and M. Kottenhahn, Forschung Chemie-Organische und Biologische Chemie, Degussa AG, for a sample of L-*tert*-butylleucine.

Supplementary Material Available: Details for the synthesis of representative templates, procedures for carrying out the addition/cyclization/transfer reaction, and analysis of telomers 6 (5 pages). Ordering information is available on any current masthead page.

Neighboring Group Activation of Acetal Cleavage: A Novel Nonacidic Strategy for the Tandem Formation of Cyclic Ethers

Simone P. Elvey and David R. Mootoo*

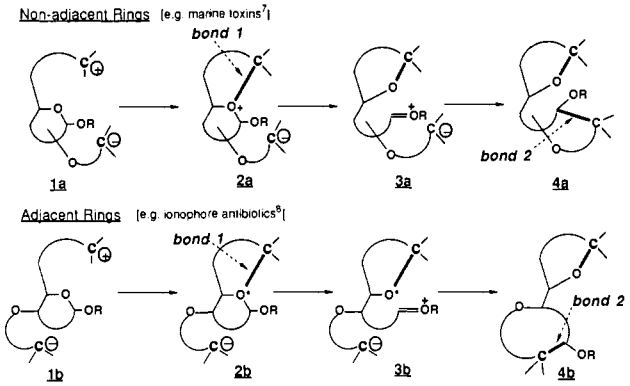
Department of Chemistry, Hunter College/CUNY
695 Park Avenue, New York, New York 10021

Received August 3, 1992

Synthetic approaches to complex polycyclic ethers invariably result in circuitous strategies in order to facilitate alcohol differentiation in polyol precursors. In this vein, carbohydrate-based approaches[1] have been popular because of the distinct reactivities of the hydroxy groups in monosaccharides.[2] Furthermore the cyclic acetal residue represents a masked hydroxy aldehyde, the elaboration of which may be strategically timed. With these considerations in mind, we envisaged a novel, tandem strategy for preparation of complex polyethers, which involves the sequencing of two different[3] ether-forming reactions on a monosaccharide template: (i) initial ether formation resulting from the attack of the ring oxygen on a remote electrophilic center, thereby leading to formation of an intermediate oxonium ion **2**, which undergoes cleavage of the internal C–O bond of the acetal to give the cyclic ether–oxocarbenium ion **3**,[4] followed by (ii) the intramolecular trapping of **3** by a carbon nucleophile[5,6] tethered to one of the hydroxy groups on the sugar. In this way adjacent and nonadjacent, bis-cyclic ether frameworks of varying ring sizes, related to important naturally occurring polyethers,[7,8] may be obtained by changing the location of the electrophile and nucleophile on different monosaccharide templates (Scheme I).

For the initial evaluation of the strategy, the alkenes **6** and **10** were prepared in three straightforward steps from the known carbohydrate building blocks **5**[9] and **9**[10] via selective formation

Scheme I



of the primary iodide,[11] followed by the Keck allyl radical coupling procedure[12] and O-alkylation of the remaining alcohol with 3-methoxybenzyl chloride or isoprenyl bromide (Scheme II).

Treatment of **6** and **10** with iodonium dicollidine perchlorate[4,13] (IDCP) in anhydrous dichloromethane under high-dilution conditions[14] (0.01 M), at room temperature, led within 10 and 45 min, respectively, to C1 epimeric pairs **7a** (60%) and **7b** (30%), each as a 6/5, cis/trans, THF (ring A) mixture, and **11** (93%), as a 5/3, cis/trans, ring A mixture. As expected from previous studies on 5-alkoxyalkenes, in neither case was THP formation observed in the initial halocyclization reaction.[15] Stereochemical assignments in the THF residues were made from comparison of ^{13}C chemical shifts in closely related compounds.[16] The structures of the cyclization products were verified, and the diastereomer composition for the THPs (ring B) was determined by conversion under zinc-mediated reductive elimination reaction conditions to the respective hydroxyalkenes, which were characterized as the acetate derivatives **8a/b** and **12**.

