4.12-4.13 (2 H, m, H-5'a,b), 4.99 (1 H, s, H-4'), 5.59 (1 H, d, H-5, $J_{5,6}$ = 8.12 Hz), 5.83 (1 H, s H-1'), 6.70-6.80 (4 H_{Arom}, m), 6.99 (1 H, br s, H-2'), 7.77 (1 H, d, H-6), 9.20 (1 H, br s, 3-NH). Anal. Calcd for $C_{17}H_{17}N_5O_5 \cdot 0.5H_2O$: C, 53.64; H, 4.76; N, 18.40. Found: C, 53.35; H, 4.63; N, 18.37.

3'-(Azidomethyl)-2',3'-didehydro-3'-deoxy-β-D-thymidine (3). To a cooled (0 °C) solution of **11a** (18 mg, 0.046 mmol) in CH_3CN/H_2O (4:1) (1.2 mL) was added CAN (51 mg, 0.092 mmol). After a procedure simular to the one used for **1**, **3** (6 mg, 46%) was isolated: mp 201-205 °C (ethyl acetate/methanol); $[\alpha]_D$ -12° (c 0.15, MeOH); ^1H NMR ($CDCl_3$) 1.84 (3 H, s, 5-CH_3), 3.10 (1 H, br s, 5'-OH), 3.80-4.20 (4 H, m, 3'-CH_2, H-5'a,b), 4.81 (1 H, br s, H-4'), 5.80 (1 H, s, H-1'), 7.01 (1 H, s, H-2'), 7.50 (1 H, s, H-6), 8.75 (1 H, br s, 3-NH). Anal. Calcd for $C_{11}H_{13}N_5O_4$: C, 47.31; H, 4.69; N, 25.08. Found: C, 47.28; H, 4.53; N, 25.10.

3'-(Azidomethyl)-2',3'-didehydro-2',3'-dideoxy-β-D-uridine (2). Reaction of **10b** (60 mg, 0.16 mmol) with CAN (181 mg, 0.33 mmol) as described above for **11a** led after purification to **2** (18 mg, 19%): mp 114-117 °C (ethyl acetate/methanol); $[\alpha]_D$ -22° (c 1, MeOH); ^1H NMR ($CDCl_3$) 3.65 (2 H, s, N_3CH_2-3'), 4.15-4.25 (2 H, m, H-5'a,b), 4.71 (1 H, s, 5'-OH), 5.07 (1 H, t, H-4', $J_{4',5'}$ = 4.7 Hz), 5.57 (1 H, d, H-5, $J_{5,6}$ = 8.10 Hz), 5.90 (1 H, s, H-1'), 6.80 (1 H, s, H-2'), 7.53 (1 H, d, H-6), 11.3 (1 H, br s, 3-NH). Anal. Calcd for $C_{10}H_{11}N_5O_4$: C, 45.28; H, 4.18; N, 26.41. Found: C, 45.25; H, 4.20; N, 26.73.

2'-Azido-2',3'-didehydro-2',3'-dideoxy-5'-O-(4-methoxyphenyl)-3'-methylidene-β-D-5-methyluridine (12). At room temperature, under argon, $Pd(OAc)_2$ (13 mg, 0.058 mmol) and PPh_3 (15 mg, 0.057 mmol) were dissolved in THF (3 mL). After 10 min, nucleoside **6a** (23 mg, 0.058 mmol) in solution in THF (3 mL) and NaN_3 (11 mg, 0.17 mmol) in THF/H_2O (9:1, 1 mL) were successively added, and the mixture was stirred for an additional 10 h. The solution was evaporated and the resulting residue poured into water (6 mL) with stirring. This solution was then extracted with chloroform (3 × 5 mL). The chloroform extract was dried ($MgSO_4$) and evaporated to give **12** containing traces of triphenylphosphine. An analytical sample was obtained by recrystallization from ethyl acetate-ether (14 mg, 65%); mp 80-83 °C; $[\alpha]_D$ -25.8° (c 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$) 2.03 (3 H, s, 5-CH_3), 3.74 (3 H, s, CH_3O), 3.98 (1 H, dd, H-5'a, $J_{5'a,4'}$ = 4.26 Hz, $J_{5'a,5'b}$ = 10.31 Hz), 4.13 (1 H, dd, H-5'b, $J_{5'b,4'}$ = 3.56 Hz), 4.80 (1 H, d, H-2', $J_{2',1'}$ = 1.77 Hz), 5.23 (1 H, br s, H-3'a), 5.44 (1 H, br s, H-3'b), 5.83 (1 H, d, H-4', $J_{4',5'}$ = 3.3 Hz), 6.29 (1 H, d, H-1'), 7.24-7.26 (4 H_{Arom}, m), 7.72-7.78 (1 H, m, H-6). Anal. Calcd for $C_{18}H_{19}N_5O_5$: C, 56.09; H, 4.97; N, 18.17. Found: C, 56.28; H, 5.14; N, 18.31.

2'-Azido-2',3'-didehydro-2',3'-dideoxy-3'-methylidene-β-D-methyluridine (4). Reaction of **12** (71 mg, 0.073 mmol) with CAN (71 mg, 0.13 mmol) in $MeCN/H_2O$ 4:1 (2 mL) according to the procedure used for **1** led after purification to **4** as an oil (5 mg, 28%): $[\alpha]_D$ -18° (c 0.5, MeOH); ^1H NMR ($CDCl_3$) 1.91 (3 H, d, 5-CH_3, J = 1.01 Hz), 3.81 (1 H, dd, H-5'a, $J_{4',5'a}$ = 3.27 Hz, $J_{5'a,5'b}$ = 12.20 Hz), 3.99 (1 H, dd, H-5'b, $J_{4',5'b}$ = 2.43 Hz), 4.77 (1 H, br s, 5'-OH), 5.29 (1 H, t, H-3''a, $J_{3''a,2'}$ = 1.97 Hz, $J_{3''a,4'}$ = 2.00 Hz), 5.42 (1 H, t, H-3''b, $J_{3''b,4'}$ = 2.03 Hz), 5.67-5.69 (1 H, m, H-4'), 5.77-5.80 (1 H, m, H-2'), 5.88 (1 H, d, H-1', $J_{1',2'}$ = 5.41 Hz), 7.65 (1 H, d, H-6, $J_{6,5}$ = 1.01 Hz), 8.13 (1 H, br s, 3-NH); MS 280 (M + 1), 297 (M + 18).

Acknowledgment. Dr. Jean-Marc Valery is gratefully acknowledged for recording the ^1H-NMR spectra and Dr. D. Klatzmann for the biological evaluation.

Reactions of Some Pyranoside Diol Monotriflates with Nucleophiles and Bases

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Reaction of pyranoside diol (equatorial) monotriflates with soft, nonbasic nucleophiles is a useful way to make axial heteroatom-substituted and "epimerized" pyranosides, particularly where a fused acetal ring inhibits ring contraction. Among the substrates examined (**1**, **2**, **3**, **4**, **35**), only **4** shows a strong tendency to give ring-contracted products. The reaction of **1-3** with more basic nucleophiles (F^-, t-BuO^-) leads to the anhydrosugars **8**, **25**, and **26**, respectively. The S_N2 reaction of **35** with tetra-n-butylammonium iodide forms the basis for a new synthesis of the Cerny epoxide **32**.

Introduction

Two factors contribute to the difficulty of carrying out bimolecular nucleophilic substitution reactions on carbohydrate substrates. First, the hindered nature of the heavily oxygenated carbohydrate carbon chain or ring greatly increases the activation energy for the S_N2 process relative to a hydrocarbon chain or ring.[1] Second, nearby hydroxyls, protecting groups, and ether oxygens can participate at the carbon undergoing substitution, resulting in rearranged or doubly-inverted products.[2] We have recently described the preparation of carbohydrate diol and triol monotriflates[3] by selective monotriflation.[4,5] Pyranoside diols can give particularly good selectivity, and the derived diol monotriflates are frequently (but not always[5,6]) stable enough to be isolated and characterized. Inasmuch as the carbohydrate triflate group is reactive toward displacement by nucleophiles,[7] and the neighboring (unprotected) hydroxyl is relatively small, this class of compounds promises to be useful for carrying out substitution reactions with inversion at the triflate-bearing

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(2) See, for example: (a) Mantell, S. J.; Ford, P. S.; Watkin, D. J.; Fleet, G. W. J.; Browne, D. *Tetrahedron Lett.* **1992**, *33*, 4503. (b) Binkley, R. W. *J. Carbohydr. Chem.* **1992**, *11*, 189. (c) Sato, K.; Hoshi, T.; Kajihara, Y. *Chem. Lett.* **1992**, 1469.

