($E^{\circ\prime}$ -1.18 V vs. NHE in acetonitrile[39]) and paraquat (-0.44 V)[37] suggests that 2,3-MPDP$^+$ could theoretically function as a more efficient redox cycling catalyst than MPP$^+$, though the significance of such is uncertain in view of the apparent short lifetime of 2,3-MPDP$^+$ in biological tissue.

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(39) MPP$^+$ undergoes a quasi-reversible 1e reduction at a Pt electrode, and the value of $E^{\circ\prime}$ given was determined by comparison to an internal ferrocenium/ferrocene couple.[40] Similar values of $E^{\circ\prime}$ were obtained by CV at a glassy carbon (GC) electrode (-1.17 V) and by OSWV (-1.20 V (Pt), -1.19 V (GC)). Reference 37 reports only that the reduction of MPP$^+$ occurs below -1.0 V in water.

(40) Gagne, R. R.; Koval, C. A.; Lisensky, G. C. *Inorg. Chem.* **1980**, *19*, 2855.

Stereospecific 1,2-Migrations in Carbohydrates. Stereocontrolled Synthesis of α- and β-2-Deoxyglycosides

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Despite the many advances made in the chemistry of carbohydrates, several problems[1] still remain in this important area of natural products. Two of the most common, but often difficult to reach, goals in carbohydrate chemistry are (a) the selective functionalization of the ring system and (b) the stereocontrolled construction of glycoside bonds, particularly in the 2-deoxy series. In this paper we report a new series of stereospecific 1,2-migrations, within the pyranoside carbohydrate framework, of a variety of groups that provide solutions to several objectives, including the two mentioned above. Specifically, we have discovered new and practical synthetic technology for (a) introduction of fluorine at C-1,[2] (b) introduction of O-, S-, and N-containing substituents at C-2, (c) inversion of configuration at C-2, (d) deoxygenation at C-2, and (e) stereocontrolled synthesis of α- and β-glycoside bonds including the hitherto difficult to construct 2-deoxy-β-glycosides.[3]

Scheme I, eq 1, outlines the mechanistic considerations that led to the design of these stereospecific migrations. Thus, it was anticipated that a migratory group at C-1 might be induced to shift to the neighboring position (C-2) by a "pull" from the "host" carbon initiated by the departure of a leaving group and (b) a "push" from the ring oxygen lone pair of electrons, providing the groups involved were stereoelectronically oriented in the proper fashion. In consideration of practical means to realize this scenario from simple and readily available starting materials, and in order to maximize the synthetic potential of the resulting products, (diethylamino)sulfur trifluoride (Et_2NSF_3, DAST) was chosen to operate on hydroxysubstrates I (Scheme I).[4] Indeed, when compounds I (X = OMe, OAc, SPh, N_3; Scheme I, eq 2) were treated with excess DAST in CH_2Cl_2 at 0-45 °C the glycosyl fluorides II were obtained in high yields (see Table I).[6] Fur-

Table I. 1,2-Migrations in Carbohydrates[a]

Entry	Substrate	Product[b]	Temperature (°C)	Yield (%)
1	X=OMe, R=Si^{t}BuMe$_2$		45	77
2	X=OMe, R=CH_2Ph		45	81
3	X=OAc, R=Si^{t}BuMe$_2$		0	91
4	X=SPh, R=Si^{t}BuMe$_2$		0	88
5	X=N_3, R=Si^{t}BuMe$_2$		45	78
6	X=OMe, R=Si^{t}BuMe$_2$		45	70
7	X=SPh, R=Si^{t}BuMe$_2$		0	93
8			0	88
9	R_1=Si^{t}BuPh$_2$, R_2=CH_2Ph		25	68
10	X=SPh, R=Me		0	86
11	X=N_3, R=Me		45	75
12	X=OCH_2Ph, R=H		25	66
13			0	88
14	R_1=CH_2Ph, R_2=Si^{t}BuMe$_2$		0	85
15	R_1=Si^{t}BuMe$_2$, R_2=Me		0	86
16	R=CH_2Ph		25	56

[a] Conditions: 3.0 equiv of Et_2NSF_3 (DAST), CH_2Cl_2. [b] In entries 3, 4, 7, 8, 10, 13, and 14 the indicated anomer was exclusively formed, whereas in the remaining entries the indicated anomer predominated in an anomeric mixture (α:β ratio): 1 (40:60), 2 (40:60), 5 (50:50), 6 (25:75), 9 (40:60), 11 (50:50), 12 (60:40), 15 (70:30), 16 (62:38).[8,9]

(1) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. Perlin, A. S. *Pure Appl. Chem.* **1978**, *50*, 1401.

