fitted with a Teflon stirbar and nitrogen inlet and outlet. After the mixture was brought to reflux, trimethyl phosphite (360 μL, 3.04 mmol) was added. The reaction was followed by reversed-phase (RP-18) TLC (methanol). The red suspensin turned blue upon addition of $(MeO)_3P$ and this color deepened over the course of 10–20 min. After the consumption of **5a** (1 h) was complete, the solvent was removed under reduced pressure (0.05 torr). The blue-green residue was quickly purified by reversed-phase flash chromatography on octadecyldimethylsilyl-modified silica gel[10] (MeOH as eluant) to yield pure **2** (356 mg, 63%).

Reaction of **5b** with $(MeO)_3P$ in refluxing toluene gave **8** in 55% yield.

Registry No. **2**, 53869-87-7; **4a**, 51372-96-4; **4b**, 525-41-7; **5a**, 96165-60-5; **5b**, 96165-61-6; **6a**, 96165-62-7; **6b**, 96165-63-8; **7a**, 96165-64-9; **8**, 96165-65-0; **9**, 96165-66-1; oxalyl chloride, 79-37-8.

Novel One-Pot Synthesis of a New Class of Compounds Involving Coupling of Sugars and Amino Acids via Triflates[1]

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A new class of pharmacologically interesting compounds has been synthesized by way of a novel C–N coupling reaction between partially blocked sugars and a variety of suitably protected naturally occurring amino acids. The free amino functions of the latter were utilized as effective nucleophiles to cause smooth S_N2 displacement of the triflyl group in benzyl 2,3-anhydro-4-triflyl-α-D-ribopyranoside and its β-L-isomer, respectively (Scheme I). The formation of a new type of aziridino sugars was also observed to a minor extent in a majority of reactions and their origin could be rationalized by a novel isomerization of an α-imino oxirane into an α-hydroxy epimine, analogus to epoxide migration (Scheme II). The reaction pathway also provided an efficient route to benzyl 2,3-anhydro-α-D- and -β-L-lyxopyranosides. The structures and conformations of all the compounds were fully supported by field desorption mass and ^1H and ^{13}C NMR spectroscopies.

Perfluoralkanesulfonic esters are important intermediates in modern synthetic as well as mechanistic organic chemistry. Particularly the trifluoromethanesulfonates, commonly referred to as triflates, have shown excellent leaving group properties and serve in numerous synthetic transformations.[2] Triflate derivatives have also been used in sugar chemistry. They are well suited for displacement reactions leading to deoxy sugars,[3,4] deoxy azido sugars,[5] deoxy halo sugars,[6] and several disaccharides.[7]

Recently we have described[8] a new and efficient approach to deoxy amino sugars. In the reaction sequence, direct displacement of the triflyl group was affected by passing gaseous ammonia into acetonic solutions of sugar triflates at low temperature. From the high selectivity observed during these reactions, it appeared that the substitution of triflyl group in partially blocked sugar triflates by the free amino functions of suitably protected naturally occurring amino acids should perform the desired C–N coupling between two important groups of natural products, resulting in novel synthesis of a new class of pharmacologically interesting compounds. We now present a full account of these studies which appear to provide an entry to the preparations of these compounds.

Results and Discussion

Benzyl 2,3-anhydro-α-D-ribopyranoside (**1**) and benzyl 2,3-anhydro-β-L-ribopyranoside (**2**) were used partially blocked sugars in the present investigations. The benzyl ether and the oxirane ring were selected as protecting groups in view of their stability in mild conditions and ease of cleavage. Both **1** and **2** were easily prepared by previously published method[9,10] from D- and L-arabinose, respectively. The dichloromethane solution of each partially

Scheme I

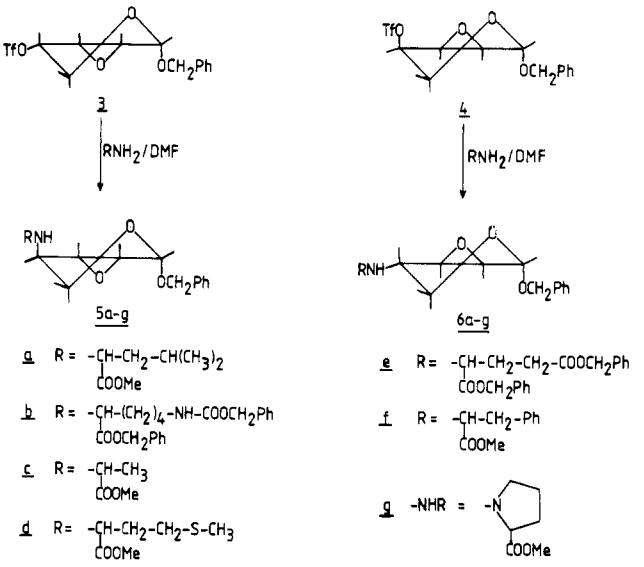

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Table I. Properties of Benzyl 2,3-Anhydro-4-deoxy-4-(substituted-amino)lyxopyranosides 5 and 6