(3) "Triflate" = trifluoromethanesulfonate. We use the term "diol monotriflate" rather than "hydroxy triflate", to emphasize that the compound was made by monotriflation of a diol.

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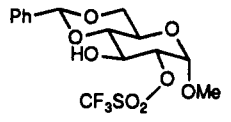
0022-3263/92/1957-7328$03.00/0

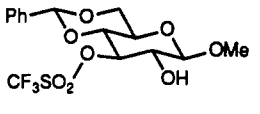
carbon. In addition, two synthetic steps, hydroxyl protection and deprotection, can in principle be saved. The challenge is to identify nucleophiles, substrates, and reaction conditions that minimize elimination, fragmentation, ring-contraction, and participation by the hydroxyl or another nearby Lewis-basic group. We report our results on displacement reactions of pyranoside diol monotriflates with a variety of nucleophiles and, for comparison, some reactions with strong bases leading to anhydro sugars. We also describe a diol monotriflate displacement reaction that leads to a new synthesis of the Cerny epoxide **32**.

Results and Discussion

Four different methyl 4,6-*O*-benzylidene-D-glycopyranoside monotriflates **1**–**4** have been prepared from the corresponding diols by selective monotriflation. In the



1



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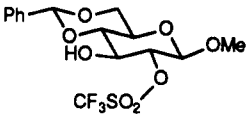

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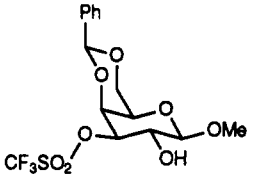
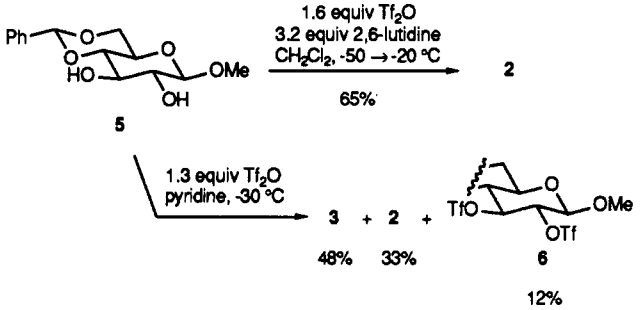


4

cases of **1** and **4**, the selectivity results from interaction of the reacting hydroxyl with a neighboring cis, vicinal ether oxygen, possibly through hydrogen-bonding.[4,8] By using triflic anhydride and 2,6-lutidine in dichloromethane solution at −50 to −20 °C, methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**5**) can be selectively sulfonylated at the C-3 hydroxyl to give **2** (65% isolated yield);[4] the selectivity may be due to the bulkiness of the (presumed) electrophile, 2,6-dimethyl-1-(trifluoromethanesulfonyl)pyridinium trifluoromethanesulfonate, which reacts at the less hindered hydroxyl.[8] We now find that changing the solvent and base to pyridine also changes the triflation selectivity—under these more basic conditions **5** gave the 2-triflate **3** as the major product. Each of the diol monotriflates **1**–**4** can be made in gram quantities and stored in the freezer for several months.



The four pyranoside diol monotriflates were treated with nucleophiles from a list that includes an oxygen nucleophile (sodium acetate), a nitrogen nucleophile (sodium azide), a mercaptide (sodium thiomethoxide), a thiocarboxylate (potassium thioacetate), and a selenium nucleophile (sodium selenophenoxide[9]). The results of successful displacements are summarized in Table I. As is commonly observed in carbohydrate reactions, each pyranoside substrate reveals a distinctive reactivity pattern. Some observations can be made: (1) displacements are frequently successful for soft, nonbasic nucleophiles (sodium azide, sodium thiomethoxide, and potassium thioacetate) in dimethylformamide solution at moderate temperatures; (2) displacements with sodium acetate appear to represent a borderline situation (**2** and **3** afford good yields, whereas **1** gives a low yield of S_N2 product); (3) the β-galactopyranoside 3-triflate **4** is the most difficult substrate for S_N2. Treatment of **4** with sodium thiomethoxide gave a displacement product **23a** in good yield, but attempted displacement with sodium azide led to the unstable ring-contracted aldehydes **24a**, which were reduced and characterized as the acetate **24c**.

All new compounds in Table I were characterized by ^1H NMR and IR spectra, optical rotation, and elemental analysis. In all cases, the stereochemistry (axial or equatorial) and the position of each C-2 or C-3 substituent was confirmed by the chemical shift and vicinal proton coupling constants of the pyranose ring hydrogens. Thioacetate **10**[10] and azide **9a**[11] match the known compounds. The thioacetate products **10**, **16**, and **21** became *O*-acetylated under the displacement conditions. Subsequent and separate *O*-acetylation of azides **9a** and **20a** gave the known derivatives **9b**[11] and **20b**.[12] Basic hydrolysis of either monoacetate **13** or **14a** gave the known allopyranoside diol, **14b**.[13] Likewise, hydrolysis of either monoacetate **19a** or **19b** gave the known mannopyranoside diol, **19c**.[14]

The S_N2 displacement of triflate from diol monotriflates **1**–**4** represents an efficient way to introduce heteroatoms onto the pyranoside ring system. In particular, diol monotriflation followed by acetate displacement is a short and simple means of inverting secondary hydroxy stereochemistry in certain pyranosides. Four families of pyranoside mono-ols are now available wherein the hydroxyl group is flanked by a cis, vicinal heteroatom (O, N, S, or Se). As the reactivity of secondary carbohydrate alcohols (toward *O*-sulfonylation, for example) is known to be profoundly affected by nearby ether oxygens,[4,8] these compounds may prove useful for further probing the nature of this effect.

For the trans, vicinal, diequatorial diol monotriflate **1**, **2**, or **3**, treatment with more basic reagents (sodium cyanide, sodium fluoride, sodium methoxide, potassium *tert*-butoxide) tends to give the 2,3-anhydro sugar as a major, high R_f product. As shown in Table II, formation of epoxides **8**,[15] **25**,[16–18] and **26**[17,18] from **1**, **2**, and **3**, respectively, can be quite efficient in the presence of fluoride or *tert*-butoxide, and this represents a good route to this class of compounds. An alternative base-promoted pathway, ring contraction to form a carboxaldehyde product,[6] does not appear to be major here.

In contrast, no high R_f product corresponding to epoxide **27** was found in the reaction of galactopyranoside substrate **4** with either potassium *tert*-butoxide or tetra-*N*-butylammonium fluoride. Several unstable, low R_f products were detected in the reactions of **4**, and ^1H NMR analysis

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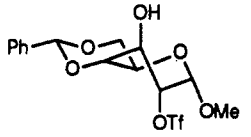
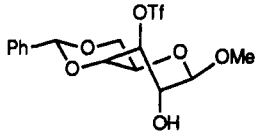
of the crude mixtures shows three aldehyde–C*H*O signals, two of which correspond to the epimers of the ring-contracted product **24a**. Sodium azide is basic enough to cause ring contraction of **4** (see Table I), so similar reactions with fluoride and *tert*-butoxide are understandable.

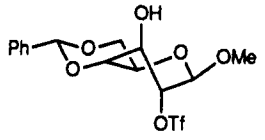
In the stable $^4C_1$ conformation, the 2,3-trans, diequatorial diol monotriflates possess the appropriate anti coplanar orbital alignment for base-promoted ring contraction, but not for epoxide formation, which ought to require a change in conformation. For **1–4**, the reactive conformations leading to epoxide formation are represented by the twist boats **28–31**, respectively. The recent investigation of the



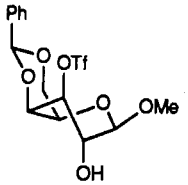
28 (from **1**)



29 (from **2**)



30 (from **3**)

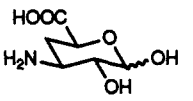


31 (from **4**)

reactions of 2,6-dideoxypyranoside 3,4-diol monotriflates with base points to ring contraction as the principal pathway for the trans, diequatorial systems, and epoxide formation for the trans, diaxial ones.[6] One difference present in substrates **1–3** is the trans-fused 1,3-dioxane ring of the benzylidene acetal, which may inhibit ring contraction owing to an increase in ring strain of the ring-contracted product. For the cis-fused ring system of **4**, however, ring contraction would not result in so great an increase in ring strain, and this may account for its differing behavior under basic conditions.[19] Eclipsing interactions involving nearby oxygen atoms are apparent at C-1,2 of **28** and C-3,4 of **31**, but **28** forms the anhydro sugar easily, whereas **31** does not.