(2) For some previous syntheses and/or utilizations of glycosylfluorides, see: Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189 and references cited therein. Nicolaou, K. C.; Dolle, R. E.; Chucholowski, A.; Randall, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1153. Nicolaou, K. C.; Chucholowski, A.; Dolle, R. E.; Randall, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1155. Hashimoto, S.; Hayashi, M.; Noyori, R. *Tetrahedron Lett.* **1984**, *25*, 1379. Rosenbrook, W.; Riley, D. A.; Lartey, P. A. *Tetrahedron Lett.* **1985**, *26*, 3. Posner, G. H.; Haines, S. A. *Tetrahedron Lett.* **1985** *26*, 5. Mukaiyama, T.; Murai, Y.; Shoda, S. *Chem. Lett.* **1981**, 431. Mukaiyama, T.; Hashimoto, Y.; Shoda, S. *Chem. Lett.* **1983**, 935. Kunz, H.; Sager, W. *Helv. Chim. Acta* **1985**, *68*, 283. Araki, Y.; Watanabe, K.; Kuan, F.-H.; Itoh, K.; Kobayashi, N.; Ishido, Y. *Carbohydr. Res.* **1984**, *127*, C5.

(3) For some previous entries into 2-deoxy-β-glycosides, see: Bock, K.; Lundt, I.; Pedersen, C. *Carbohydr. Res.* **1984**, *130*, 125 and references cited therein.

(4) For the use of DAST to prepare α-fluoro-β-amino acids from β-hydroxy-α-amino acids via nitrogen 1,2-shift, see: Somekh, L.; Shanzer, A. *J. Am. Chem. Soc.* **1982**, *104*, 5836.

(5) The starting materials utilized in this work (Schemes I and II and Table I) were prepared by standard methods from commercially available carbohydrates and are optically active.

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Scheme I. 1,2-Migrations in Carbohydrate System

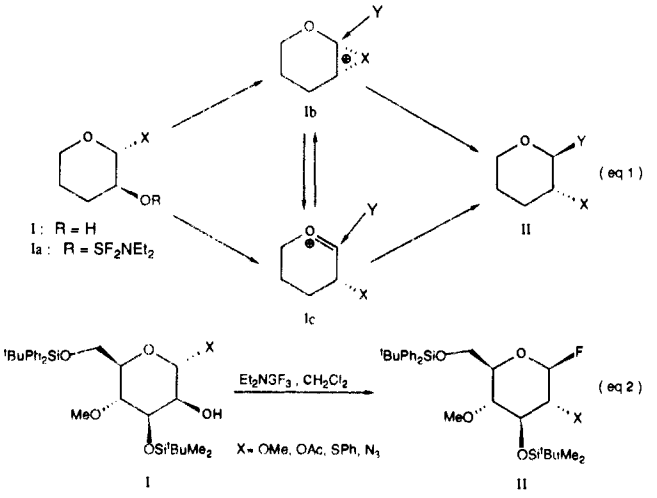


Table II. Stereocontrolled Synthesis of α- and β-Glycosides

entry	reactants	solvent/reagents[a]	yield, %	α:β ratio[c]
1	IV, V	Et_2O	92	1:16
2		CH_2Cl_2	90	10:1
3		CH_2/Cl_2/20 equiv Me_2S	90	1:13
4		THF (1.2 equiv of $AgClO_4$)[b]	(50)	(1:3)
5	XII, V	Et_2O	93	1:0[10]
6		CH_2Cl_2	91	1:0[10]

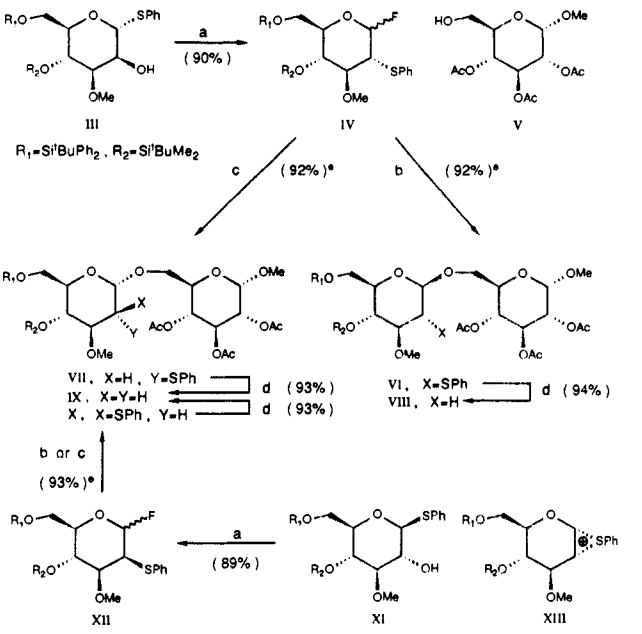
[a] Reaction Conditions: 1.8 equivof $SnCl_2$, 4-Å MS, −15 °C. [b] In the absence of $AgClO_4$ the reaction did not proceed. [c] Determined by ^1H NMR spectroscopy.

thermore, a variety of other substrates and substituents (e.g., OCH_2Ph, OCOPh, O-sugar) were found to undergo the C-1 to C-2 shift as Table I demonstrates.[7] Thus, in one step, this operation introduces a variety of useful functional groups at C-2 and simultaneously a fluorine substituent at C-1 with inversion of stereochemistry at both centers.[8,9]