compd[f]	-NHR	isomer	salt form	%yield[a]	mp,[b] °C	$[\alpha]^{25}_D$,[c] deg	mol form	anal. calcd, found C	H	N
5a	-Leu-OMe	β-L	HCl	59	115–116 (M–Et)	+44.3	$C_{19}H_{28}NClO_5$	59.14, 59.23	7.31, 7.24	3.63, 3.62
5b	-Lys(Z)-OBzl	β-L		43	oil	+34.8	$C_{33}H_{38}N_2O_7$	68.69, 68.48	6.67, 6.50	4.87, 4.78
5c	-Ala-OMe	β-L	*g*	*g*	*g*	*g*	*g*	*g*	*g*	*g*
5d	-Met-OMe	β-L	TsOH	56	135 (E–Et)	+22.5	$C_{25}H_{33}NO_8S_2$	55.67, 55.53	6.16, 6.12	2.60, 2.56
5e	-Glu(OBzl)-OBzl	β-L		52	oil	+34.5	$C_{31}H_{33}NO_7$	70.04, 70.10	6.26, 6.13	2.63, 2.55
5f	-Phe-OMe	β-L	TsOH	68	163–164 (M–Et)	+48.6[d]	$C_{29}H_{33}NO_8S$	62.68, 62.98	5.98, 6.05	2.52, 2.53
5g	-Pro-OMe	β-L		70	oil	+16.9	$C_{18}H_{23}NO_5$	65.05, 64.93	6.98, 6.90	4.21, 4.30
6a	-Leu-OMe	α-D		78.4	32 (Et)	+34.2	$C_{19}H_{27}NO_5$	65.31, 65.20	7.79, 7.71	4.01, 3.98
6b	-Lys(Z)-OBzl	α-D		45	75 (E–Et–H)	+22.6	$C_{33}H_{38}N_2O_7$	68.97, 68.63	6.67, 6.58	4.87, 4.89
6c	-Ala-OMe	α-D	TsOH	58	142 (E–Et)	+51.5	$C_{23}H_{29}NO_8S$	57.60, 58.03	6.10, 6.32	2.92, 2.96
6d	-Met-OMe	α-D		62.6	oil	+35.6[e]	$C_{18}H_{25}NO_5S$	58.84, 58.51	6.86, 6.77	3.81, 3.63
6e	-Glu(OBzl)-OBzl	α-D		55.6	oil	+29.6	$C_{31}H_{33}NO_7$	77.64, 77.47	6.26, 6.01	2.63, 2.55
6f	-Phe-OMe	α-D	TsOH	54	134 (E–Et)	+52.5	$C_{29}H_{33}NO_8S$	62.68, 63.24	5.98, 5.91	2.52, 2.50
6g	-Pro-OMe	α-D	TsOH	70	140 (E–Et)	+35.6	$C_{25}H_{31}NO_8S$	59.39, 59.56	6.18, 6.24	2.77, 2.74
5c′	benzyl 2,4-dideoxy-2-bromo-4-(-Ala-OMe)-β-L-xylopyranoside hydrogen bromide			46	180 (D-Et)	+41.7	$C_{16}H_{23}NO_5Br_2$	40.95, 40.54	4.94, 4.95	2.98, 2.99

[a] Isolated yield. [b] Solvents for crystallization are given in parentheses: E, ethanol; Et, diethyl ether; H, *n*-hexane; D, dichloromethane; M, methanol. [c] The optical rotations were measured in $CHCl_3$ except at otherwise stated. [d] MeSO. [e] C_6H_6. [f] The amino acid moieties are always of the L_s configuration. [g] See **5c′**.

protected carbohydrate (**1**, **2**) was reacted with triflic anhydride in the presence of pyridine at 0 °C to provide the corresponding triflates **3** and **4**).[5] On the other hand, representatives of different classes of amino acids were used to demonstrate the scope of the reaction. These include methyl esters of L-alanine, L-phenylalanine, L-leucine, L-proline, and L-methionine along with dibenzyl ester of L-glutamic acid and benzyl ester of $N\epsilon$-(benzyloxycarbonyl)-L-lysine. All of these were respectively used to displace the triflyl group in **3** and **4**. The reactions were performed in DMF under the conditions described in the Experimental Section. The target compounds **5a–g** and **6a–g** were formed in major concentration and could be isolated from the product mixtures of silica gel column chromatography (Scheme I). These were characterized as such or through their crystalline salts, except in one case where attempted salt formation with ethereal hydrogen bromide at room temperature also resulted in trans diaxial epoxide cleavage to provide benzyl 2,4-dideoxy-2-bromo-4-(Ala-OCH_3)-β-L-xylopyranoside hydrogen bromide (**5c′**). The structure and 1C conformation of this compound was assigned on the basis of mass and 400-MHz NMR spectra. The physical and analytical data of all the products are presented in Table I.

The facile substitution at C-4 can be attributed to the excellent leaving properties of the triflyl group, the nucleophilicity of the protected amino acids, and the enhanced reactivity due to the neighboring oxirane ring.[11] Moreover, the approach of the attacking nucleophiles is favored trans to the oxirane ring due to molecular geometry which shows the dipole moment in the direction of C–O bond and not parallel to the newly forming C–N bond.[5]

The reactions described in the foregoing account invariably lead to lyxo products due to stereochemical inversion at C-4. The key evidence to this effect was provided by the coupling constants in ^1H NMR spectra at 100 MHz, particularly $J_{3,4}$ and $J_{4,5'}$. In the reacting sugars 3-H has a cis relationship with 4-H and a $J_{3,4}$ value of ca. 3.6 Hz is obtained whereas in the products the two protons have a trans relationship and practically no coupling was observed. Moreover, for **3** the $J_{4,5'}$ value of 8.1 Hz was obtained because of the quasi-axial, axial relationship between 4-H and 5′-H while the $J_{4,5'}$ values for the corresponding products where 4-H and 4′-H have a quasi-equatorial,axial relationship varied from 1 to 4 Hz.[12]

The relationship between 4-H and 5′-H is exactly reversed in the case of **4** and its products, and the observation of the $J_{4,5'}$ value served again as an additional means of diagnosing the configurational inversion at C-4. The formation of inverted products can only be rationalized by an S_N2 or ion pair mechanism. However, the observation that the reaction rates varied considerably with the nature and concentration of amino esters suggested strongly the operation of an S_N2 mechanism rather than a unimolecular process.

The conformations adopted by pyranoside rings in compounds **5b–g** and **6a–g** were determined by vicinal coupling constants, chemical shift correlations, and long-range coupling constants in the ^1H NMR spectra. In the series **6a–g**, it is clear that $J_{4,5'}$ or $J_{4,5}$ is the important parameter. For all these compounds Table II shows that $J_{4,5'}$ is large (7–9 Hz), indicating a diaxial relationship for 4-H and 5′-H; the conformation is therefore predominantly $^0H_5$. In the other series, the conformation is less easy to determine on the basis of vicinal coupling constant, as 4-H and 5′-H are in an axial–quasi-equatorial,quasi-equatorial–axial relationship in the two possible conformations. However, the chemical shift correlations indicate clearly that $^0H_5$ is the predominant conformation. The chemical shift of 1-H appears to be the most helpful of all parameters in assigning conformations to the 13 compounds. It remains fairly constant for each series and shows close agreement to methyl 2,3-anhydro-α-D- and -β-L-lyxopyranosides for which equatorial orientation of 1-H and hence $^0H_5$ conformations have already been established.[13] The other chemical shifts of the ring protons vary quite widely, owing in the main to the orientation of the proton relative to the plane of the epoxide ring, which is thought to exhibit a large diamagnetic anisotropic effect.[14]