The ability to effect THP, in addition to THF, formation in the first stage of the reaction significantly increases the versatility of the methodology. This scenario requires an RO6 triggered reaction, and in order to test the feasibility of this plan, the homologous derivatives **13** and **16** were prepared from a three-step hydroboration–oxidation–methylenation sequence on the RO5 precursors, **6** and **10**. Application of the standard cyclization conditions led to bis-THP mixtures **14a/b** and **17** in 70 and 89% yields, after 16 h and 45 min, respectively. The stereochemistry of the initially formed THP in **17** was assignd by careful analysis of the ^1H NMR spectrum of the major isomer, and that for **14** was deduced from comparison of the ^{13}C NMR chemical shifts of the two compounds. Not surprisingly, the stereoselectivities in the formation of ring B for both RO5 and RO6 triggered reactions were similar. In particular, the reactions of the 1,2-*O*-isopropylidene substrates which afforded a single, ring B diastereomer are noteworthy. This result presumably reflects the stereochemical bias of nucleophilic addition to the intermediate cyclic oxocarbenium species.

These results indicate that the triggering RO5 and RO6 participation reactions were highly efficient in both the pyranoside

(1) For examples of carbohydrate-based approaches to polyethers, see the following. Lasalocid: (a) Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155. Calcimycin: (b) Nakahara, Y.; Beppu, K.; Ogawa, T. *Tetrahedron* **1986**, *42*, 6465. X-14574A: (c) Edwards, M. P.; Ley, S. V.; Lister, S. G.; Palmer, B. D.; Williams, D. J. *J. Org. Chem.* **1984**, *49*, 3503. Okadaic acid: (d) Isobe, M.; Ichikawa, Y.; Goto, T. *Tetrahedron Lett.* **1986**, *27*, 963.

(2) Haines, A. H. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 11.

(3) For an example of tandem THF formation involving the same repeating reaction, see: (a) Schultz, W. J.; Etter, M. C.; Pocius, A. V.; Smith, S. *J. Am. Chem. Soc.* **1980**, *102*, 7981. (b) Hoye, T. R.; Suhadolnik, J. C. *Tetrahedron* **1986**, *42*, 2855 and references cited therein.

(4) Mootoo, D. R.; Date, V.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 2662.

(5) For carbocyclization reactions of oxonium ions derived from the acid-promoted cleavage of acetals, see: (a) Blumenkopf, T. A.; Bratz, M.; Castaneda, A.; Look, G. C.; Overman, L. E.; Rodriguez, D.; Thompson, A. S. *J. Am. Chem. Soc.* **1990**, *112*, 4386. (b) Yamada, J.; Tetsuya, A.; Kadota, I.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 6066 and references cited therein.

(6) For a related study in the carbohydrate field involving intramolecular capture of cyclic oxonium ions derived from exocyclic C–O acetal bond cleavage, see: Martin, O. R.; Prahlada Rao, S.; Kurz, K. G.; El-Shenawy, H. A. *J. Am. Chem. Soc.* **1988**, *110*, 8698.

(7) For nonadjacent, fused polycyclic ethers, see: Faulkner, D. J. *Nat. Prod. Rep.* **1986**, *3*, 1; **1984**, *1*, 251.

(8) For adjacently linked polycyclic ethers, see: *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Westley, J. W., Ed.; Marcel Dekker: New York, 1983; Vols. 1 and 2.

(9) Stoffyn, A.; Stoffyn, P. *J. Org. Chem.* **1967**, *32*, 4001.

(10) Levine, P. A.; Raymond, A. L. *J. Biol. Chem.* **1933**, *102*, 317. No. 21 is commercially available from Pfanstiehl Laboratories, Inc.

(11) Garegg, P. J.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866.

(12) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079.

(13) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190.

(14) At higher concentrations, significant proportions of the aldehyde products were observed, presumably resulting from hydrolysis of the collidinium acetal which would have arisen from the intermolecular capture of the intermediate oxocarbenium ion by the collidine ligand in the reagent.

