.42–5.34 (2 H, m, 2-H, 3-H)*, 5.10–5.03 (1 H, m, 4-H)*, 4.19 (1 H, b d, J = 13.2, 5-H), 3.91 (1 H, dd, J = 13.2, 1.7, 5-H), 2.13, 2.09, 2.01 (3 H each, s, CH_3C=O's). ^{13}C NMR ($CDCl_3$) δ 169.9, 169.6 (CH_3C=O's), 89.5 (C-1), 67.8, 67.7, 67.4 (C-2, 3, 4), 64.5 (C-5), 20.6, 20.5, 20.3 (CH_3C=O's).

1,5-Anhydro-L-*arabino*-pentitol (103). To a suspension of the bromide **102** (3.5 g, 10.3 mmol) in diethyl ether (10 mL) was added a catalytic amount of azobisisobutyronitrile (AIBN) followed by the dropwise addition of tributyltin hydride (3.23 mL, 12.0 mmol). After the mixture was stirred at room temperature under nitrogen for 5 h, a solution of KF·2H_2O (2 g) in 10 mL of H_2O was added and the mixture was stirred vigorously for 0.5 h. The white precipitate was then filtered, and the filtrate was concentrated in vacuo. This acetylated anhydroarabinitol was deacetylated with NaOMe/MeOH and neutralized with Dowex 50 (H^+) according to the procedure of Gray and Barker.[28] The product was a white solid, mp 94–96 °C. The yield from **102** was 45%. ^{1}H NMR (D_2O) δ 3.78–3.60 (4 H, m, 1-H$_e$, 2-, 4-, 5-H's), 3.45 (1 H, dd, J = 8.3, 3.2, 3-H), 3.39 (1 H, dd, J = 12.3, 1.6, 5-H), 3.02 (1 H, dd, J = 10.7, 9.0, 1-H$_a$). ^{13}C NMR (D_2O) δ 72.7, 69.5, 68.9, 68.0, 67.0.

4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-L-*arabino*-pentitol (104). This compound was prepared from **103** according to the same procedure used in the synthesis of **86**. The desired product was purified by flash chromatography (25% EtOAc/hexane). The overall yield from **103** was 59%. ^{1}H NMR ($CDCl_3$) δ 8.14 (2 H, d, J = 8.0, ortho H's), 7.46 (1 H, t, J = 7.3, para H), 7.32 (2 H, dd, J = 8.0, 7.3, meta H's), 5.16 (1 H, ddd, J = 7.4, 6.4, 4.0, 2-H), 5.10 (1 H, td, J = 5.2, 2.6, 4-H), 4.03–3.96 (1 H, m, 3-H), 4.00 (1 H, dd, J = 11.6, 4.0, 1-H), 3.85 (1 H, dd, J = 12.1, 5.2, 5-H), 3.54 (1 H, dd, J = 12.1, 2.6, 5-H), 3.40 (1 H, dd, J = 11.6, 7.4, 1-H), 3.12 (1 H, b s, OH), 2.03 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 170.6 (CH_3C=O), 166.2 (PhC=O), 133.4, 129.8, 128.5, 128.3 (Ar C's), 71.2, 70.5, 69.3, 66.6, 66.5 (C-1, 2, 3, 4, 5), 21.0 (CH_3C=O). Anal. Calcd for $C_{14}H_{16}O_6$: C, 60.00; H, 5.75. Found: C, 60.04; H, 5.70. A minor product, 3-*O*-acetyl-1,5-anhydro-2-*O*-benzoyl-L-*arabino*-pentitol, was also isolated. ^{1}H NMR ($CDCl_3$) of this minor product: δ 7.99 (2 H, d, J = 8.0, ortho H's), 7.57 (1 H, t, J = 7.5, para H), 7.44 (2 H, dd, J = 8.0, 7.5, meta H's), 5.38 (1 H, ddd, J = 8.2, 7.8, 4.4, 2-H), 5.25 (1 H, dd, J = 8.2, 3.2, 3-H), 4.19–4.15 (1 H, m, 4-H), 4.12 (1 H, dd, J = 11.6, 4.4, 1-H), 3.90 (1 H, dd, J = 12.1, 4.5, 5-H), 3.68 (1 H, dd, J = 12.1, 2.2, 5-H), 3.49 (1 H, dd, J = 11.6, 7.8, 1-H), 2.24 (1 H, d, J = 5.3, OH), 2.10 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of this minor product: δ 170.2 (CH_3C=O), 168.0 (PhC=O), 133.4, 129.8, 129.6, 128.5 (Ar C's), 79.7, 72.4, 69.5, 68.3, 67.2 (C-1,2,3,4,5), 21.0 (CH_3C=O).