Long-range coupling constants are well-known in the carbohydrate field, usually occurring between protons which are both equatorial and separated by four bonds, in the coplanar *W* configuration.[15] Hall[16] later demon-

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Table II. Mass[a] and ^{1}H NMR[b,c] Spectral Data of Compounds 15a-g and 6a-g

compd	MS m/z (M^+)	chem shifts[d,e] in δ units relative to Me_4Si	conformation
5a	349[g]	5.16 (1 H, d, $J_{1,2}$ = 2.9 Hz, 1-H), 4.21 (1 H, m, α-H), 4.0 (1 H, dd, $J_{5,4}$ = 1.4, $J_{5,5}$ = 11.5 Hz, 5-H), 3.9 (1 H, dd, $J_{5',4}$ = 1.99, $J_{5',5}$ = 11.6 Hz, 5'-H), 3.81–3.72 (2 H, m, 2-H, 3-H), 3.74 (3 H, s, OCH_3), 3.43 (1 H, m, 4-H), 2.11–1.70 (3 H, m, β-H_2, γ-H), 1.01 (3 H, d, J = 6.1 Hz, δ-H_3), 0.96 (3 H, d, J = 6.1 Hz, δ'-H_3)	$^0H_5$
5b	574	7.32 (10 H, m, Ar H), 5.13, 5.06 (2 H, s, OCH_2Ph), 4.95 (1 H, d, $J_{1,2}$ = 1.87 Hz, 1-H), 3.84 (1 H, dd, $J_{5,4}$ = 1.1, $J_{5,5'}$ = 12.0 Hz, 5-H), 3.36 (1 H, t, J = 6.2 Hz, α-H), 3.26 (1 H, dd, $J_{5',4}$ = 2.35, $J_{5',5}$ = 12.0 Hz, 5'-H), 3.19 (2 H, m, 2-H, 3-H), 3.08 (2 H, t, J = 6.4 Hz, ϵ-H_2), 2.86 (1 H, m, 4-H), 1.74–1.33 (6 H, m, β-H_2, γ-H_2, δ-H_2)	$^0H_5$
5c[f]	389/387[g]	4.64 (1 H, d, $J_{1,2}$ = 8.6 Hz, 1-H), 4.49 (1 H, dd, $J_{5',4}$ = 5.1, $J_{5',5}$ = 11.8 Hz, 5'-H), 4.42 (1 H, t, J = 6.9 Hz, α-H), 4.32 (1 H, m, 3-H), 4.11 (1 H, dd, $J_{5,4}$ = 8, $J_{5,5'}$ = 11.8 Hz, 5-H), 3.83 (3 H, s, OCH_3), 3.71 (1 H, dd, $J_{2,1}$ = 8.6, $J_{2,3}$ = 9.9 Hz, 2-H), 3.33 (1 H, m, 4-H), 1.83 (3 H, d, J = 6.9 Hz, β-H_3)	$1C$
5d	351[g]	7.44 (4 H, dd, J = 8 Hz, $CH_3C_6H_4$), 5.07 (1 H, d, $J_{1,2}$ = 2.95 1-H), Hz, 1-H), 4.44–4.23 (1 H, dd, $J_{5,4}$ = 1.5, $J_{5,5'}$ = 11.7 Hz, 5-H), 4.15–3.61 (4 H, m, 5'-H, α-H, 2-H, 3-H), 3.72 (3 H, s, OCH_3), 3.30 (1 H, m, 4-H), 2.71–2.31 (4 H, m, β-H_2, γ-H_2), 2.34 (3 H, s, $CH_3C_6H_4$), 1.99 (3 H, s, SCH_3)	$^0H_5$
5e	531	7.31 (10 H, m, Ar H), 5.14 5.08 (2 H, s, OCH_2Ph), 4.92 (1 H, d, $J_{1,2}$ = 1.7 Hz 1-H), 3.81 (1 H, dd, $J_{5,4}$ = 1.1, $J_{5,5'}$ = 11.7 Hz, 5-H), 3.42 (1 H, t, J = 6.57 Hz, α-H), 3.23 (1 H, dd, $J_{5',4}$ = 2.3, $J_{5',5}$ = 11.7 Hz, 5'-H), 3.14 (2 H, m, 2-H, 3-H), 2.85 (1 H, m, 4-H), 2.48 (2 H, m, γ-H_2), 2.1–1.65 (2 H, m, β-H_2)	$^0H_5$
5f[h]	383[g]	7.37 (4 H, dd, J = 8 Hz, $CH_3C_6H_4$), 7.28 (5 H, m, Ar H), 5.13 (1 H, d, $J_{1,2}$ = 2.9 Hz, 1-H), 4.50 (1 H, m, α-H), 3.72–3.68 (3 H, m, $J_{5',4}$ = 1.99 Hz, 5-H_2, 4-H), 3.55 (3 H, s, OCH_3), 3.32 (1 H, m, 2-H), 3.13 (1 H, d, $J_{3,2}$ = 3.8 Hz, 3-H), 2.98 (2 H, d, J = 3.7 Hz, β-H_2), 2.28 (3 H, s, $CH_3C_6H_4$)	$^0H_5$
5g	333	4.97 (1 H, d, $J_{1,2}$ 2.6 Hz, 1-H), 3.93 (1 H, dd, $J_{5,4}$ = 0.9, $J_{5,5}$ = 12.3 Hz, 2.3, 5-H), 4.2–3.0 (5 H, m, α-H, 5'-H, 2-H, 3-H, 4-H), 3.66 (3 H, s, OCH_3), 2.91 (2 H, J = 7.5 Hz, δ-H_2), 2.6–1.8 (4 H, m, β-H_2 γ-H_2)	$^0H_5$
6a	349	4.97 (1 H, s, 1-H), 3.71 (3 H, s, OCH_3), 3.65 (1 H, m, α-H), 3.50 (1 H, dd, $J_{5,4}$ = 2.4, $J_{5,5'}$ = 12 Hz, 5-H), 3.28 (1 H, dd, $J_{5',4}$ = 8.1, $J_{5',5}$ = 12 Hz, 5'-H), 3.12 (1 H, d, $J_{2,3}$ = 3.5 Hz, 2-H), 3.07 (1 H, d, $J_{3,2}$ = 3.5 Hz, 3-H), 2.97 (1 H, m, 4-H), 1.87–1.35 (4 H, m, β-H_2, γ-H, NH), 0.91 (3 H, d, J = 6 Hz, δ-H_3), 0.89 (3 H, d, J = 6 Hz, δ'-H_3)	$^0H_5$
6b	574	7.33 (10 H, m, Ar H), 5.14, 5.07 (2 H, s, OCH_2Ph), 4.96 (1 H, s, 1-H), 3.44 (1 H, dd, $J_{5,4}$ = 2.93, $J_{5,5'}$ = 10.8 Hz, 5-H), 3.41 (2 H, m, $J_{5',4}$ = 8.1, $J_{5',5}$ = 10.8 Hz, 5'-H, α-H), 3.3–3.0 (5 H, m, 4-H, 3-H, 2-H, ϵ-H_2), 1.67–1.24 (6 H, m, β-H_2, γ-H_2, δ-H_2)	$^0H_5$
6c[i]	307[g]	7.43 (4 H, dd, J = 8 Hz, CHC_6H_4), 5.1 (1 H, s, 1-H), 4.29 (1 H, q, J = 7.4 Hz, α-H), 3.77 (3 H, s, OCH_3), 3.74 (1 H, dd, $J_{5,4}$ = 2.1 $J_{5,5'}$ = 12 Hz, 5-H), 3.69–3.60 (2 H, m, $J_{5',4}$ = 7.9, $J_{5',5}$ = 12 Hz, 5'-H 4-H), 3.56 (1 H, d, $J_{3,2}$ = 3.52 Hz 3-H), 3.3 (1 H, d, $J_{2,3}$ = 3.52 Hz, 2-H), 2.29 (3 H, s, $CH_3C_6H_4$), 1.53 (3 H, d, J = 7.4 Hz, β-H_3)	$^0H_5$
6d[k]	351	4.92 (1 H, s, 1-H), 3.57 (1 H, dd, $J_{5,4}$ = 2.6 $J_{5,5}$ = 11.6 Hz, 5-H), 3.31 (1 H, dd, $J_{5',4}$ = 8.4, $J_{5',5}$ = 11.6 Hz, 5'-H), 3.30–3.18 (1 H, m, α-H), 3.23 (3 H, s, OCH_3), 3.1–2.85 (3 H, m, 4-H, 3-H, 2-H), 2.34 (2 H, t, J = 7 Hz, γ-H_2), 1.7 (3 H, s, SCH_3), 1.95–1.4 (2 H, m, β-H_2)	$^0H_5$
6e	531	7.32 (10 H, m, Ar H), 5.14, 5.08 (2 H, s, OCH_2Ph), 4.95 (1 H, s, 1-H), 3.49 (1 H, dd, $J_{5,4}$ = 2.9, $J_{5,5}$ = 11.8 Hz, 5-H), 3.4–3.32 (2 H, m, $J_{5',4}$ = 8, $J_{5',5}$ = 11.8 Hz, 5'-H, α-H), 3.15 (1 H, d, $J_{2,3}$ = 3.7 Hz, 2-H), 3.05 (1 H, d, $J_{3,2}$ = 3.7 Hz, 3-H), 3.23–2.53 (1 H, m, 4-H), 2.44 (2 H, m, J = 6.6 Hz, γ-H_2), 2.09–1.87 (2 H, m, β-H_2)	$^0H_5$
6f[j]	383[g]	7.38 (4 H, dd, J = 8.1 Hz, $CH_3C_6H_4$), 7.14 (5 H, m, Ar H), 4.8 (1 H, s, 1-H), 4.25 (1 H, m, α-H), 3.72 (1 H, dd, $J_{5,4}$ = 2.3, $J_{5,5'}$ = 11.9 Hz, 5-H), 3.65–3.53 (2 H, m, $J_{5',4}$ = 8, $J_{5',5}$ = 11.9 Hz, 5'-H, 4-H), 3.46 (3 H, s, OCH_3), 3.24 (1 H, d, $J_{2,3}$ = 3.8 Hz, 2-H), 3.11 (1 H, d, $J_{3,2}$ = 3.8 Hz, 3-H), 2.96 (2 H, d, J = 3.5 Hz, β-H_2), 2.26 (3 H, s, $CH_3C_6H_4$)	$^0H_5$
6g	333[g]	7.39 (4 H, dd, J = 8.2 Hz, $CH_3C_6H_4$), 4.87 (1 H, s, 1-H), 4.37 (1 H, m, α-H), 4.2–3.5 (6 H, m, 5-H_2, δ-H_2, 2-H, 3-H), 3.75 (3 H, s, OCH_3), 3.16 (1 H, m, 4-H), 2.29 (3 H, s, $CH_3C_6H_4$), 2.3–2.0 (4 H, m, β-H_2, γ-H_2)	$^0H_5$