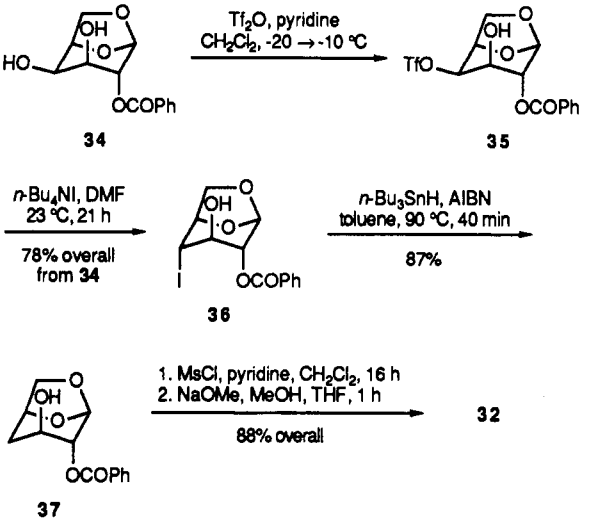
A diol monotriflate displacement reaction has led to a new synthesis of the Cerny epoxide, 1,6:2,3-dianhydro-4-deoxy-β-D-allopyranose (**32**).[20,21] This compound has been used for the synthesis of various 4-deoxy sugars,[22,23] including ezoaminuroic acid **33**,[24] and as a precursor to (−)-*cis*-rose oxide.[25] The racemic version has been used in syntheses of DL-glucose, -galactose, and -allose.[26–28] We viewed this epoxide as an ideal precursor to various protected, (C-6)-reduced, ezoaminuroic acid substrates for use in glycosylation studies and for eventual application to the synthesis of the ezomycin antibiotics.[29]

32



33

Selective monotriflation[5] of 1,6-anhydro-2-*O*-benzoyl-β-D-galactopyranose[30,31] (**34**) (an improved preparation is given in the Experimental Section) occurred at the less hindered, equatorial[8] C-4 hydroxyl to give triflate **35**. Treatment of **35** with tetra-*n*-butylammonium iodide gave the axial [J(H-4/H-5) = J(H-1/H-2) = 0] iodide **36**. The absence of a ring-contracted product may again be the result of prohibitive ring strain in the transition state for such a process. The epimeric "pair" **35** and **36** represents potential precursors to various 4-substituted pyranoses, depending upon successful displacement of triflate and iodide, respectively.[32] Free-radical reduction of **36** afforded the deoxy pyranose **37**; mesylation and then treatment with sodium methoxide led efficiently to the epoxide **32**.[20,21] Overall, the route encompasses five steps (about 60%) from **34** and conveniently provides gram quantities of **32**.



Experimental Section[33]

Methyl 4,6-*O*-(Phenylmethylene)-2-*O*-[(trifluoromethyl)sulfonyl]-β-D-glucopyranoside (3). Trifluoromethanesulfonic anhydride (1.1 mL, 6.54 mmol, 1.3 equiv) was added to a stirred solution of 1.40 g (5 mmol, 1 equiv) of methyl 4,6-*O*-(phenylmethylene)-β-D-glucopyranoside (**5**) in 100 mL of dry pyridine at −30 °C. The reaction mixture turned orange immediately, and a white precipitate was deposited. The flask was shaken to break apart the solid, which dissolved over a period of about 4 h. After 12 h at −30 °C, the reaction was quenched by addition of 500 mL of water. The reaction mixture was concentrated in vacuo, and the resulting residue was chromatographed on silica with 3:1 petroleum ether/ethyl ether as the eluant to afford, in order of elution, 0.484 g of the 2-triflate **3**, 0.838 g of a mixture of **3** and the ditriflate **6**, and 0.678 g (33%) of the 3-triflate **2**. The mixture was crystallized from dichloromethane/petroleum ether to afford an additional 0.502 g of **3** (total 0.986 g, 48%). The mother liquor was concentrated to afford 0.330 g (12%) of ditriflate **6** containing trace amounts of **3**. The three

(19) A 3,4-cis-fused acetonide, however, does not inhibit ring contraction of some 2-*O*-sulfonyl galactopyranosides: (a) Fleet, G. W. J.; Seymour, L. C. *Tetrahedron Lett.* **1987**, *28*, 3015. (b) Ahmed, F. M. E. S., David, S.; Vatele, J.-M. *Carbohydr. Res.* **1986**, *155*, 19. Here, as always, caution must be exercised in comparing reactions of dissimilar carbohydrate substrates.

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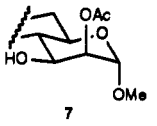
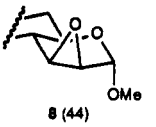
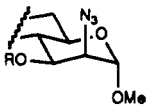
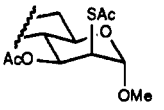
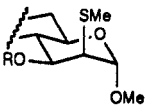
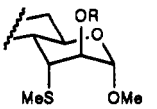
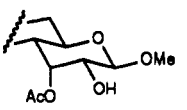
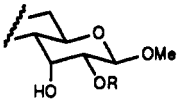
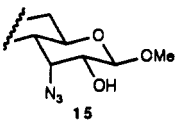
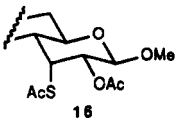
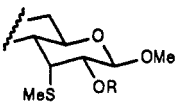
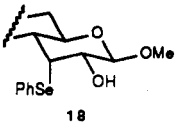
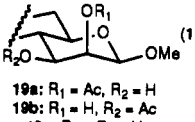
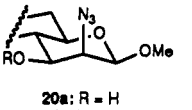
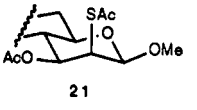
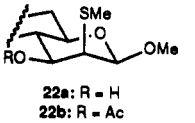
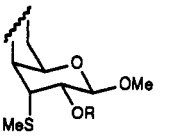
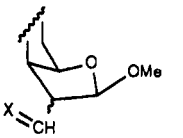
(33) Proton nuclear magnetic resonance (NMR) spectra were obtained on deuteriochloroform solutions unless otherwise specified. J values are given in Hz; IR values are given in cm^{-1}. Additional general information on reagents and apparatus may be found in ref 4.

Table I. Displacement Reactions of Pyranoside Diol Monotriflates

triflate	condns	S_N2 product	% yield	other prods (% yield)
1	NaOAc (10 equiv) DMF, 6 d	 **7**	22	 **8** (44) + recovered **1** (6)
1	NaN_3 (10 equiv) DMF, 4 d	 **9a**: R = H **9b**: R = Ac	79	recovered **1** (5)
1	KSAc DMF, 2 h	 **10**	85	
1	NaSMe DMF, 2 h	 **11a**: R = H **11b**: R = Ac	15	 **12a**: R = H (61) **12b** R = Ac
2	NaOAc (10 equiv) DMF, 1 d	 **13**	86	 **14a**: R = Ac (4) **14b**: R = H
2	NaN_3 (10 equiv) DMF, 1 h (from ref. 4)	 **15**	85	
2	n-Bu_4NN_3 (5 equiv) benzene, 1 h	**15**	75	
2	KSAc (10 equiv) DMF, 2 d	 **16**	85	
2	NaSMe (10 equiv) DMF, -40 °C	 **17a**: R = H **17b**: R = Ac	89	
2	NaSePh THF, EtOH	 **18**	60	
3	NaOAc (10 equiv) DMF, 2 d	 **19a**: R_1 = Ac, R_2 = H **19b**: R_1 = H, R_2 = Ac **19c**: R_1 = R_2 = H	92 (**19a/b** = 6:1)	
3	NaN_3 (10 equiv) DMF, 3 d	 **20a**: R = H **20b**: R = Ac	85	
3	KSAc (10 equiv) DMF, 2.5 d	 **21**	81	
3	NaSMe (10 equiv) DMF, -40 °C, 2 h	 **22a**: R = H **22b**: R = Ac	28	
4	NaSMe (10 equiv) DMF, -40 °C, 2 h	 **23a**: R = H **23b**: R = Ac	65	
4	NaN_3 (2 equiv) DMF, 18 h	 **24a**: X = O (57) **24b**: X = H, OH **24c**: X = H, OAc		

products matched authentic samples[4] by TLC and NMR analysis.

