selectivity (α:β = 1:3). Attempts to glycosylate the alcohol **11** using an oxazolidine derivative were unsuccessful presumably because of steric congestion at the secondary hydroxyl group. Reductive acetylation of the azide **12** using thiolacetic acid[19] and selective saponification gave the 4′-alcohol **13** (59%). Finally, sulfation of **13** using sulfur trioxide·pyridine in DMF[20] (73%) and global catalytic debenzylation gave bulgecin C (**3**) (80%). The material was identical in all respects (TLC, IR, ^{1}H NMR, ^{13}C NMR, FAB HRMS, and $[\alpha]_D$) with an authentic sample of the natural product.

It is clear from these results that the radical substitution of pyrrolidine derivatives provides a convenient method for the stereospecific generation of bulgecinine (**4**). Additionally the electrochemical/radical strategy and the glycosylation technology are applicable to the synthesis of alternative bulgecin systems. Further aspects of these studies will be published in due course.

Acknowledgment. We thank the National Institutes of Health for support of our program (AI-23034) and for the purchase of a 400-MHz NMR spectrometer (RR-01672) and a high-resolution mass spectrometer (RR-03245) used in these studies. We additionally thank Takeda Chemical Industries, Ltd., for providing an authentic sample of bulgecin C (**3**) and G. D. Searle and Company for the microanalysis of new compounds.

Supplementary Material Available: Experimental data for **3** and **4** (2 pages). Ordering information is given on any current masthead page.

(19) Rosen, T.; Lico, I. M.; Chu, D. T. W. *J. Org. Chem.* **1988**, *53*, 1580.
(20) Guiseley, K. B.; Ruoff, P. M. *J. Org. Chem.* **1961**, *26*, 1248. Wolfrom, M. L.; Shen Han, T. M. *J. Am. Chem. Soc.* **1959**, *81*, 1764.

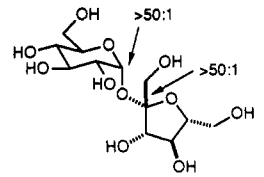
Redox Glycosidation: A Stereoselective Synthesis of Sucrose‡

Anthony G. M. Barrett,*,[1] Barend C. B. Bezuidenhoudt, and Laura M. Melcher
Department of Chemistry, Northwestern University, Evanston, Illinois 60208
Received July 16, 1990

Summary: Sucrose was stereoselectively prepared from D-glucose by esterification using D-arabinoic acid and subsequent methylenylation, iodoetherification, and radical-mediated substitution.

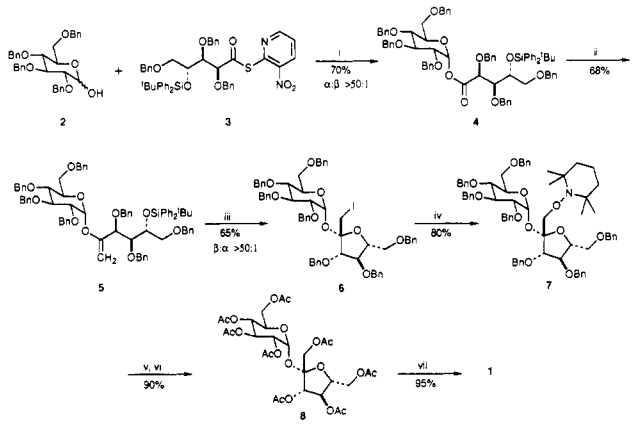
The construction of glycosides is frequently nontrivial in consequence of poor α- versus β-diastereoselectivities and low chemical yields. Classically glycosides are prepared by the Koenig–Knorr reaction of a protected glycosyl halide with a sugar alcohol in an alkylation process mediated by a silver (I) or mercury (II) salt.[2] In the past decade numerous variations of this alkylation strategy have been developed.[3] However, there is, as yet, no generally reliable method available such that the assembly of oligosaccharides is routine and straightforward.[4] Recently we described a procedure whereby disaccharides were assembled via glycosyl aldonic esters, Tebbe methylenylation, and subsequent cyclization.[5] Additionally we observed that disaccharides could be prepared via glycosyl aldonic acid thionoesters, reductive S-methylation, and cyclization.[6] These redox glycosidation procedures provide novel methods[7] for the elaboration of the glycosidic bond.

Sucrose is a target considerable historic importance[8] that is not straightforward to synthesize. It contains two synthetically challenging units: a cis α-glucopyranoside and a β-fructofuranoside residue, which contains a tertiary glycosyl oxygen. Herein we report the application of the titanium redox glycosidation methodology for the total synthesis of sucrose from D-glucose and D-arabinoic acid. The approach is noteworthy in consequence of the outstanding kinetic stereoselectivities achieved in the construction of both anomeric centers.