[a] The molecular ion peaks were observed in field desorption mass spectra. [b] At 90 MHz in $CDCl_3$ unless otherwise noted. [c] d = doublet, dd = doublet of doublets, m = multiplet, q = quartet, s = singlet, t = triplet. [d] The signals of 1-OCH_2Ph were consistently observed at δ 7–7.5 (5 H, m) and 4.2–4.8 (2 H, dd, J_{gem} = 11–12 Hz). These are not repeated in the text for the sake of simplicity. [e] The relative assignments of 5'-H and 5-H were made on the basis of $J_{1,5}$ = 0.48–0.65 Hz. Similarly the assignments of 3-H and 2-H were confirmed by the value of $J_{3,5}$ = 0.99 Hz. [f] At 400 MHz. [g] Obtained for the corresponding liberated base. [h] CD_2Cl_2. [i] Me_2SO-d_6. [j] D_2O. [k] C_6D_6.

strated conclusively that four-bond couplings can also occur between an equatorial and an axial proton, through the ring oxygen in pyranose derivatives. In the case of the anhydro sugars, an additional spur to long-range coupling lies in the nature of the epoxide ring, which acts similarly to a double bond in enhancing pseudoallylic coupling, previously found in propylene oxide and indene oxide.[17] The long-range couplings found in this work were used in addition to assign multiplets to protons where other evidence was ambiguous.