These facile migrations have a number of obvious and useful applications. Thus, the glycosyl fluorides obtained can be used in coupling reactions[2] to afford various types of O-, S-, N-, and C-glycosides. This powerful reaction also offers the possibility of transplanting a group in a predictable stereochemical fashion at C-2 after introduction at C-1, the most activated position of the carbohydrate framework. Easy deprotection of some of these groups (e.g., OAc, OCH_2Ph) results in a new and practical method for inversion of stereochemistry at C-2, whereas the successful introduction of the azido group has important implications in the synthesis of amino sugars. The PhS group with its rich and synthetically fertile chemistry promises new ventures in carbohydrate chemistry including deoxygenation at C-2 and control of glycosidation stereochemistry.

The application of this new technology to the stereocontrolled construction of α- and β-glycosides was then demonstrated by

Scheme II. Stereocontrolled Synthesis α- and β-Deoxyglycosides[a]



[a] (a) 3.0 equiv of DAST, CH_2Cl_2, 0 °C; (b) 0.9 equiv of V, 1.8 equiv of $SnCl_2$, 4 Å MS, Et_2O, −15 °C; (c) 0.9 equiv of V, 1.8 equiv of $SnCl_2$, 4 Å MS, CH_2Cl_2, −15 °C; (d) Raney Ni, EtOH, Δ; (e) yield based on V.

efficient syntheses of two isomeric disaccharides. This important objective was achieved by (a) introduction of a PhS group at C-2, (b) α- or β-directed glycosidation by neighboring group and/or solvent participation, and (c) desulfurization to afford the 2-deoxy-α-glycoside or its β-isomer. Scheme II illustrates this three-step sequence which is of particular importance for 2-deoxy-β-glycosides, compounds normally not directly accessible from 2-deoxy sugars,[3] leading to the α-linked disaccharides VII and X[10] and the β-linked isomer VI with high stereocontrol. Of special interest was the solvent effect on the stereochemical outcome of these glycosidation reactions in the presence of $SnCl_2$ as Table II shows. It appears that in the presence of a tin-complexing solvent or reagent (e.g., entries 1, 3, and 5, Table II) the SPh group remains free to direct the glycosidation via a transient intermediate such as XIII (Scheme II), whereas in the absence of a complexing medium (e.g., entries 2 and 6, Table II) the catalyst may be engaging the sulfur, thus preventing it from participating in the coupling reaction.[10]

The described chemical transformations are expected to (a) increase the usefulness of carbohydrates in organic synthesis, (b) enhance our ability to synthesize various useful and/or rare sugars from other readily available carbohydrates, and (c) facilitate the construction of oligosaccharide chains with stereocontrol at the glycoside bonds. Further extensions of these discoveries and applications to the synthesis of naturally occurring substances are in progress.[11]

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Supplementary Material Available: Listing of ^1H NMR data for compounds II (X = OMe, OAc, SPh, N_3), IV–X, and XII and ^{13}C NMR data for VIII and IX (5 pages). Ordering information is given on any current masthead page.

(6) For a previous report of C-1 to C-2 shift involving a thiophenyl and a mesylate group under basic conditions, see: Ryan, K. J.; Acton, E. M.; Goodman, L. *J. Org. Chem.* **1971**, *36*, 2646.

(7) It was also demonstrated that a trimethylsilylated hydroxyl group at C-2 allows the reaction, presumably by leading to the same intermediate Ia (Scheme I, eq 1).

(8) The indicated stereochemistry at C-1 and C-2 in these compounds was expected on mechanistic grounds and was confirmed by ^1H NMR data. Thus, the crystalline product obtained from II (Scheme I, X = OMe) by desilylation (n-Bu_4NF) with concomitant anomerization (α-anomer) exhibited $J_{1,2}$ = 2.6 and $J_{2,3}$ = 9.5 Hz (^1H, NMR, 250 MHz). Furthermore, the structure of the product from the mannose derivative in entry 6, Table I, was proven by an alternative synthesis from the corresponding glucose derivative: (a) NaH–MeI, THF, 0 °C; (b) Me_3SiSPh–n-Bu_4NI–ZnI_2, $ClCH_2CH_2Cl$, 60 °C; (c) DAST–NBS, CH_2Cl_2, −15 °C (50% overall).

(9) Anomerization of these fluorides may easily be envisioned under the reaction conditions but usually has no significant effect on the stereoseletivity of coupling reactions of these substrates.

(10) In both entries 5 and 6, Table II, the α-anomer is expected as observed, since sulfur participation and the anomeric effect direct the stereochemistry to the α-configuration.

(11) All new compounds exhibited satisfactory ^1H NMR, IR, MS, and analytical and/or high-resolution mass spectral data. Yields refer to chromatographically and spectroscopically homogeneous materials.