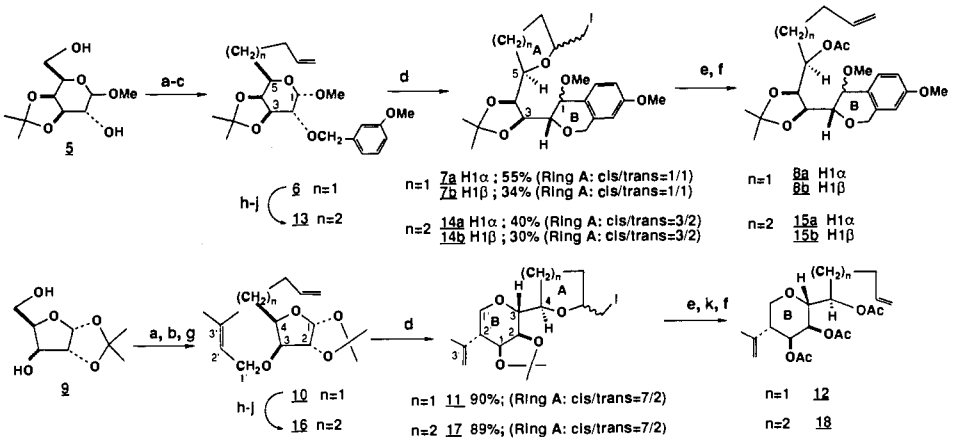
(15) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963. Ting, P. C.; Bartlett, P. A. *J. Am. Chem. Soc.* **1984**, *106*, 2668.

(16) The resonances for the methylene carbons of the cis THF were observed to be consistently upfield relative to those of the trans isomer in related compounds whose structures were verified by degradation to both diastereomers of 5-methyltetrahydrofuran-2-methanol.[17]

(17) Brown, H. C.; Lynch, G. T. *J. Org. Chem.* **1981**, *46*, 938.

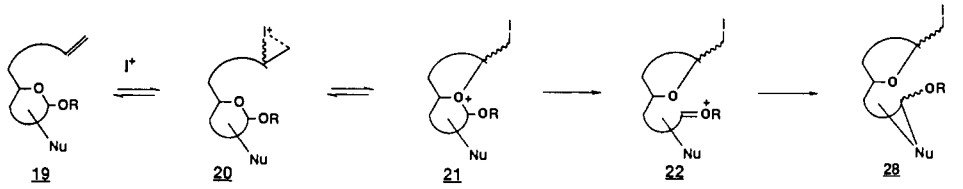
0002-7863/92/1514-9685$03.00/0

Scheme II[a]



[a] Reagents: (a) PhH, Ph_3P, I_2, imidazole; (b) allyltributyltin, AIBN, PhH, 80 °C; (c) NaH, 3-$MeOC_6H_4CH_2Cl$, Bu_4NI, DMF; (d) $I(coll)_2ClO_4$, CH_2Cl_2; (e) Zn, EtOH, reflux; (f) Ac_2O, DMAP, EtOAc; (g) $(Me)_2C{=}CHCH_2Br$, NaH, Bu_4NI, DMF; (h) 9-BBN, THF, then Na_2O_2; (i) Swern's oxidation; (j) $Ph_3P{=}CH_2$, THF; (k) MeOH, HCl.

Scheme III



and furanoside substrates. Since these test compounds are very sterically crowded and conformationally restricted, this reaction should be equally successful for simpler systems, where the transition state for this step is expected to be less highly strained. It should also be noted that products arising from direct electrophilic attack on the nucleophilic residues were not observed in any of these cases. Since these nucleophiles are very electron rich, electrophile–nucleophile compatibility problems are not anticipated for less electron rich nucleophiles.

