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n-PENTENYL 2-AMINO-2-DEOXY GLYCOSIDES UNDERGO STEREOSELECTIVE COUPLING UNDER MILD, CHEMOSPECIFIC CONDITIONS

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Abstract: *n-Pentenyl 2-deoxy-2-phthalimido and 2-anisylimino-2-deoxy-D-gluco-pyranosides undergo ready iodonium ion induced coupling with a variety of sugar alcohols to give β and α disaccharides, respectively, in moderate to excellent yields. The procedure is tolerant of a wide variety of protecting groups.*

Recent advances in the isolation of complex polysaccharides and the determination of their conformational properties have helped to establish the important roles that these compounds play in intercellular recognition, and thereby led to significant breakthroughs in cell biology.[1-3] These glycans are considered as molecular messengers,[3-6] the chemical messages being encoded in their primary structures and their spatial conformations. Consequently, there has been widespread interest in the synthesis of these compounds for immunological and enzymological studies.

In this context, we have recently shown that n-pentenyl glycosides **1** are versatile glycosyl donors that can be activated under mild conditions by halonium ions.[7] The reactions presumably proceed *via* the initial attachment of the electrophile to the olefin to give the cyclic halonium ion **2**, which is in equilibrium with the cyclic oxonium ion **3**. Subsequent release of the halomethyltetrahydrofuran liberates the oxocarbonium ion **4**, which may be trapped by an alcohol donor.

The ratio of α- and β glycosides **5** obtained in the coupling process is of utmost importance in the synthesis of complex oligosaccharides (**5**, S=saccharide), and indeed,

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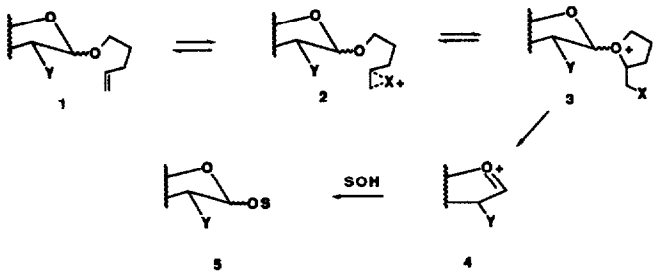
favorable selectivity was obtained with a number of n-pentenyl glycosides bearing a C-2 benzyloxy substituents (Y=OBn).[7c] In these cases, the α:β ratio of the disaccharide products were found to depend on the nature of the protected sugar alcohol used, as well as the reaction solvent.[7c]

SCHEME 1



Alternatively, it is well known that selectivity in saccharide coupling reactions can be influenced by use of a C-2 participating group (e.g., **4**, Y=OCOOR).[8] However, our initial experiments with these substrates indicated that such compounds were highly unreactive,[7b] and therefore the concept of anomeric stereocontrol *via* C2-esters did not appear to be promising for n-pentenyl glycosides. In our continuing investigation of the effect of C-2 substitution on these novel substrates, we have extended our study to the 2-amino-2-deoxy derivatives, and these results are reported herein.

Two basic types of n-pentenyl glycosides were investigated: 2 phthalimido, **8**, and 2-p-methoxybenzylimino, **9**. Both compounds were prepared from the common precursor **7**, which was obtained by the tin(IV) chloride catalyzed glycosidation of 1,3,4,6-*tetra*-O-acetyl-2-deoxy-2-phthalimido-α/β-D-glucopyranose **6**[9] with 4-penten-1-ol, using the procedure of Campos-Valdez and co-workers.[10]

The pentenyl glycoside **7** was easily transformed, after manipulation of the protecting groups into the 2-phthalimido glycosyl donor **8** in 68% yield. The desired 2-imino glycosyl donor **9** was then obtained from **8** by removal of the phthalimido group,[11] and condensation of the free amine with p-anisaldehyde.

The glycosidations were carried out in dichloromethane and were complete within 1 hour for the glycosyl donors **8** and **9**.[12] The triacetate donor **7** was less reactive and glycosidations utilizing this compound resulted in reduced yields. As shown in Table 1, excellent β selectivity was observed for the reaction of the 2-phthalimido glycoside **8** with various alcohol donors; the complementary result was achieved using the 2-imino derivative **9** to obtain the α anomers.

Although similar selectivities have been obtained in glycosidations involving the corresponding N-substituted glycosyl halides,[9,13] important advantages of the n-pentenyl glycoside methodology involves the sturdiness of the glycosyl donor and the mildness of the

activation procedure. These attributes allow for the incorporation of a wide variety of sensitive protecting groups in the glycosyl donor, and is exemplified by the preparation of the 2-imino pentenyl glycosides **9**. For such substrates, preparation of the corresponding glycosyl halide would be severely challenging in view of the lability of the imino and isopropylidene functionalities.