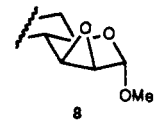
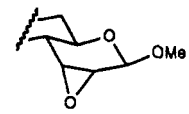
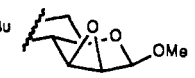
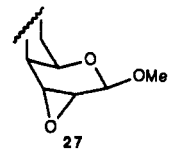
General Procedure for Triflate Displacement Reactions. A 0.05 M solution of the pyranoside diol monotriflate (**1**, **2**, **3**, or **4**) in dimethylformamide was treated with 10 equiv of sodium azide, sodium acetate, sodium thiomethoxide, or potassium thioacetate at 23 °C unless otherwise indicated in Table I, and the solution was allowed to stir for the indicated time. Progress of the reactions was monitored by TLC analysis of concentrated aliquots. Attempts to increase the rate of displacements by heating above room temperature led to the appearance of undesired products (TLC analysis). The reaction mixture was concentrated in vacuo, and the residue was partitioned between dichloromethane and water. The organic phase was dried over magnesium sulfate and concentrated. The product was isolated by chromatography on silica with ether/hexane mixtures as the eluant. Solid products were typically crystallized from ethyl ether/hexane or dichloromethane/hexane. When deemed necessary for characterization, acetylation of the product alcohols was carried out by using a solution of 20 equiv of acetic anhydride and 0.1 equiv of 4-(*N*,*N*-dimethylamino)pyridine in pyridine. Acetylated products were isolated as described above.

General Procedures for Epoxide Formation. (A) With Potassium *tert*-Butoxide. A 0.05 M solution of the pyranoside diol monotrilfate (**1**, **2**, **3**, or **4**) in 2-methyl-2-propanol (dried over 4-Å molecular sieves) was treated with 2.0 equiv of solid, sublimed potassium *tert*-butoxide. The reaction was kept at 23 °C for 2 h, at which time TLC analysis indicated the disappearance of starting material. The reaction was quenched by addition of 1 mL of saturated aqueous sodium bicarbonate and then concentrated and partitioned between ethyl acetate and water. The organic phase was dried over magnesium sulfate, concentrated, and chromatographed and crystallized according to the reported procedures.

(B) With Tetra-*n*-butylammonium Fluoride. The general procedure for displacement reactions was followed, except that tetra-*n*-butylammonium fluoride was used as the "nucleophile" and benzene as the reaction solvent.

Methyl 2-*O*-acetyl-4,6-*O*-(phenylmethylene)-α-D-mannopyranoside (7): $[\alpha]_D = +14.0°$ ($c = 0.65$, $CHCl_3$) (lit.[14] $[\alpha]_D$ +26°, $c = 0.8$, $CHCl_3$); NMR (300 MHz) 2.17 (s, OAc), 2.36 (d, $J = 4.2$,

Table II. Anhydro Sugar Formation from Diol Monotriflates

substrate	condns	anhydro sugar	% yield
1	KO*t*-Bu, HO*t*-Bu 23 °C, 2 h	 8	86
2	KO*t*-Bu, HO*t*-Bu 23 °C, 2 h	 25	98
3	KO*t*-Bu, HO*t*-Bu 23 °C, 2 h	 26	90
3	*n*-Bu$_4$NF, benzene 23 °C, 1 h	26	90
4	KO*t*-Bu, HO*t*-Bu 23 °C, 2 h	 27	0
4	*n*-Bu$_4$NF, benzene 23 °C, 1 h	27	0

OH), 3.39 (s, OCH_3), 3.78–3.93 (m, 3 H), 4.28–4.33 (m, 2 H), 4.69 (d, J = 1.5, H-1), 5.21 (dd, J = 3.7, 1.5, H-2), 5.60 (s, PhC*H*), 7.26–7.39 (m, 3 H_{arom}), 7.46–7.51 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 3595 (OH), 1745 (OAc). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.08; H, 6.30.

Methyl 2,3-anhydro-4,6-*O*-(phenylmethylene)-α-D-mannopyranoside (8): mp 143–144 °C from methanol (lit.[15] mp 145–147 °C); $[\alpha]_D$ = +105.0° (c = 1.11, $CHCl_3$) (lit.[15] $[\alpha]_D$ +107°, c = 1.6, $CHCl_3$); NMR (300 MHz, benzene-d_6) 3.22 (d, J = 3.6, H-2), 3.35 (s, OCH_3), 3.60 (d, J = 3.6, H-3), 3.77 (t, J = 10.2, H-6_{ax}), 3.91 (d, J = 9.5, H-4), 4.07 (td, J = 9.9, 4.7, H-5), 4.39 (dd, J = 10.2, 4.6, H-6_{eq}), 4.97 (s, H-1), 5.55 (s, PhC*H*), 7.45–7.57 (m, 3 H_{arom}), 7.91–7.93 (m, 2 H_{arom}); IR (KBr) 3020, 2860, 1080.

Methyl 2-Azido-2-deoxy-4,6-*O*-(phenylmethylene)-α-D-mannopyranoside (9a) and Its Acetate (9b). For **9a**: $[\alpha]_D$ = +68.1° (c = 1.04, $CHCl_3$) (lit.[11] $[\alpha]_D$ +69.5°, c = 1.06, $CHCl_3$); NMR (300 MHz) 2.84 (d, J = 4.0, OH), 3.36 (s, OCH_3), 3.73–3.89 (m, H-2,3,4,6_{ax}), 4.20 (td, J = 9.5, 4.0, H-5), 4.23 (partially obscured dd, J = 9.3, 3.8, H-6_{eq}), 4.65 (d, J = 1.5, H-1), 5.54 (s, PhC*H*), 7.25–7.30 (m, 3 H_{arom}), 7.45–7.50 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 3600 (OH), 2110 (azido); DCI-MS 308 (M^+ + 1). Anal. Calcd for $C_{14}H_{17}N_3O_5$: C, 54.72; H, 5.58; N, 13.67. Found: C, 54.88; H, 5.42; N, 13.45. For **9b**: $[\alpha]_D$ = +39.4° (c = 1.87, $CHCl_3$); NMR (300 MHz) 2.15 (s, OAc), 3.42 (s, OCH_3), 3.81 (t, J = 10.2, H-6_{ax}), 3.88 (td, J = 10.2, 4.0, H-5), 4.06 (t, J = 9.2, H-4), 4.14 (dd, J = 3.9, 1.5, H-2), 4.25 (dd, J = 9.2, 3.8, H-6_{eq}), 4.68 (d, J = 1.4, H-1), 5.42 (dd, J = 10.1, 3.9, H-3), 5.55 (s, PhC*H*), 7.35–7.42 (m, 3 H_{arom}), 7.45–7.55 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 2105 (azido), 1748 (OAc). Anal. Calcd for $C_{16}H_{19}N_3O_6$: C, 55.01; H, 5.48; N, 12.03. Found: C, 55.06; H, 5.54; S, 12.08.

Methyl 3-*O*,2-*S*-diacetyl-4,6-*O*-(phenylmethylene)-2-thio-α-D-mannopyranoside (10): mp 127–128 °C from ether/petroleum ether (lit.[10] mp 130–131 °C from ethanol); $[\alpha]_D$ = +34.2° (c = 0.45, $CHCl_3$) (lit.[10] $[\alpha]_D$ +31.6, c = 0.76, $CHCl_3$); NMR (400 MHz) 2.00 (s, OAc), 2.39 (s, SAc), 3.41 (s, OCH_3), 3.76 (t, J = 9.8, H-4), 3.79 (t, J = 10.3, H-6_{ax}), 3.98 (td, J = 10.0, 4.7, H-5), 4.26 (dd, J = 10.3, 4.7, H-6_{eq}), 4.37 (dd, J = 4.8, 1.2, H-2), 4.73 (br s, H-1), 5.54 (s, PhC*H*), 5.63 (dd, J = 10.3, 4.9, H-3), 7.34–7.38 (m, 3 H_{arom}), 7.43–7.47 (m, 2 H_{arom}); IR (film) 1740 (OAc), 1695 (SAc); DCI-MS 383 (M^+ + 1). Anal. Calcd for $C_{18}H_{22}O_7S$: C, 56.53; H, 5.80; S, 8.38. Found: C, 56.74; H, 5.51; S, 8.56.