The relative reactivities observed for the different substrates are interesting from a mechanistic standpoint. Since the intramolecular trapping of **3** is expected to be fast, the higher reactivities for the more strained furanoside compared to the pyranoside substrates in both RO5 (**10**, <10 min vs 6, ~45 min) and RO6 (**16**, ~45 min vs **13**, ~16 h) initiated reactions suggest that the slow step in the overall transformation **1** → **3** is the cleavage process (**2** → **3**), rather than the participation reaction (**1** → **2**). In view of this observation and the proven reversibility of oxonium ion formation in the related halocyclization reaction of alkoxyalkene derivatives,[15,18] a mechanism in which all steps leading to the formation of the bicyclic oxonium ion intermediate **21** are reversible, followed by a slow, irreversible fragmentation step, is postulated (Scheme III).

In summary, this methodology illustrates the way in which neighboring group participation mechanisms may be used to effect regiospecific cleavage of acetal bonds under mild, nonacidic, reaction conditions, leading to oxonium ions which may be then subjected to known chemistry. Specifically, by using monosaccharides as the acetal templates, highly substituted oxocarbenium ions are accessible, and their trapping by strategically located internal carbon nucleophiles constitutes a novel approach to bis-cyclic ether frameworks containing several stereogenic centers. Our current investigations are probing stereochemical aspects and also the use of other combinations of electrophilic and nucleophilic residues, particularly aimed at effecting efficient medium ring formation.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

Supplementary Material Available: Listing of experimental and spectral details for the cyclization precursors and products (4 pages). Ordering information is given on any current masthead page.

(18) Reitz, A. B.; Nortey, S. O.; Maryanoff, B. E.; Liotta, D.; Monahan, R., III *J. Org. Chem.* **1987**, *52*, 4191.

Synthesis and Characterization of an Aluminosilsesquioxane Framework That Violates Loewenstein's Rule

Frank J. Feher,* Keith J. Weller, and Joseph W. Ziller

Department of Chemistry, University of California Irvine, California 92717

Received August 10, 1992

According to "Loewenstein's rule"[1-4] the distribution of aluminum atoms in aluminosilicates is not entirely random:

(1) Loewenstein, W. *Am. Mineral.* **1954**, *39*, 92–96.

(2) For selected reviews with discussions of Si/Al ordering in aluminosilicates, see: (a) Fyfe, C. A.; Feng, T.; Grondey, H.; Kokotailo, G. T.; Gies, H. *Chem. Rev.* **1991**, *91*, 1525–43. (b) Klinowski, J. C. *Chem. Rev.* **1991**, *91*, 1459–79. (c) Engelhardt, G.; Michel, D. *High Resolution Solid-State NMR of Silicates and Zeolites*; Wiley: New York, 1987. (d) Thomas, J. M.; Catlow, C. R. A. *Prog. Inorg. Chem.* **1987**, *35*, 1–49. (e) Klinowski, J. *Prog. NMR Spectrosc.* **1984**, *16*, 237–309. (f) Liebau, F. *Structural Chemistry of Silicates*; Springer-Verlag: Heidelberg, 1985. (g) Barrer, R. M. *Hydrothermal Chemistry of Zeolites*; Academic Press: New York, 1982. (h) Barrer, R. M. *Zeolites and Clay Minerals as Sorbents and Molecular Sieves*; Academic Press: New York, 1978. (i) Breck, D. W. *Zeolite Molecular Sieves: Structure, Chemistry and Use*; Wiley: London, 1974.

(3) Other discussions of Si/Al ordering: (a) Earley, C. W. *Inorg. Chem.* **1992**, *31*, 1250–5. (b) Klinowski, J.; Ramdas, S.; Thomas, J. M.; Fyfe, C. A.; Hartman, J. S. *J. Chem. Soc., Faraday Trans. 2* **1982**, *78*, 1025–50. (c) Barron, P. F.; Slade, P.; Frost, R. L. *J. Phys. Chem.* **1985**, *89*, 3880–5. (d) Lipsicas, M.; Raythatha, R. H.; Pinnavaia, T. J.; Johnson, I. D.; Giese, R. F.; Costanzo, P. M.; Robert, J.-L. *Nature* **1984**, *309*, 604–6. (e) Melchior, M. T.; Vaughan, D. E. W.; Jacobson, A. J. *J. Am. Chem. Soc.* **1982**, *104*, 4859–64.

0002-7863/92/1514-9686$03.00/0