The relative assignments of 5-H and 5'-H were made on the basis of vicinal coupling with 4-H and the long-range coupling to 1-H. Invariably the coupling lies between 1-H and 5'-H in a quasi-equatorial–axial relationship, proven by the evidence of a similar coupling in the hexose series where 5-H is replaced by CH_2OH.[16] Finally, in the assignment of 2-H and 3-H, there is an additional coupling to 5-H of ca. 0.99 Hz. As a five-bond coupling of this magnitude seems unlikely, whereas a four bond coupling is quite favorable, 3-H is assigned as the high-field epoxide proton, coupling to 5-H. Similar chemical shift ranges are found for solutions in deuterium oxide, dimethyl-d_6 sulfoxide, and other deuterated solvents, although the assignments of the epoxide protons and of 5-H and 5'-H are sometime reversed relative to deuteriochloroform, owing to solvent effects rather than to conformation changes.[13] The coupling products as well as the corresponding free anhydro sugars exist predominantly in $^0H_5$ conformation from which it can be deduced that introduction of amino acid moiety in position 4 does not change the conformational stability (Table II). The majority of reactions also lead consistently to a novel and new type of aziridino sugar. Their formation can be rationalized by a classical intramolecular isomerization of an α-imino oxirane into an α-hydroxy epimine.

These compounds were, however, formed in extremely low concentration and could only be isolated pure from

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Table III. Physical Properties and Analytical Data of Aziridine Sugars

compd	% yield[a]	mp[b], °C	$[\alpha]^{25}_D$,[c] deg	mol form	anal. calcd (found) C, H, N
7a	9.3	oil	+56.5	$C_{19}H_{27}NO_5$	65.31 (65.11), 7.79 (7.62), 4.01 (4.11)
8a	10.5	75 (H–Et)	+10.2	$C_{19}H_{27}NO_5$	65.31 (65.22), 7.79 (7.71), 4.01 (4.07)
7b	8.8	86 (E–Et–H)	+35.4	$C_{33}H_{38}N_2O_7$	68.97 (68.39), 6.67 (6.63), 4.87 (5.06)
8b	9.9	136–137 (E)	+4.8	$C_{33}H_{38}N_2O_7$	68.97 (68.69), 6.67 (6.59), 4.87 (4.90)

[a] Isolated yield. [b] The solvents for crystallization are given in parentheses: H, *n*-hexane; Et, diethyl ether; E, ethanol. [c] The optical rotations were measured in $CHCl_3$.

Table IV. Mass[a] and ^{1}H NMR[b,c] Spectral Data of Aziridino Sugars 7a,b and 8a,b

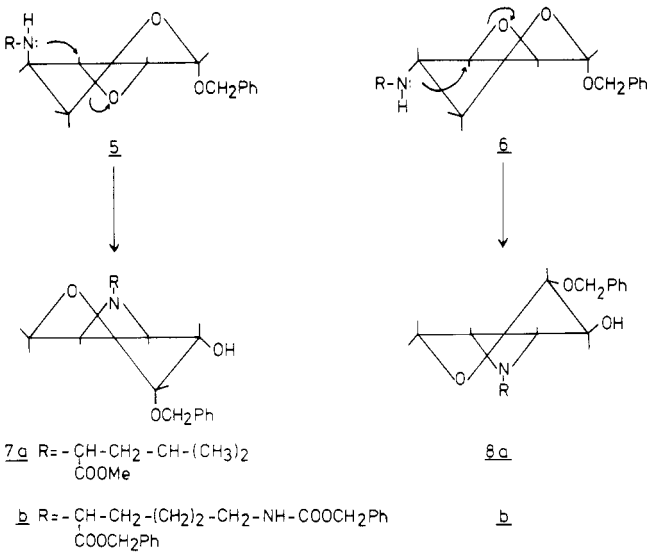
compd	MS, *m/z*	chemical shifts[d,e] in δ units relative to Me_4Si	conformation
7a	349	4.69 (1 H, d, $J_{1,2}$ = 3.8 Hz, 1-H), 4.01 (1 H, d, $J_{5,5'}$ = 12.2 Hz, 5-H), 3.90 (1 H, dd, $J_{5',4}$ = 2.5, $J_{5',5}$ = 12.2 Hz, 5′-H), 3.85 (1 H, d, $J_{2,1}$ = 3.8 Hz, 2-H), 3.71 (3 H, s, OCH_3), 2.36 (1 H, t, J = 6.7 Hz, α-H), 1.96 (1 H, d, $J_{3,4}$ = 4.3 Hz, 3-H), 1.91 (1 H, dd, $J_{4,5'}$ = 2.5, $J_{4,3}$ = 4.3 Hz, 4-H), 1.85–1.6 (3 H, m, β-H_2, γ-H), 0.9 (3 H, d, J = 6 Hz, δ-H_3), 0.89 (3 H, d, J = 6 Hz, δ-H_3)	$^0H_1$
7b	574	7.32 (10 H, m, Ar H), 5.14, 5.07 (2 H, s, OCH_2Ph), 4.65 (1 H, d, $J_{1,2}$ = 3.8 Hz, 1-H), 3.88–3.81 (3 H, m, 5-H_2, 2-H), 3.25–3.0 (2 H, m, ε-H_2), 2.29 (1 H, t, J = 5.8 Hz, α-H), 1.86 (2 H, m, 4-H, 3-H), 2.0–1.62 (2 H, m, δ-H_2), 1.62–1.30 (4 H, m, β-H_2, γ-H_2)	$^0H_1$
8a[f]	349	4.17 (1 H, d, $J_{5',5}$ = 12.3 Hz, 5′-H), 4.03 (1 H, d, $J_{1,2}$ = 7.15 Hz, 1-H), 3.83 (1 H, dd, $J_{5,4}$ = 1.75, $J_{5,5'}$ = 12.3 Hz, 5-H), 3.77 (1 H, d, $J_{2,1}$ = 7.15 Hz, 2-H), 3.71 (3 H, s, OCH_3), 2.43 (1 H, t, J = 6.7 Hz, α-H), 1.94 (1 H, d, $J_{3,4}$ = 4.2 Hz, 3-H), 1.73 (1 H, dd, $J_{4,5}$ = 1.75, $J_{4,3}$ = 4.2 Hz, 4-H), 1.81–1.57 (3 H, m, β-H_2, γ-H), 0.92 (3 H, d, J = 6.4 Hz, δ-H_3), 0.88 (3 H, d, J = 6.4 Hz, δ′-H_3)	$^1H_0$
8b	574	7.29 (10 H, m, Ar H), 5.15, 5.07 (2 H, s, OCH_2Ph), 4.14 (1 H, d, $J_{5',5}$ = 12.3 Hz, 5′-H), 4.01 (1 H, d, $J_{1,2}$ = 7.33 Hz, 1-H), 3.78 (1 H, dd, $J_{5,4}$ = 1.5, $J_{5,5'}$ = 12.3 Hz, 5-H), 3.67 (1 H, d, $J_{2,1}$ = 7.33 Hz, 2-H), 3.12 (2 H, m, ε-H_2), (1 H, t, J = 5.86 Hz, α-H), 2.02–1.63 (4 H, m, 3-H, 4-H, δ-H_2), 1.63–1.23 (4 H, m, β-H_2, γ-H_2)	$^1H_0$