Methyl 2-*S*-Methyl-4,6-*O*-(phenylmethylene)-2-thio-α-D-mannopyranoside (11a) and Its Acetate (11b). For **11a**: NMR (300 MHz) 2.24 (s, SCH_3), 2.66 (d, J = 7.1, C-3 OH), 3.16 (dd, J = 4.8, 1.8, H-2), 3.36 (s, OCH_3), 3.65–3.83 (m, 3 H), 4.18–4.26 (m, 1 H), 4.33 (ddd, J = 9.6, 7.1, 4.9, H-3), 4.91 (s, H-1), 5.54 (s, PhC*H*), 7.31–7.38 (m, 3 H_{arom}), 7.44–7.49 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 3600 (free OH), 3505 (H-bonded OH). For **11b**: oily semisolid, mp 48 °C; $[\alpha]_D$ = +0.90° (c = 0.67, $CHCl_3$); NMR (300 MHz) 2.09 (s, OAc), 2.17 (s, SCH_3), 3.38 (s, OCH_3), 3.43 (dd, J = 4.8, 0.7, H-2), 3.81 (app t, J = 9.9, H-6_{ax}), 3.91 (td, J = 10, 4.3, H-5), 4.04 (app t, J = 10.0, H-4), 4.23 (dd, J = 9.8, 4.2, H-6_{eq}), 4.86 (s, H-1), 5.46 (dd, J = 10.1, 4.8, H-3), 5.55 (s, PhC*H*), 7.32–7.38 (m, 3 H_{arom}), 7.43–7.46 (m, 2 H_{arom}). Anal. Calcd for $C_{17}H_{22}O_6S$: C, 57.61; H, 6.26; S, 9.05. Found: C, 57.90; H, 6.34; S, 8.90.

Methyl 3-*S*-Methyl-4,6-*O*-(phenylmethylene)-3-thio-α-D-altropyranoside (12a) and Its Acetate (12b). For **12a**: mp 131.5–133 °C from ether/hexane; $[\alpha]_D$ = +19.8° (c = 1.11, $CHCl_3$); NMR (300 MHz) 2.20 (s, SCH_3 and OH), 3.23 (br t, J = 3.3, H-3), 3.38 (s, OCH_3), 3.76–3.84 (m, 1 H), 4.14 (br s, H-2), 4.23–4.37 (m, 3 H), 4.55 (s, H-1), 5.59 (s, PhC*H*), 7.32–7.38 (m, 3 H_{arom}), 7.44–7.49 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 3610 (sharp, free OH), 3430 (H-bonded OH). Anal. Calcd for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45; S, 10.26. Found: C, 57.60; H, 6.52; S, 10.08. For **12b**: oily semisolid, mp 58 °C; $[\alpha]_D$ = +42.2° (c = 1.51, $CHCl_3$); NMR (300 MHz) 2.15 (s, OAc), 2.24 (s, SCH_3), 3.22 (dd, J = 3.7, 2.7, H-3), 3.38 (s, OCH_3), 3.80 (td, J = 11.5, 2.5, H-5), 4.16 (dd, J = 9.2, 4.3, H-6_{eq}), 4.27–4.37 (m, 2 H), 4.54 (br s, H-1), 5.14 (dd, J = 3.7, 1.3, H-2), 5.60 (s, PhC*H*), 7.31–7.38 (m, 3 H_{arom}), 7.43–7.49 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 1735 (OAc). Anal. Calcd for $C_{17}H_{22}O_6S$: C, 57.61; H, 6.26; S, 9.05. Found: C, 57.82; H, 6.37; S, 8.86.

Methyl 3-*O*-Acetyl- and 2-*O*-Acetyl-4,6-*O*-(phenylmethylene)-β-D-allopyranoside (13 and 14a, Respectively). For **13** (lower R_f, silica, 3:2 ether/hexane): mp 126–127 °C from ether/hexane; $[\alpha]_D$ = −55.8° (c = 0.77, $CHCl_3$); NMR (400 MHz) 2.18 (s, OAc), 2.37 (br s, OH), 3.60 (s, OCH_3), 3.66–3.71 (m, H-2 and H-4), 3.77 (t, J = 10.3, H-6_{ax}), 3.94 (td, J = 9.8, 4.9, H-5), 4.40 (dd, J = 10.3, 4.9, H-6_{eq}), 4.61 (d, J = 7.9, H-1), 5.54 (s, PhC*H*), 5.78 (t, J = 2.9, H-3), 7.26–7.37 (m, 3 H_{arom}), 7.41–7.44 (m, 2 H_{arom}); IR (film) 3490 (OH), 1745 (OAc). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.23; H, 6.22. Found: C, 59.43; H, 6.35. For **14a** (higher R_f, silica, 3:2 ether/hexane): mp 161–162.5 °C from ether/hexane; $[\alpha]_D$ = −78.0° (c = 0.20, $CHCl_3$); NMR (400 MHz) 2.17 (s, OAc), 2.27 (s, OH), 3.54 (s, OCH_3), 3.68 (dd, J = 9.3, 2.3, H-4), 3.80 (t, J = 10.3, H-6_{ax}), 4.06 (td, J = 9.5, 5.1, H-5), 4.42 (dd, J = 10.3, 4.9, H-6_{eq}), 4.48 (t, J = 2.4, H-3), 4.79 (dd, J = 8.1, 2.8, H-2), 4.85 (d, J = 8.3, H-1), 5.60 (s, PhC*H*), 7.26–7.41 (m, 3 H_{arom}), 7.47–7.50 (m, 2 H_{arom}); IR (film) 3487 (OH), 1716 (OAc); DCI-MS 325 (M^+ + 1). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.23; H, 6.22. Found: C, 59.69; H, 6.24. Basic hydrolysis of either **13** or **14a** gave the known[13] methyl 4,6-*O*-(phenylmethylene)-β-D-allopyranoside **14b**: mp 171–173 °C from ethanol (lit.[13] mp 173–174 °C); $[\alpha]_D$ = −45.1° (c = 0.48, $CHCl_3$) (lit.[13] $[\alpha]_D$ −43.0°, c = 1.0, $CHCl_3$); NMR (400 MHz) 2.55 (s, C-3 OH), 2.65 (d, J = 6.4, C-2 OH), 3.48–3.53 (m, H-2), 3.58 (s, OCH_3), 3.59 (partially obscured dd, J = 9.3, 2.4, H-4), 3.76 (t, J = 10.3, H-6_{ax}), 4.00 (td, J = 9.8, 4.9, H-5), 4.38 (br s, H-3), 4.40 (dd, J = 10.4, 5.1, H-6_{eq}), 4.62 (d, J = 7.8, H-1), 5.58 (s, PhC*H*), 7.34–7.39 (m, 3 H_{arom}), 7.48–7.54 (m, 2 H_{arom}); IR (dilute CCl_4) 3495, 3345, 3255 (free and H-bonded OH's).

Methyl 2-*O*,3-*S*-diacetyl-4,6-*O*-(phenylmethylene)-3-thio-β-D-allopyranoside (16): mp 118–120 °C from dichloromethane/petroleum ether; $[\alpha]_D$ = −85.2° (c = 0.79, $CHCl_3$); NMR (300 MHz) 2.03 (s, OAc), 2.39 (s, SAc), 3.49 (s, OCH_3), 3.55 (td, J = 9.6, 5.0, H-5), 3.73 (t, J = 10.4, H-6_{ax}), 3.94 (dd, J = 9.4, 4.2, H-4), 4.32 (dd, J = 10.5, 5.0, H-6_{eq}), 4.53 (d, J = 8.2, H-1), 4.67 (t, J = 4.3, H-3), 5.02 (dd, J = 8.2, 4.4, H-2), 5.57 (s, PhC*H*), 7.33–7.38 (m, 3 H_{arom}), 7.42–7.47 (m, 2 H_{arom}); IR (dilute CCl_4) 1750 (OAc), 1695 (SAc); DCI-MS 383 (M^+ + 1). Anal. Calcd for $C_{18}H_{22}O_7S$: C, 56.53; H, 5.80; S, 8.38. Found: C, 56.42; H, 5.80; S, 8.11.