‡ Dedicated to Professor Leonard N. Owen on the occasion of his 76th birthday.

Scheme I[a]



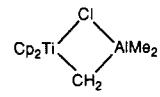
[a] Reagents: (i) nBuLi (1.6 M), THF, −78 °C; (ii) $TiCl_4$, TMEDA, Zn, CH_2Br_2, THF; (iii) Bu_4NF on silica, THF; I_2, KO^{t}Bu, THF; (iv) TEMPO, Bu_3SnH, PhH, $h\nu$; (v) Na, NH_3, THF; (vi) Ac_2O, pyridine; (vii) NaOMe, MeOH.

Sequential reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**2**)[9] with *n*-butyllithium and the thioester **3**[10] gave

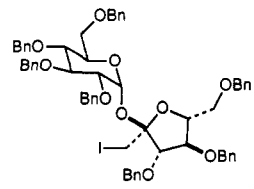
(1) Address correspondence to the author at the Department of Chemistry, Colorado State University, Fort Collins, CO 80523.
(2) Igarashi, K. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 243.
(3) For examples of recent developments in glycosidation chemistry, see: Mootoo, D. R.; Konradsson, P.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1989**, *111*, 8540. Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661. Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6656. Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212. Nicolaou, K. C.; Ladduwahetty, J. L. R.; Chuchulowski, A. *J. Am. Chem. Soc.* **1986**, *108*, 2466. Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189. Nicolaou, K. C.; Dolle, R. E.; Chucholowski, A.; Randall, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1153.
(4) In contrast to oligosaccharide chemistry, syntheses of oligonucleotides and polypeptides are now highly sophisticated. For examples, see: Letsinger, R. L. "Chemical Synthesis of Oligodeoxyribonucleotides; A Simplified Procedure" In *Genetic Engineering: Principles and Methods*; Setlow, J. K., Hollaender, A., Eds.; Plenum Press: New York, 1983; Vol. 5, pp 191–209. Merrifield, B. *Science* **1986**, *232*, 341.
(5) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Gasiecki, A. F.; Howell, A. R.; Russell, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 1392.

0022-3263/90/1955-5196$02.50/0

the α-glucopyranosyl ester 4[11] (Scheme I). This transesterification[12,13] proceeded with good α-stereoselectivity at −30 °C (α:β = 9:1) and superior selectivity at −78 °C *when only the α-anomer was produced* (α:β > 50:1). Much to our chagrin, attempts to convert the ester **4** into the vinyl ether **5** by methylenylation[5] using the Tebbe reagent **9** were unsuccessful. However methylenylation using the Nozaki–Takai protocol[14] readily afforded alkene **5**. Alkene **5** was desilylated with tetrabutylammonium fluoride on silica and the resultant alcohol cyclized by using iodine and base *in the presence of silica to provide only the β-D-fructofuranosyl system* **6**. This remarkable and fortuitous diastereoselectivity requires further comment. When the iodoetherification was carried out without silica present both **6** (36%) and **10** (34%) were formed. Additionally, in a blank experiment, **10** was not destroyed under the iodoetherification conditions in the presence of silica. It appears, therefore, that the silica kinetically biases the stereochemistry of cyclization. This effect of silica may be of use in other iodoetherification reactions.



9



10

Much to our disappointment the iodide **6** proved to be refractory toward S_N2 displacement by oxygen-centered nucleophiles even under forcing conditions. However radical-mediated substitution[15] gave the hydroxylamine **7**. Global deprotection via dissolving metal reduction gave sucrose, which was conveniently isolated as the octaacetate **8**.[16] Finally Zemplen methanolysis regenerated sucrose **1**.[17]

These results clearly demonstrate the validity of redox glycosidation for the highly stereoselective elaboration of sucrose. The application of the chemistry to more complex systems and mechanistic studies of the origin of stereocontrol are currently under investigation.

Acknowledgment. We thank the National Institutes of Health (Grant GM-40949) and G.D. Searle and Company for support of our research; the National Institutes of Health (Grants RR-02314 and RR-03245) for the purchase of a 400-MHz NMR spectrometer and a high resolution mass spectrometer used in these studies; FRD DSIR, Pretoria for financial support to B.C.B.B.; and Drs. Amy R. Howell and Mark A. Russell for preliminary studies on the preparation of **4**.