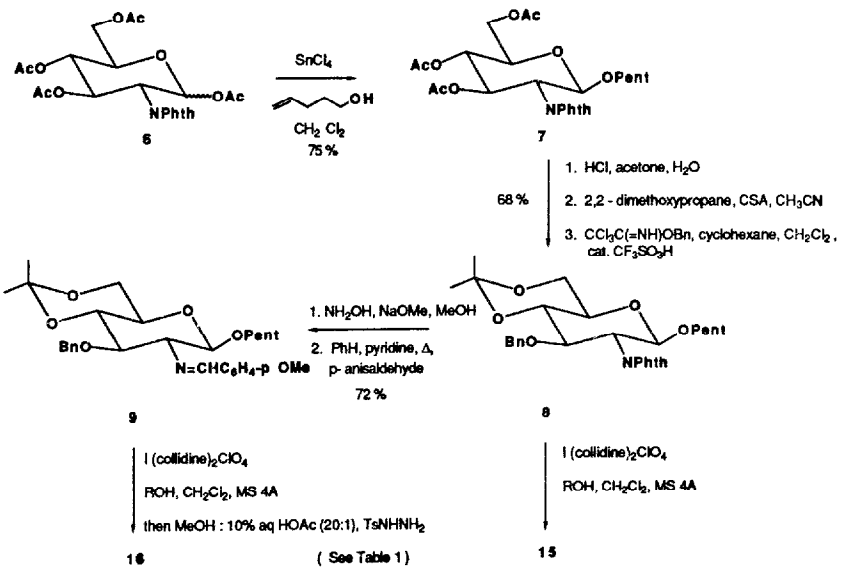
TABLE 1 Reaction of Alcohol Donors with 2- Phthalimido and 2-Anisylimino Pentenyl Glycosides

Alcohol Donor ROH / Disaccharide Product	10	11	12	13	dl- 14
β - Phthalimido Glycoside (% Yield)	15a (90)	15b (81)	15c (88)	15d (77)	
α - Amino Glycoside (% Yield)	16a (60)	16b (66)	16c (64)	16d (64)	16e (68)*

* 1 : 1 mixture of diastereoisomers

The foregoing considerations therefore bear particular significance for oligosaccharide synthesis, since the number of hydroxyl group differentiations subsequent to saccharide

SCHEME 2



coupling may be reduced, thereby increasing the convergence of the process. Of related importance is the chemoselectivity of the activation procedure. Thus, reaction of the pentenyl glycosides **9** with the tri-O-allyl inositol derivative **14** afforded moderate yields of coupled products **16e** in which the allylic olefins were unaffected.

In summary, protected n-pentenyl 2-amino glycosides have been shown to be highly stable glycosyl donors, which tolerate a wide spectrum of protecting groups, and are conveniently prepared on large scales. Furthermore, excellent α/β selectivity has been obtained in saccharide couplings, depending on the nature of the amino protecting group. These results are extremely important and timely for the synthesis of amino polysaccharides, which are important constituents of blood group determinants, antigenic determinants cell surfaces,[14] and glycolipids,[15] and amino glycoside antibiotics.[16]

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Note. An invention disclosure has been filed for the processes described in this communication.

References

1. Hughes, R. C. Membrane Glycoproteins. London: Butterworths; 1976.
2. Montreuil, J. *Adv. Carbohydr. Chem. Biochem.*; **1980**; *37*: 1157.
3. Hakamori, S. *Ann. Rev. Biochem.*; **1981**; *50*: 733.
4. (a) Sharon, N. Complex Carbohydrates. *Their Chemistry, Biosynthesis, and Functions*. Reading, Massachusetts: Addison Wesley; 1975; (b) Sharon, N.; Lis, H. *Chem. Eng. News*; **1981**; *58*(13): 21.
5. Feizi, T.; Childs, R. A. *Trends Biochem. Sci.*; **1985**; *19*: 24.
6. Lemieux, R. U. *Chem. Soc. Rev.*; **1978**; *7*: 423.
7. (a) Mootoo, D. R.; Date, V.; Fraser-Reid, B. *J. Am. Chem. Soc.*; **1988**; *110*: 2662; (b) Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.*; **1988**; *110*: 5583; (c) Fraser-Reid, B.; Konradsson, P.; Mootoo, D. R.; Udodong, U. *J. Chem. Soc., Chem. Comm.*; **1988**: 823.
8. Frush, H. L.; Isbell, H. S. *J. Res. Nat. Bur. Stand.*; **1941**; *27*: 413; Isbell, H. S. *Ann. Rev. Biochem.*; **1940**; *9*: 65; Pascu, E. *Advan. Carbohydr. Chem. Biochem.*; **1945**; *1*: 77.
9. Lemieux, R. U.; Takeda, T.; Chung, B. Y. *ACS Symposium Series*; **1976**; *39*: 90.
10. Compos-Valdez, M. T.; Marino-Albernas, J. R.; Verez-Bencomo, V. *J. Carbohydr. Chem.*; **1987**; *6*: 509.
11. Neunhoeffer, O.; Lehmann, G.; Haberer, D.; Steinle, G. *Annalen*; **1968**; *712*: 208.
12. For a standard procedure, see reference 7c. For the glycosidations involving the 2-imino pentenyl glycosides, the crude product was treated with 10% aqueous acetic acid in methanol (1:20), and tosylhydrazine (1 equiv.) for 20 minutes to give the free amine. All new compounds cited in this article gave satisfactory elemental analyses and spectral data.
13. Umezawa, S. *Adv. Carbohydr. Chem. Biochem.*; **1974**; *30*: 111.
14. Kabot, E. A. Blood and Tissue Antigens. New Yrok: Academic Press; 1970: 187, Ed., Aminoff, D.
15. Watkins, W. M. Glycoproteins. Amsterdam: Elsevier; 1972: 830, Ed. Gottschalk, A.
16. Umezawa, S. *Adv. Carbohydr. Chem. Biochem.*; *1974*; *30*: 111.

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