[a] Molecular ion peaks were observed by field desorption mass spectra. [b] At 400 MHz in $CDCl_3$ unless otherwise noted. [c] d = doublet, dd = doublet of doublets, *m* = multiplet, s = singlet, t = triplet. [d] The signals of 1-OCH_2Ph were consistently observed at δ 7-7.5 (5 H, m) and 4.2–4.8 (2 H, dd, J_{gem} = 11–12 Hz). These are not repeated in the text for simplicity. [e] The coupling constants are described in hertz and signals of 5′-H and 5-H were assigned on the basis of $J_{1,5'}$ = 0.57–0.65 Hz. [f] C_6D_6.

the coupling reactions of methyl ester of L-leucine and benzyl ester of *N*ε-(benzyloxycarbonyl)-L-lysine, respectively (Scheme II). A reaction analogous to this type of internal S_N2 displacement has earlier been described in literature to explain epoxide migration in some 2,3- and 3,4-anhydropyranosides.[5,18] The reactions illustrated in Scheme II are jointly mediated by the trans-oriented secondary amino functions and the solvent medium. In **5g** and **6g**, where the ring nitrogen is tertiary, no isomerization was observed despite careful search by the chromatographic techniques. The coupling products were also stirred in a series of solvents at room temperature for 48 h when more rearrangement took place in the protic solvents, particularly ethanol and methanol, respectively. The physical constants and analytical data of compounds **7a,b** and **8a,b** are provided in Table III.

^{1}H NMR spectroscopy at 400 MHz was used to define the conformation of aziridino sugars. The chemical shift of 1-H was again found to be the strongest parameter in conformational assignments. In **7a** and **7b** the position of anomeric proton peaks corresponds to equatorial orientation and the predominant conformation is, therefore, $^0H_1$. On the other hand, in **8a** and **8b** the anomeric proton peaks have moved appreciably upfield, and those of 5-H and 5′-H downfield. The coupling constant $J_{1,2}$ is also larger (7–7.5 Hz) than that for **7a** and **7b**, indicating that a change of conformation has occurred. The compounds **8a** and **8b** are clearly in $^1H_0$ conformation in which the anomeric proton is axial and 2-H pseudoaxial. It may be stated in the context of this data that the anomeric effect determines the conformation in most of the 2,3- and 3,4-anhydropentopyranosides,[19] and the predominant conformation is the one with the glycosidic group axial. The anomaly in the compounds **8a** and **8b** is probably due to the effect of steric and electrostatic repulsions between the axial benzyloxy group and the epimine ring nitrogen in $^0H_1$ conformation. This hypothesis is strongly supported by the fact that methyl 3,4-anhydro-β-L-arabinopyranoside and methyl 3,4-anhydro-α-D-arabinopyranoside, which show close structural resemblance to the isomerized products, have been reported to exist in $^0H_1$ and $^1H_0$ conformations, respectively[13] (Table IV). The ^{13}C NMR spectra of the coupling and isomeric products were also recorded (Table V), not only to lend further support to the assigned structures but also because of the fact that the ^{13}C NMR data of 2,3-anhydropyranosides and the aziridino sugars are not frequently available in the literature.

Scheme II



In all the reactions described in the foregoing account, benzyl 2,3-anhydro-β-L-lyxopyranoside (**9**) and benzyl 2,3-anhydro-α-D-lyxopyranoside (**10**) were respectively obtained as side products from **3** and **4**. The origin of these compounds can be explained through the competing nu-

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Table V. ^{13}C NMR Spectral Data[a]