Methyl 3-*S*-Methyl-4,6-*O*-(phenylmethylene)-3-thio-β-D-allopyranoside (17a) and Its Acetate (17b). For **17a**: $[\alpha]_D$ = −81.7° (c = 0.80, $CHCl_3$); NMR (400 MHz) 2.28 (s, SCH_3), 2.96 (d, J = 7.9, C-2 OH), 3.56 (s, OCH_3), 3.58 (overlapped dd, J = 8.6, 4.2, H-3), 3.73 (td, J = 8.0, 4.7, H-2), 3.77 (t, J = 10.4, H-6_{ax}), 3.84 (dd, J = 9.1, 3.7, H-4), 4.02 (td, J = 9.8, 5.1, H-5), 4.31 (d, J = 8.1, H-1), 4.37 (dd, J = 10.5, 5.3, H-6_{eq}), 5.56 (s, PhC*H*),

7.35–7.40 (m, 3 H_{arom}), 7.47–7.50 (m, 2 H_{arom}); IR (dilute CCl_4) 3591 (free OH), 3480 (H-bonded OH). Anal. Calcd for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45; S, 10.26. Found: C, 57.64; H, 6.52; S, 10.15. For **17b**: $[\alpha]_D$ = −71.6° (*c* = 1.44, $CHCl_3$); NMR (400 MHz) 2.17 (s, OAc), 2.23 (s, SCH_3), 3.53 (s, OCH_3), 3.74–3.82 (m, H-6_{ax} and H-3), 3.91 (dd, *J* = 9.2, 3.7, H-4), 4.12 (td, *J* = 9.8, 5.2, H-5), 4.38 (dd, *J* = 10.4, 5.1, H-6_{eq}), 4.67 (d, *J* = 8.3, H-1), 4.85 (dd, *J* = 8.3, 4.6, H-2), 5.54 (s, PhC*H*), 7.32–7.36 (m, 3 H_{arom}), 7.38–7.47 (m, 2 H_{arom}); FT-IR (3% in $CHCl_3$) 1740 (OAc). Anal. Calcd for $C_{17}H_{22}O_6S$: C, 57.61; H, 6.26; S, 9.05. Found: C, 57.79; H, 6.22; S, 8.94.

Methyl 3-Deoxy-4,6-*O*-(phenylmethylene)-3-(phenylseleno)-β-D-allopyranoside (18). Sodium borohydride (27.5 mg, 0.726 mmol, 2 molar equiv) was added to a stirred solution of 177 mg (1.81 mmol, 5 equiv) of diphenyl diselenide in 4 mL of absolute ethanol at −10 °C. The solution turned yellow as the sodium borohydride dissolved. A solution of 150 mg (0.363 mmol, 1 equiv) of triflate **2** in 4 mL of THF was added, and the resulting reaction mixture was allowed to warm to 23 °C over 3 h and then was stirred at 23 °C for 1 h. The reaction was quenched with 2 mL of saturated aqueous sodium bicarbonate, concentrated, and then extracted by using 10 mL of water and 35 mL of ethyl acetate. The organic phase was dried over magnesium sulfate, concentrated, and chromatographed on silica with 5:1, and then 2:1, hexane/ethyl ether as the eluant to afford 92 mg (60%) of selenide **18** as a colorless solid, mp 129.5–131 °C: $[\alpha]_D$ = −157.3 (*c* = 0.93, $CHCl_3$); NMR (400 MHz) 3.05 (d, *J* = 8.4, OH), 3.58 (s, OMe), 3.68 (td, *J* = 8.3, 4.6, H-2), 3.79–3.85 (m, H-4, H-5, H-6_{eq}), 4.04 (dd, *J* = 4.5, 3.8, H-3), 4.26 (d, *J* = 8.1, H-1), 4.39 (dd, *J* = 8.5, 3.1, H-6_{ax}), 5.62 (s, PhC*H*), 7.17–7.47 (m, 8 H_{arom}), 7.67 (d, *J* = 7.0, 2 H_{arom}) IR (dilute CCl_4) 3605, 3495 (free and H-bonded O-H); DCI-MS *m/z* 422 (M^+ + 1). Anal. Calcd for $C_{20}H_{22}O_5Se$: C, 57.01; H, 5.26. Found: C, 56.99; H, 5.02.

Methyl 2-*O*-acetyl- and 3-*O*-acetyl-4,6-*O*-(phenylmethylene)-β-D-mannopyranoside (19a and 19b, respectively): NMR of 6:1 mixture (400 MHz; signals due to **19b** are underlined) 2.14 (s, OAc), 2.18 (s, OAc), 2.45–2.70 (br s, C-2 OH), 2.70–3.05 (br s, C-3 OH), 3.37 (app octet, *J* = 5.0, H-5), 3.43–3.60 (m, H-5), 3.51 (s, OCH_3), 3.55 (s, OCH_3), 3.84 (t, *J* = 9.8, H-4), 3.87 (t, *J* = 10.8, H-6_{ax}), 3.91 (dd, *J* = 9.7, 3.5, H-3), 4.11 (t, *J* = 10.2, H-4), 4.20 d, *J* = 2.7, H-2), 4.34 (dd, *J* = 10.5, 4.9, H-6_{eq}), 4.44 (d, *J* = 1.1, H-1), 4.48 (s, H-1), 5.05 (dd, *J* = 10.2, 3.2, H-3), 5.41 (dd, *J* = 3.4, 1.1, H-2), 5.54 (s, PhCH), 5.57 (s, PhCH), 7.35–7.54 (m, 5 H_{arom}).

Methanolysis of the 6:1 mixture of **19a** and **19b** (sodium methoxide in methanol solution) gave quantitatively the known diol, methyl 4,6-*O*-(phenylmethylene)-β-D-mannopyranoside (**19c**), mp 178–180 °C from ether/petroleum ether (lit.[14] mp 181–182 °C from benzene): $[\alpha]_D$ = −95.0° (*c* = 0.62, $CHCl_3$) (lit.[14] $[\alpha]_D$ −98.0°, *c* = 1.3, $CHCl_3$); NMR (400 MHz) 2.77 (br s, C-2 OH), 2.91 (br d, *J* = 4.4, C-3 OH), 3.33 (td, *J* = 10.1, 5.0, H-5), 3.56 (s, OCH_3), 3.76–3.81 (m, H-3), 3.84 (t, *J* = 10.3, H-6_{ax}), 3.87 (t, *J* = 9.4, H-4), 4.06 (d, *J* = 3.2, H-2), 4.33 (dd, *J* = 10.5, 5.0), 4.42 (d, *J* = 1.1, H-1), 5.54 (s, PhC*H*), 7.34–7.39 (m, 3 H_{arom}), 7.48–7.51 (m, 2 H_{arom}); IR (dilute CCl_4) 3585, 3440 (free and H-bonded OH).

Methyl 2-Azido-2-deoxy-4,6-*O*-(phenylmethylene)-β-D-mannopyranoside (20a) and Its Acetate (20b). For **20a**: $[\alpha]_D$ = −135.7° (*c* = 0.4, $CHCl_3$); NMR (400 MHz) 2.59 (br s, OH), 3.34 (td, *J* = 9.8, 4.9, H-5), 3.58 (s, OCH_3), 3.77 (t, *J* = 9.5, H-4), 3.85 (d, *J* = 10.3, H-6_{ax}), 3.91 (dd, *J* = 9.5, 3.9, H-3), 4.03 (dd, *J* = 3.9, 1.1, H-2), 4.34 (dd, *J* = 10.5, 4.9, H-6_{eq}), 4.55 (d, *J* = 1.1, H-1), 5.55 (s, PhC*H*), 7.36–7.41 (m, 3 H_{arom}), 7.46–7.49 (m, 2 H_{arom}); IR (thin film) 3360 (OH), 2110 (azido). Anal. Calcd for $C_{14}H_{17}N_3O_5$: C, 54.72; H, 5.58; N, 13.67. Found: C, 54.66; H, 5.50; N, 13.51. For **20b**: mp 126–127 °C (from ether/hexane); NMR (300 MHz) 2.16 (s, OAc), 3.43 (td, *J* = 9.7, 4.5, H-5), 3.57 (s, OCH_3), 3.86 (t, *J* = 9.6, H-6_{ax}), 3.97 (t, *J* = 10.2, H-4), 4.20 (dd, *J* = 3.7, 1.3, H-2), 4.33 (dd, *J* = 10.6, 4.9, H-6_{eq}), 4.62 (d, *J* = 1.3, H-1), 5.06 (dd, *J* = 10.2, 3.8, H-3), 5.53 (s, PhC*H*), 7.35–7.39 (m, 3 H_{arom}), 7.41–7.48 (m, 2 H_{arom}); IR (KBr) 2115 (azido), 1740 (OAc). Anal. Calcd for $C_{16}H_{19}N_3O_6$: C, 55.01; H, 5.48; N, 12.03. Found: C, 55.12; H, 5.54; N, 11.78.