4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-oxo-L-*arabino*-pentitol (105). Oxidation of **104** with pyridinium chlorochromate followed a procedure identical with that used in the preparation of **80**. The yield was 80%. ^{1}H NMR ($CDCl_3$) δ 8.06 (2 H, d, J = 8.0, ortho H's), 7.59 (1 H, t, J = 7.4, para H), 7.45 (2 H, dd, J = 8.0, 7.4, meta H's), 5.61 (1 H, dd, J = 6.1, 4.5, 2-H), 5.46 (1 H, dd, J = 6.3, 4.3, 4-H), 4.15 (1 H, dd, J = 12.0, 4.5, 1-H), 4.10 (1 H, dd, J = 12.1, 4.3, 5-H), 4.08 (1 H, dd, J = 12.0, 6.1, 1-H), 3.96 (1 H, dd, J = 12.1, 6.3, 5-H), 2.18 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) δ 196.6 (C-3), 169.3 (CH_3C=O), 165.0 (PhC=O), 133.7, 130.0, 128.8, 128.6 (Ar C's), 75.0, 74.7, 71.6, 71.5 (C-1,2,4,5), 20.6 (CH_3C=O). The hydrate form of **105** was also detected by NMR. ^{1}H NMR ($CDCl_3$) of the hydrate form: δ 8.05 (2 H, d, J = 8.0, ortho H's), 7.57 (1 H, t, J = 7.4, para H), 7.43 (2 H, dd, J = 8.0, 7.4, meta H's), 5.26 (1 H, dd, J = 5.7, 3.3, 2-H), 5.09 (1 H, dd, J = 6.7, 3.7, 4-H), 3.99-3.87 (2 H, m, 1-H, 5-H), 3.79 (1 H, dd, J = 11.8, 5.7, 1-H), 3.64 (1 H, dd, J = 11.6, 6.7, 5-H), 2.18 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of the hydrate form: δ 171.1 (CH_3C=O), 166.7 (PhC=O), 133.8, 130.1, 129.4, 128.7 (Ar C's), 92.7 (C-3), 72.9, 72.2, 67.1, 66.8 (C-1,2,4,5), 21.1 (CH_3C=O).

4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-oxo-L-*arabino*-pentitol (*p*-Tolylsulfonyl)hydrazone (55). This compound was prepared from **105** based on the coupling described in the general procedures. Both syn and anti isomers (2:1) were obtained and separated by flash chromatography (25% EtOAc/hexane). The total yield was 90%. ^{1}H NMR ($CDCl_3$) of the major isomer: δ 9.35 (1 H, b 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, b 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 ($CDCl_3$) of the major isomer: 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. ^{1}H NMR ($CDCl_3$) of the minor isomer: δ 9.79 (1 H, b s, NH), 8.00 (2 H, d, J = 7.8, ortho H's), 7.61 (1 H, t, J = 7.5, para H), 7.45 (2 H, dd, J = 7.8, 7.5, meta H's), 7.75, 7.23 (2 H each, d, J = 8.3, Ts H's), 5.44 (1 H, b s, 4-H), 5.41 (1 H, dd, J = 10.7, 6.3, 2-H), 4.25 (1 H, d, J = 13.2, 5-H), 4.19 (1 H, dd, J = 10.7, 6.3, 1-H), 3.76 (1 H, dd, J = 13.2, 1.9, 5-H), 3.57 (1 H, t, J = 10.7, 1-H), 2.35 (3 H, s, Ts-Me), 2.05 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of the minor isomer: δ 169.0 (CH_3C=O), 168.0 (PhC=O), 146.2 (C-3), 144.1, 134.3, 130.2, 129.4, 128.7, 128.1, 128.0 (Ar C's), 70.2, 69.8, 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 447.1195.