(6) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Howell, A. R.; Lee, A. L.; Russell, M. A. *J. Org. Chem.* **1989**, *54*, 2275.
(7) For a discussion of alternative nonclassical approaches to prepare glycosides, see: Briner, K.; Vasella, A. *Helv. Chim. Acta* **1989**, *72*, 1371 and references therein.
(8) For earlier studies on the synthesis of sucrose, see: Lemieux, R. U.; Huber, G. *J. Am. Chem. Soc.* **1953**, *75*, 4118. Tsuchida, H.; Komoto, M. *Agric. Biol. Chem.* **1963**, *29*, 239. Ness, R. K.; Fletcher, H. G., Jr. *Carbohydr. Res.* **1971**, *17*, 465. Fraser-Reid, B. *Int. Symp. Carbohydr. Chem. VIIth, Bratislava*, **1974**. Khan, R. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 235. Iley, D. E.; Fraser-Reid, B. *Can. J. Chem.* **1979**, *57*, 645.
(9) Commercially available from Sigma Chemical Co.
(10) Prepared from 2,3,5-tri-*O*-benzyl-D-arabinoic acid γ-lactone and used directly in the esterification, see: Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Dhanak, D.; Gasiecki, A. F.; Howell, A. R.; Lee, A. L.; Russell, M. A. *J. Org. Chem.* **1989**, *54*, 3321.
(11) All new compounds were fully authenticated by spectroscopic data and microanalyses or HRMS.
(12) This procedure is general for the preparation of α-D-glucopyranosyl esters. Barrett, A. G. M.; Bezuidenhoudt, B. C. B. *Heterocycles* **1989**, *28*, 209.
(13) For the preparation of the α-glucosyl ester from simple acyl chlorides and alkoxides, see: Pfeffer, P. E.; Rothman, E. S.; Moore, G. G. *J. Org. Chem.* **1976**, *41*, 2926.
(14) Okazoe, T.; Takai, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 4410 and references therein.
(15) Kinney, R. J.; Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 7902. Howell, A. R.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1990**, *2*, 103.
(16) The product was identical with authentic sucrose octaacetate (Aldrich) (TLC, mp, $[\alpha]_D$, IR, 400-MHz ^{1}H NMR, 101-MHz ^{13}C NMR, HRMS).
(17) The product was identical with authentic sucrose (TLC, mp $[\alpha]_D$, IR, 400-MHz ^{1}H NMR, 101-MHz ^{13}C NMR, HRMS).

$SnCl_4$ Chelation of an *N*-Acyloxazolidinone: An NMR Investigation[1]

Stephen Castellino

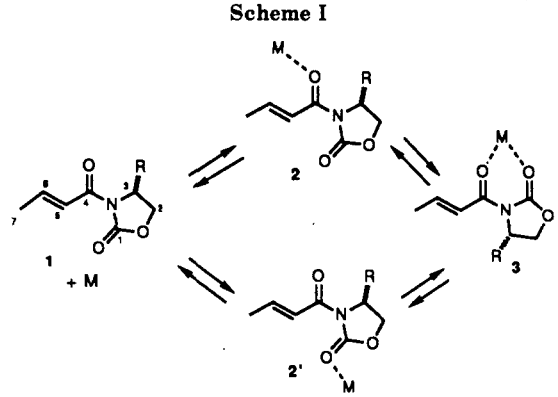
Department of Chemistry, North Dakota State University, Fargo, North Dakota 58105-5516

Received July 9, 1990

Summary: The $SnCl_4$ chelate of oxazolidinone, **1** (R = isopropyl), has been characterized by ^{119}Sn, ^{13}C, and ^{1}H NMR.

The *N*-acyloxazolidinones, **1**, pioneered by Evans as an asymmetric template, incorporate all the important design features necessary for efficient asymmetric synthesis.[2] The use of neutral Lewis acids to enhance reactivity and stereoselectivity in Diels–Alder additions between **1** and cyclopentadiene has also been examined by Evans.[2b] Our interests in the structure and reactivity of Lewis acid

Scheme I



(1) Presented at the 199th National Meeting of the American Chemical Society, Organic Division, paper 25, Boston, April 22, 1990.
(2) (a) Evans, D. A.; Clark, J. S.; Metternich, R.; Novack, V. J.; Sheppard, G. S. *J. Am. Chem. Soc.* **1990**, *112*, 866. (b) Evans, D. A.; Chapman, K. T.; Bisaka, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238. (c) Evans, D. A.; Chapman, K. T.; Hung, D. T.; Kawaguchi, A. T. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1184. (c) Evans, D. A. *Aldrichim. Acta* **1982**, *15*, 23 and references therein.

0022-3263/90/1955-5197$02.50/0