Methyl 3-*O*,2-*S*-diacetyl-4,6-*O*-(phenylmethylene)-2-thio-β-D-mannopyranoside (21): mp 118–119 °C from ether/hexane; $[\alpha]_D$ = −57.6° (*c* = 0.82, $CHCl_3$); NMR (300 MHz) 1.98 (s, OAc), 2.38 (s, SAc), 3.51 (td, *J* = 9.9, 4.8, H-5), 3.53 (s, OCH_3), 3.78 (app q, *J* = 10.2, H-4 and H-6_{ax}), 4.32 (dd, *J* = 10.4, 4.8, H-6_{eq}), 4.51 (dd, *J* = 4.4, 1.8, H-2), 4.77 (d, *J* = 1.8, H-1), 5.31 (dd, *J* = 10.1, 4.3, H-3), 5.51 (s, PhC*H*), 7.33–7.36 (m, 3 H_{arom}), 7.40–7.43 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 1745 (OAc), 1700 (SAc). Anal. Calcd for $C_{18}H_{22}O_7S$: C, 56.53; H, 5.80; S, 8.38. Found: C, 56.51; H, 5.60; S, 8.00.

Methyl 2-*S*-Methyl-4,6-*O*-(phenylmethylene)-2-thio-β-D-mannopyranoside (22a) and Its Acetate (22b). For **22a**: $[\alpha]_D$ = −98.8° (*c* = 0.55, $CHCl_3$); NMR (400 MHz) 2.30 (s, SCH_3), 2.93 (d, *J* = 8.9, OH), 3.31 (dd, *J* = 4.9, 1.7, H-2), 3.36 (td, *J* = 9.9, 4.9, H-5), 3.52 (t, *J* = 9.3, H-4), 3.58 (s, OCH_3), 3.82 (t, *J* = 10.3, H-6_{ax}), 4.03 (td, *J* = 9.1, 4.9, H-3), 4.32 (dd, *J* = 10.5, 4.9, H-6_{eq}), 4.65 (d, *J* = 1.7, H-1), 5.54 (s, PhC*H*), 7.33–7.38 (m, 3 H_{arom}), 7.47–7.50 (m, 2 H_{arom}); IR (dilute CCl_4) 3599 (free OH), 3495 (H-bonded OH). For **22b**. Anal. Calcd for $C_{17}H_{22}O_6S$: C, 57.62; H, 6.26; S, 9.05. Found: C, 57.33; H, 6.18; S, 9.21.

Methyl 3-*S*-Methyl-4,6-*O*-(phenylmethylene)-3-thio-β-D-gulopyranoside (23a) and Its Acetate (23b). For **23a**: $[\alpha]_D$ = −40.9° (*c* = 1.43, $CHCl_3$); NMR (400 MHz) 2.29 (s, SCH_3), 2.59 (d, *J* = 5.6, C-2 OH), 3.34 (dd, *J* = 4.8, 2.7, H-3), 3.57 (s, OCH_3), 3.88 (d, *J* = 1.3, H-5), 4.07–4.12 (m, H-2 and H-6), 4.16 (d, *J* = 2.1, H-4), 4.35 (dd, *J* = 12.5, 1.3, H-6_{eq}), 4.44 (d, *J* = 8.3, H-1), 5.55 (s, PhC*H*), 7.35–7.38 (m, 3 H_{arom}), 7.51–7.53 (m, 2 H_{arom}); FT-IR (dilute CCl_4) 3691 (free OH), 3589 (H-bonded OH); DCI-MS 313 (M^+ + 1). For **23b**: mp 145–146 °C from dichloromethane/petroleum ether; $[\alpha]_D$ = −43.1° (*c* = 0.57, $CHCl_3$); NMR (300 MHz) 2.10 (s, OAc), 2.19 (s, SCH_3), 3.51 (s, OCH_3), 3.54 (overlapped dd, *J* = 4.9, 2.9, H-3), 3.88 (br s, H-5), 4.02–4.09 (m, H-4 and H-6_{ax}), 4.32 (dd, *J* = 12.5, 1.5, H-6_{eq}), 4.68 (d, *J* = 8.4, H-1), 5.20 (dd, *J* = 8.3, 5.0, H-2), 5.52 (s, PhC*H*), 7.32–7.35 (m, 3 H_{arom}), 7.49–7.52 (m, 2 H_{arom}); IR (dilute CCl_4 and $CHCl_3$) 1742 (OAc). Anal. Calcd for $C_{17}H_{22}O_6S$: C, 57.62; H, 6.26; S, 9.05. Found: C, 57.63; H, 6.39; S, 8.87.

Methyl 2-Deoxy-2-*C*-formyl-4,6-*O*-(phenylmethylene)-β-D-xylo(lyxo)furanoside (24a) and Its Derived Alcohol (24b) and Acetate (24c). Treatment of triflate **4** with sodium azide according to the general procedure followed by chromatography with 2:1 petroleum ether/ethyl acetate as the eluant afforded 300 mg (57%) of an unstable syrup. NMR analysis of the product showed the presence of two aldehydes in a ratio of about 3:1 xylo/lyxo: δ 3.49 (s, OMe, lyxo), 3.51 (s, OMe, xylo), 9.80 (s, −C*H*O, xylo), 9.88 (d, *J* = 3, −C*H*O, lyxo). A portion of this product was reduced with excess sodium borohydride in methanol solution to afford the xylo carbinol **24b** (only one isomer was isolated), and this was characterized as the derived (acetic anhydride, pyridine) acetate **24c**: NMR (400 MHz) 2.71 (br t, *J* = 6.5, H-2), 3.50 (s, OCH_3), 3.90 (s, H-3), 4.14 (dd, *J* = 13.2, 2.9, H-5), 4.17 (d, −CH_2OAc), 4.34 (d, *J* = 2.9, H-4), 4.43 (d, *J* = 13.2, H-5′), 4.95 (d, *J* < 1, H-1), 5.46 (s, PhC*H*), 7.35–7.51 (m, 5 H_{arom}); IR (film) 1732 (OAc). Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 61.95; H, 6.48. The xylo (epimerized) stereochemistry is assigned to **24c** based on the small H-1,2 coupling constant (<1 Hz), and the apparent enrichment in this isomer upon reduction of the mixture **24a**.

Methyl 2,3-anhydro-4,6-*O*-(phenylmethylene)-β-D-allopyranoside (25): mp 137–138 °C from ether/hexane (lit.[16] mp 136–137 °C; lit.[17] mp 138 °C); $[\alpha]_D$ = −14.8° (*c* = 1.35, $CHCl_3$) (lit.[16] $[\alpha]_D$ −17°; lit.[17] $[\alpha]_D$ −15.6°); NMR[18] (300 MHz, benzene-d_6) 3.05 (d, *J* = 4.3, H-2), 3.12 (d, *J* = 4.2, H-3), 3.15 (s, OCH_3), 3.43 (t, *J* = 10.1, H-6_{ax}), 3.60 (dd, *J* = 9.1, 0.5, H-4), 3.78 (td, H = 10.1, 4.9, H-5), 4.07 (dd, *J* = 10.1, 4.9, H-6_{eq}), 4.57 (s, H-1), 5.26 (s, PhC*H*), 7.08–7.34 (m, 3 H_{arom}), 7.57–7.61 (m, 2 H_{arom}); IR ($CHCl_3$) 3005, 2865, 1105.

Methyl 2,3-anhydro-4,6-*O*-(phenylmethylene)-β-D-mannopyranoside (26): mp 183–184 °C (lit.[17] 183 °C); $[\alpha]_D$ = −30.8° (*c* = 0.72, $CHCl_3$ at 18 °C) (lit.[18] $[\alpha]_D$ −30.7°, *c* = 0.82, $CHCl_3$ at 18 °C); NMR[18] (300 MHz, benzene-d_6) 2.71 (d, *J* = 3.7, H-2), 2.98 (td, *J* = 9.7, 4.6, H-5), 3.17 (d, *J* = 3.7, H-3), 3.30 (s, OCH_3), 3.45 (t, *J* = 10.3, H-6_{ax}), 3.55 (d, *J* = 9.4, H-4), 4.03 (dd, *J* = 10.3, 4.6, H-6_{eq}), 4.33 (s, H-1), 5.14 (s, PhC*H*), 7.12–7.22 (m, 3 H_{arom}), 7.55–7.58 (m, 2 H_{arom}); IR (3% in $CHCl_3$) 3005, 2940, 2880, 1100.