compd	C1	C2	C3	C4	C5	1-OCH$_2$Ph	C_α	C_β	C_γ	C_δ	others
5a	92.5	51.2[d]	56.1	52.3[d]	57.4	69.8	48.1	39.2	24.9	22.9	169 (C=O), 52.9 (OCH$_3$), 21.1 ($C_{\delta'}$)
5b	92.4	51.1	59.8	51.1	60.3	69.1	52.1	29.6	22.7	33.4	175.2, 153.4 (C=O), 66.8, 66.6 (*C*H$_2$Ph), 40.8 (C_ϵ)
5c'	101.6	59.8	72.4	57.3	61.7	71.5	54.0	15.8			169.1 (C=O), 53.7 (OCH$_3$)
5d	92.5	51.7[d]	56.0	52.2[d]	57.4	69.6	48.2	29.3	29.3		168.5 (C=O), 52.2 (OCH$_3$), 14.9 (SCH$_3$)
5e	92.3	51.4[d]	59.4	51.1[d]	59.4	69.1	52.0	28.6	30.5		174.8, 172.8 (C=O), 67.0, 66.3 (*C*H$_2$Ph)
5f[b]	92.5	51.3	56.0	50.8	59.1	69.1	47.8	35.6			168.9 (C=O), 52.6 (OCH$_3$), 20.7 (*C*H$_3$C$_6$H$_4$)
5g	92.6	51.3[d]	53.5	51.8[d]	62.0	69.2	58.9	30.0	23.4	50.7	175.0 (C=O), 51.8 (OCH$_3$)
6a	94.2	50.2	58.0	49.4	59.5	69.8	51.8	43.0	24.8	22.7	176 (C=O), 54.7 (OCH$_3$), 22.0 ($C_{\delta'}$)
6b	93.9	49.8	59.0	49.1	59.0	69.4	54.2	29.3	22.4	33.0	174.5, 156 (C=O), 66.4, 66.1 (CH$_2$Ph), 40.5 (C_ϵ)
6c[b]	103.4	59.3	62.7	58.9	64.3	79.2	56.7	30.3			179.4 (C=O), 62.4 (OCH$_3$), 24.4 (*C*H$_3$C$_6$H$_4$)
6d[c]	94.8	50.3	58.4	50.3	59.9	69.8	51.5	33.1	30.5		175.0 (C=O), 54.7 (OCH$_3$), 15.2 (SCH$_3$)
6e	94.1	50.2	58.7	49.4	59.4	69.8	54.4	28.6	30.5		174.8, 172.8 (C=O), 67.0, 66.3 (*C*H$_2$Ph)
6f	93.9	50.5[d]	55.5	49.6	59.9	70.1	50.2[d]	36.2			168.1 (C=O), 52.8 (OCH$_3$), 21.3 (*C*H$_3$C$_6$H$_4$)
6g	94.1	50.9	55.3	49.1	63.5	70.5	54.8	28.9	22.0	48.8	167.7 (C=O), 51.1 (OCH$_3$), 21.2 (*C*H$_3$C$_6$H$_4$)
7a	94.5	70.1	41.2	35.9	60.0	69.4	65.0	41.7	24.8	22.6	172.9 (C=O), 51.8 (OCH$_3$), 22.6 ($C_{\delta'}$)
8a	94.5	70.0	41.0	36.8	64.4	68.9	68.1	41.7	24.8	22.7	172.8 (C=O), 51.9 (OCH$_3$), 22.6 ($C_{\delta'}$)
7b	94.5	70.9	41.3	36.3	59.8	70.0	65.0	29.9	23.0	32.1	171.8, 156.5 (C=O), 66.6 (*C*H$_2$Ph), 40.8 (C_ϵ)
8b	102.1	70.6	41.5	36.9	64.3	69.9	68.0	29.8	23.0	31.9	171.6, 155.6 (C=O), 66.6 (*C*H$_2$Ph), 40.7 (C_ϵ)

[a] Data are given in ppm, relative to Me$_4$Si standard. All spectra were measured in $CDCl_3$ unless otherwise noted. The assignments were supported by signal multiplicity obtained by off-resonance decoupling experiments. The aromatic protons are not described for the sake of simplicity. [b] Me$_2$SO-d_6. [c] C_6D_6. [d] The assignments can be reversed.

cleophilic displacement of the triflyl group by the moisture present in DMF. None of these compounds were obtained when displacement reactions were carried out in acetonitrile of high purity grade. Compound **9**, which was hitherto unreported, could also be obtained as major product by stirring **3** in 98% DMF with tetrabutylammonium nitrite or pyridine. The yield of **10** could likewise be improved considerably, providing an alternate and efficient route to this epoxy sugar from L-arabinose, following the earlier synthesis reported by one of us, departing from D-xylose.[5]

Experimental Section

Methods. Melting points were not corrected. Thin-layer chromatography was done on precoated silica gel plates with fluorescence indicator. Column chromatography was performed on silica gel 60, particle size 0.063–0.200 mm. The triflic anhydride was prepared from triflic acid by the reported method.[20] All the other chemicals were obtained from E. Merck and Aldrich and used as received. All carbohydrates and amino acids were commercial samples from E. Merck and Sigma Chemical Co. The amino esters were synthesized according to the reported procedures.[21-25]

General Procedure for the Coupling Reactions. Each of the sugar triflate **3** and **4** (1 mmol) was dissolved in DMF Selectipur (Merck) and added the corresponding amino ester (2.5 mmol) at −20 °C. The reaction mixture was slowly warmed to room temperature, followed by continuous stirring for further 5 h. Reactions were monitored by TLC using solvent system acetone/dichloromethane/toluene (1:1:1). In all the cases except proline three types of products, coupling compounds (R_f 0.53–0.7), aziridino sugars (R_f 0.38–0.5), and the free anhydro sugars **9** and **10** (R_f 0.3), were observed. The chromatographic R_f's for each product of each reaction have already been described in preliminary paper.[1] The solvent was removed under high vacuum after the disappearance of all starting triflate. The residue was taken up in ethyl acetate, washed repeatedly with sodium carbonate solution and water, dried (Na_2SO_4), and freed of solvent. The compounds described in Tables I and III were isolated pure by column chromatography using the same solvent system. Their spectral data are given in Table II, IV, and V.

In a modified procedure, DMF was replaced by acetonitrile of high purity grade not only because of ease of removal of solvent but also to prevent the formation of side products. The reactions were carried out at room temperature for 48 h and improved yields of the coupling products were obtained.

Optimum Procedure for the Synthesis of 9 and 10. Each of the sugar triflates **3** and **4** (1 mmol) was dissolved in 98% DMF (10 mL) and added pyridine or tetrabutylammonium nitrate (1 mmol) at room temperature. The reaction mixture was stirred at room temperature for 48 h when the major conversion to a slower running product was observed on TLC. The solvent was removed under high vacuum; the residue as taken up in dichloromethane and successively washed with 1% hydrochloric acid, water, 1% sodium bicarbonate solution, and finally again with water. On drying and removal of solvent an oily residue was obtained which was chromatographed over silica gel by using a 1:1 mixture of ethyl acetate and petroleum ether. Crystallization from ether/petroleum ether afforded **9** and **10** in excellent yields.

Benzyl 2,3-anhydro-β-L-lyxopyranoside (9): 68% yield; mp 83–85 °C; $[\alpha]^{25}_D$ +68.6° (*c* 1, $CHCl_3$); FD mass spectrum, *m/z* 222 (M+); ^1H NMR (100 MHz, $CDCl_3$) δ 7.28 (5 H, m, Ar H), 4.96 (1 H, d, $J_{1,2}$ = 2.8 Hz, 1-H), 4.64 (2 H, dd, J_{gem} = 12.2 Hz, OC*H*$_2$Ph), 3.94 (1 H, dd, $J_{5,4}$ = 1.4, $J_{5,5'}$ = 12.4 Hz, 5-H), 3.63 (1 H, m, 4-H), 3.37 (1 H, dd, $J_{5',4}$ = 1.9, $J_{5',5}$ = 12.4 Hz, 5'-H), 3.25 (2 H, m, 2-H, 3-H), 2.07 (1 H, br s, OH); ^{13}C NMR ($CDCl_3$) δ 92.1 (d, C1), 51.2 (d, C2), 51.5 (d, C3), 64.1 (d, C4), 61.4 (t, C5), 69.2 (t, O*C*H$_2$Ph).