4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-deoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-L-*lyxo*-pentitol (70) and 4-*O*-Acetyl-1,5-anhydro-2-*O*-benzoyl-3-deoxy-3-[2-(*p*-tolylsulfonyl)hydrazino]-L-*arabino*-pentitol (71). Reduction of **55** with $NaBH_3CN$ was accomplished by the method described in the general procedures. Two products, **70** and **71**, were isolated by flash chromatography (5% EtOAc/$CHCl_3$) with a total yield of 70%. ^{1}H NMR ($CDCl_3$) of **70**: δ 8.02 (2 H, d, J = 7.3, ortho H's), 7.59 (1 H, t, J = 7.4, para H), 7.44 (2 H, dd, J = 7.4, 7.3, meta H's), 7.73, 7.25 (2 H each, d, J = 8.1, Ts H's), 6.41 (1 H, b s, NH), 5.46 (1 H, b t, J = 3.0, 2-H), 4.92 (1 H, ddd, J = 10.8, 9.7, 5.0, 4-H), 4.05 (1 H, dd, J = 10.8, 5.0, 5-H), 3.59 (1 H, d, J = 11.9, 1-H), 3.52 (1 H, buried, NH), 3.50 (1 H, dd, J = 11.9, 3.0, 1-H), 3.38 (1 H, ddd, J = 9.7, 7.4, 3.0, 3-H), 3.30 (1 H, t, J = 10.8, 5-H), 2.40 (3 H, s, Ts-Me), 2.11 (3 H, s, CH_3C=O). ^{1}H NMR ($CDCl_3$) of **71**: δ 8.08 (2 H, d, J = 7.1, ortho H's), 7.65 (1 H, t, J = 7.4, para H), 7.51 (2 H, dd, J = 7.4, 7.1, meta H's), 7.53, 6.99 (2 H each, d, J = 8.1, Ts H's), 6.27 (1 H, d, J = 2.7, NH), 5.29 (1 H, b s, 4-H), 5.10 (1 H, ddd, J = 9.6, 9.5, 5.0, 2-H), 4.09 (1 H, dd, J = 11.1, 5.0, 1-H), 3.98 (1 H, dd, J = 12.7, 2.7, 5-H), 3.57 (1 H, dd, J = 12.7, 1.6, 5-H), 3.55 (1 H, b d, J = 3.0, NH), 3.49 (1 H, dd, J = 9.6, 3.0, 3-H), 3.48-3.45 (1 H, m, NH), 3.40 (1 H, dd, J = 11.1, 9.5, 1-H), 2.31 (3 H, s, Ts-Me), 2.13 (3 H, s, CH_3C=O). ^{13}C NMR ($CDCl_3$) of **71**: δ 171.3 (CH_3C=O), 166.3 (PhC=O), 133.7-128.1 (Ar C's), 68.4, 67.8, 66.8, 63.0, 55.9 (C-1,2,3,4,5), 21.6 (Ts-Me), 21.0 (CH_3C=O). High-resolution FAB-MS: calcd for $C_{21}H_{25}N_2O_7S$ $(M + H)^+$ 449.1382, found 449.1346.

When the reduction was carried out with $NaBD_3CN$, the intensity of the 3-H peak of both **70** and **71** was diminished by 45%. This corresponds to a 45% deuterium incorporation at the imino carbon C-3.

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Supplementary Material Available: Experimental data for **1-12, 14-25, 28-43, 51-53, 65-68,** and **106-108** (17 pages). Ordering information is given on any current masthead page.

Preparation and Absorption Spectra of Arylhydrazones from α,β-Unsaturated Carbonyl Compounds

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Substituted arylhydrazones **2-17, 19,** and **23-29** were prepared from several α,β-unsaturated carbonyl compounds and their absorption spectra examined. The dependence on concentration of certain near-infrared bands of the spectra has been associated with aggregation and appears to correlate with structural elements of the compounds in a way suggesting significant intermolecular effects, either hydrogen bonding or charge transfer or both.

Arylhydrazones are important intermediates for a number of synthetically useful transformations of carbonyl compounds,[1] such as the Fischer indole synthesis,[2] and are valuable derivatives of long-recognized merit for the characterization of aldehydes and ketones.[3] Recent work[4] has emphasized the sensitivity of these materials toward the conditions of their preparation and the importance of obtaining a better understanding of their properties; this work has further pointed out the somewhat surprising fact that much remains unknown in their chemistry. For example, some aromatic hydrazines display a high degree of

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