1,6:2,3-Dianhydro-4-deoxy-β-D-allopyranose (32). A solution of 1.75 mL (22.61 mmol) of methanesulfonic anhydride and 4.13 g (16.52 mmol) of deoxysugar **37** in 7.5 mL (92.73 mmol) of pyridine and 35 mL of dichloromethane was stirred at 23 °C for

16 h. The reaction mixture was partitioned between 110 mL of additional dichloromethane and 150 mL of water. The organic phase was dried and concentrated to give the crude mesylate, which was used as such for the next reaction.

A solution of the crude mesylate in 60 mL of 1:1 methanol/tetrahydrofuran was treated with 23 mL of 1 M methanolic sodium methoxide, and the reaction was stirred at 23 °C for 1 h. The reaction mixture was neutralized with Amberlite IR-120 (H^+) resin, concentrated, and then chromatographed with 1:1 and then 3:2 petroleum ether/ethyl acetate as the eluant to give 1.87 g (88%) of the Cerny epoxide **32** with mp 60–62 °C (lit.[21] mp 66–67 °C): $[\alpha]_D$ +30.6° (c = 0.16, H_2O) (lit.[21] $[\alpha]_D$ +30°, c = 1.8, H_2O); NMR (200 MHz) 1.70 (dd, J = 15.6, 5.3, H-4_{eq}), 2.46 (dd, J = 15.6, 5.0, H-4_{ax}), 2.98 (d, J = 4.3, H-2), 3.15 (ddd, J = 0.5, 5.3, 4.3, H-3), 3.74 (dd, J = 7.4, 1.6, H-6_{endo}), 3.91 (dd, J = 7.4, 5.8, H-6_{exo}), 4.40 (m, H-5), 5.58 (s, H-1); ^{13}C NMR (50 MHz) 33.0 (C-4), 47.6, 48.5 (2 oxirane C), 68.8, 71.1, 97.1 (C-1).

1,6-Anhydro-2-*O*-benzoyl-β-D-galactopyranose (34). 1,6-Anhydro-3,4-*O*-(dimethyl)methylene-β-D-galactopyranose was prepared according to the literature procedure[31] from 23.85 g of β-D-galactose pentaacetate. Chromatography with 2:1 and then 1:1 petroleum ether/ethyl acetate as the eluant and crystallization from 100 mL of 1:1 petroleum ether/dichloromethane afforded 5.83 g (45%) of the anhydrosugar, mp 143–144 °C. This material (28.86 mmol) was 2-*O*-benzoylated with 4 mL (34.46 mmol) of benzoyl chloride and 35 mg (0.29 mmol) of 4-(*N*,*N*-dimethylamino)pyridine in pyridine solution (30 mL) at 23 °C for 30 min. The reaction mixture was partitioned between ether and 1 N aqueous hydrochloric acid, and the organic phase was dried and concentrated to a syrup. The acetonide was removed by treatment with 25 mL of 4 N aqueous hydrochloric acid in 60 mL of 5:1 methanol/dichloromethane at 50 °C for 6 h. The reaction mixture was cooled, quenched by addition of triethylamine, concentrated, and chromatographed with 1:1 petroleum ether/ethyl acetate as the eluant to afford 7.01 g (91% overall yield) of diol **34**, mp 154–157 °C (lit.[30] mp 164–165 °C), $[\alpha]_D$ + 45.5° (c = 0.15, $CHCl_3$) (lit.[30] $[\alpha]_D$ + 47.2°, c = 0.8, $CHCl_3$).

1,6-Anhydro-2-*O*-benzoyl-4-deoxy-4-iodo-β-D-glucopyranose (36). Trifluoromethanesulfonic anhydride (4.7 mL, 27.94 mmol) was added to a stirred solution of 6.45 g (24.25 mmol) of 1,6-anhydro-2-*O*-benzoyl-β-D-galactopyranose[30,31] (**34**) in 19.7 mL (243.6 mmol) of pyridine and 300 mL of dichloromethane at −20 °C. The mixture was stirred at −20 °C for 4 h, −10 °C for 2 h, and then quenched by adding 300 mL of water. The organic phase was dried and concentrated to give a residue containing the 4-triflate **35**. The crude triflate was dissolved in 200 mL of dimethylformamide and treated with 14.30 g (38.71 mmol) of tetra-*n*-butylammonium iodide. The solution was stirred for 21 h at 23 °C, and then quenched with 500 mL of 10% aqueous sodium thiosulfate. The aqueous phase was back-extracted with ether (950 mL total), and the combined organic extracts were dried and concentrated. Chromatography with 4:1 and then 3:1 petroleum ether/ethyl acetate as the eluant afforded 7.11 g (78%) of iodide **36** with mp 97–99 °C: $[\alpha]_D$ + 7.8° (c = 1.5, $CHCl_3$); NMR (200 MHz) 3.61 (d, J = 5.5, OH), 3.66 (dd, J = 7.8, 4.8, H-6_{exo}), 4.23 (s, H-4), 4.28 (d, J = 7.8, H-6_{endo}), 4.38 (d, J = 5.5, H-3), 4.81 (d, J = 4.8, H-5), 4.90 (s, H-2), 5.64 (s, H-1), 7.39–8.18 (m, 5 H_{arom}); ^{13}C NMR (50 MHz) 24.6 (C-4), 67.6, 71.4, 73.5, 78.1, 99.7 (C-1), 128.4, 129.0, 130.2, 133.5 (4 C_{arom}), 165.8 (C=O); FT-IR (film) 3457 (OH), 2963, 1723 (OBz), 1269, 1113, 1026. Anal. Calcd for $C_{13}H_{13}O_5I$: C, 41.51; H, 3.48; I, 33.74. Found: C, 41.65; H, 3.31; I, 33.71.

1,6-Anhydro-2-*O*-benzoyl-4-deoxy-β-D-glucopyranose (37). A solution of 6.40 mL (23.79 mmol) of tri-*n*-butyltin hydride, 25 mg of azobis(isobutyronitrile), and 7.11 g (18.91 mmol) of iodide **36** in 60 mL of toluene was heated at 90 °C for 40 min. The reaction mixture was cooled, concentrated, and chromatographed with 3:1 and then 2:1 petroleum ether/ether as the eluant to give 4.13 g (87%) of deoxysugar **37** with mp 89–92 °C: $[\alpha]_D$ +23.1° (c = 0.75, $CHCl_3$); NMR (200 MHz), 1.81 (d, J = 14.8, H-4_{eq}), 2.36 (dt, J = 14.8, 4.6, H-4_{ax}), 3.06 (d, J = 4.9, OH), 3.74 (dd, J = 6.8, 5.5, H-6_{exo}), 3.97 (dd, J = 4.9, 4.6, H-3), 4.25 (d, J = 6.8, H-6_{endo}), 4.59 (dd, J = 5.5, 4.6, H-5), 4.83 (s, H-2), 5.58 (s, H-1), 7.38–8.06 (m, 5 H_{arom}); ^{13}C NMR (50 MHz) 33.0 (C-4), 66.3, 67.5, 71.7, 72.1, 99.5 (C-1), 128.4, 129.4, 129.8, 133.4 (4 C_{arom}), 165.7 (C=O); FT-IR (film) 3462 (OH), 2961, 2899, 1718 (OBz), 1265, 1115, 997. Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.19; H, 5.52.

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Friedel–Crafts α-Aminoacylation of Alkylbenzene with a Chiral *N*-Carboxy-α-amino Acid Anhydride without Loss of Chirality

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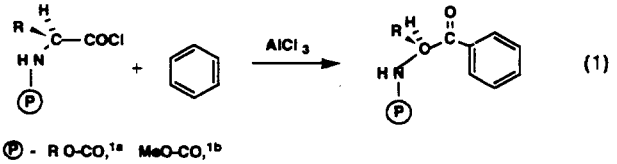
A Friedel–Crafts-type α-aminoacylation of alkylbenzene with *N*-carboxy anhydrides of five L-α-amino acids was developed. Five new α-aminoalkyl *p*-methylphenyl ketones and other α-aminoalkyl aryl ketones were obtained and isolated as free bases or hydrochloride salts. The chiralities of the original L-α-amino acids were retained during this acylation.

A Freidel–Crafts-type α-aminoacylation of benzene with N-protected α-amino acid chlorides has recently been developed by several chemists[1a–c] (eq 1). The reaction affords α-aminoalkyl phenyl ketones, which have been used as precursors of biologically active medicines such as ephedrine.[1a] The optically active N-protected α-amino ketones obtained from the reaction shown in eq 1 cannot be easily converted to the corresponding α-amino ketone free bases (abbreviated as F-B) without loss of chirality.



(1)

P - R O-CO,[1a] MeO-CO,[1b] and CF_3CO,[1c]

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