Anal. Calcd for $C_{12}H_{14}O_4$ (222.24): C, 64.85; H, 6.35. Found C, 64.59; H, 6.33.

Benzyl 2,3-anhydro-α-D-lyxopyranoside (10): 72% yield, mp 65–66 °C (lit.[5] mp 65 °C); $[\alpha]^{25}_D$ +60.1° (*c* 1, $CHCl_3$); ^1H NMR (100 MHz, $CDCl_3$) δ 7.24 (5 H; m, Ar H), 4.95 (1 H, s, 1-H), 4.69 (2 H, dd, J_{gem} = 11.6 Hz, OC*H*$_2$Ph), 3.93 (1 H, m, 4-H), 3.68 (1 H, dd, $J_{5,4}$ = 1.87, $J_{5,5'}$ = 12.1 Hz , 5-H), 3.51 (1 H, dd, $J_{5',4}$ = 7.9, $J_{5',5}$ = 12.1 Hz, 5'-H), 3.28 (1 H, d, $J_{2,3}$ = 3.8 Hz, 2-H), 3.15 (1 H, dd, $J_{3,2}$ = 3.8, $J_{3,4}$ = 0.59 Hz, 3-H), 2.62 (1 H, br s, OH); ^{13}C NMR ($CDCl_3$) δ 94.5 (d, C1), 51.1 (d, C2), 54.0 (d, C3), 62.6 (d, C4), 61.0 (t, C5), 70.3 (t, O*C*H$_2$Ph).

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95066-13-0; **5g**, 95066-20-9; **6a**, 95066-10-7; **6b**, 95066-26-5; **6c**, 95066-11-8; **6d**, 95066-19-6; **6e**, 95066-24-3; **6f**, 95066-15-2; **6g**, 95066-21-0; **7a**, 96728-24-4; **7b**, 96728-25-5; **8a**, 96728-26-6; **8b**, 96728-27-7; **9**, 95066-28-7; **10**, 71204-43-8; L-leucine methyl ester, 2666-93-5; N_ϵ-(benzyloxycarbonyl)lysine benzyl ester, 24458-14-8; L-alanine methyl ester, 10065-72-2; L-methionine methyl ester, 10332-17-9; L-glutamic acid dibenzyl ester, 2768-50-5; L-phenylalanine methyl ester, 2577-90-4; L-proline methyl ester, 2577-48-2.

Solvolysis of 2-Adamantyl Trifluoromethanesulfonate: A Y_{OTf} Scale[1]

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The solvolysis of 2-adamantyl trifluoromethanesulfonate proceeds at a convenient rate at temperatures below ambient in a wide variety of pure and aqueous organic solvents and in ethanol–2,2,2-trifluoroethanol mixtures. A scale of Grunwald–Winstein Y values (Y_{OTf}) is developed for 26 solvents and it is found to much more closely resemble the corresponding Y_{OClO_3} scale than the corresponding scale of Y_{OTs} values. In aqueous ethanol, there is a preference for product formation by interaction with water molecules by a factor of *ca.* 1.5, essentially independent of solvent composition (96–50% ethanol).

Because of their extremely high nucleofugality, about 10^4–10^5 times higher than that for the *p*-toluenesulfonate (tosylate) ion,[2-4] the trifluoromethanesulfonate (triflate) and other perfluoroalkanesulfonate ions have found extensive use in both synthetic and mechanistic studies.[5] Their ability to depart from esters with formation of relatively unstable carbenium ions has been utilized in the generation of carbocations from cyclopropyl triflates,[6] of α-keto cations,[7] of carbenium ions destabilized by one or more α-trifluoromethyl groups or by a α-cyano group,[8] of disubstituted carbenium ions (vinyl cations),[4,9,10] and of carbocations from polycyclic structures.[6,11-13] The solvolysis of 7-norbornyl triflate has recently been used to establish Y_{OTf} values for eight solvents.[13] These are recommended for use within the Grunwald-Winstein equation (eq. 1) for solvolyses of triflate esters. In eq 1, k and k_0

$$\log\left(\frac{k}{k_0}\right)_{ROTf} = mY_{OTf} \qquad (1)$$

represent the specific rates of solvolysis in the solvent under consideration and in the standard solvent (80% ethanol), Y represents the solvent ionizing power of the solvent under consideration, and m represents the sensitivity of the rate of solvolysis of the substrate to changes in solvent ionizing power.

Attempts to correlate the rates of solvolysis of triflate esters against Y values (based on *tert*-butyl chloride solvolysis) or Y_{OTs} values (based on adamantyl tosylate solvolysis[14,15]) have met with varying success. In aqueous–ethanol mixtures, vinyl,[4,9,16-19] cyclopropyl,[20] and bridgehead[12] triflates have been correlated against Y values with reasonable m values. Correlations of cyclopropyl and bridgehead triflates against Y values in aqueous–acetone mixtures led[6] to lower m values, reminiscent of the behavior of 2-adamantyl perchlorate.[15] However, when a more extensive range of solvents was incorporated into a study of α-trifluoromethyl-destabilized carbocations, plots of specific solvolysis rates against Y_{OTs} values showed both dispersion and variable m values for different mixed-solvent systems,[8a] again reminiscent of 2-adamantyl perchlorate solvolysis,[15] and the need for a thorough study of the solvent dependence of triflate reactivities was emphasized. The rates of solvolyses of 7-norbornyl triflate also correlated rather poorly with Y_{OTs} values.[13] The rates of solvolysis of several vinyl triflates have also been correlated[21] by using the extended Grunwald–Winstein equation with N_{OTs} and Y_{OTs} scales[14a] (eq 1, with the addition of a lN term, which is governed by solvent nucleophilicity and the sensitivity of the solvolysis rate of a given substrate toward changes in solvent nucleophilicity).

The extremely slow solvolyses of 7-norbornyl triflate, except in solvents of high ionizing power,[13] limit the range

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