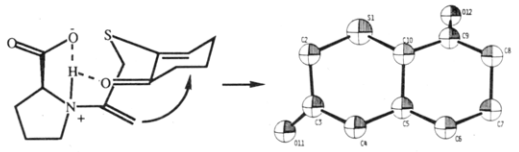
"90% ee" solution of **1** exhibited visible shoulders for many of its peaks in the Eu(hfc)$_3$ spectrum, we conclude that the optical purity of **1** is ≥95%. On the basis of the assumption that recrystallized **1** exhibiting a rotation of −311° is optically pure, an enantiomeric excess of 19% can be assigned for the cyclization conducted at room temperature, and a value of 28% for the reaction conducted at −15 °C. When **5** was cyclized by using unnatural D-proline, and the product recrystallized twice from THF, a compound identical in all respects with **1** but having a rotation of +307° (*c* 0.975, $CHCl_3$) was obtained.

The recrystallized compound (−)-**1** was then subjected to single-crystal X-ray structure analysis.[5] The diffraction data was refined to an unweighted residual value of 0.059 for the structure **1** with the absolute configuration shown below (C-5 and C-10 having the *S* configuration). A model

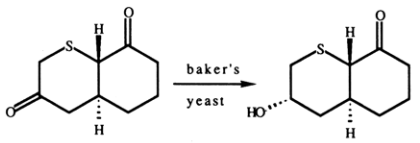


6 **1**

similar to that proposed by Agami[6] for the intramolecular aldol reaction of Hajos and Parrish[7] can be used to explain the stereoselectivity of this intramolecular Michael process. In our model (**6**), an enamine-like adduct between proline and the side-chain ketone is initially formed. Hydrogen bonds between the protonated nitrogen of the amino acid and the enone carbonyl then direct the Michael addition preferentially to one face of the carbocyclic ring.

Our next problem became the regioselective differentiation of the ketone groups of the bicyclic products. Initial attempts at monoreduction (one hydride equivalent of L-selectride, $LiAlH_4$, or $NaBH_4$) produced mixtures of ketols, diols, or starting material. The attempted monoketalization with ethylene glycol also showed poor selectivity. Discrimination between the two ketones was achieved by use of actively fermenting bakers' yeast.

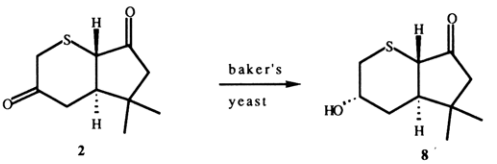
A broth of actively fermenting bakers' yeast was prepared according to the method of Ridley,[8] (−)-**1** was added,



1 **7**

and the suspension was stirred for 18 h. After silica gel chromatography the monoreduced product (−)-**7** was isolated as a crystalline solid (69%). Only the ketone contained in the thiopyran ring had been reduced. The structure and stereochemistry at the hydroxyl-bearing center were confirmed by single-crystal X-ray analysis.[9]

The corresponding *trans*-thiahydrindan **2** was also selectively reduced with bakers' yeast to give alcohol **8**, as a single diastereomer, in 59% yield.



2 **8**

From these studies one may conclude that either antipode of *trans*-diketothiadecalin **1** is available in optically pure form by an intramolecular Michael reaction catalyzed by D- or L-proline. The two chemically similar carbonyls of thiadecalin **1** can be differentiated by a stereoselective bakers' yeast reduction. Additionally, the diketothiahydrindans **2** and **3** can be produced in approximately a 1:1 ratio of cis and trans diastereomers. Thiahydrindan **2** can also be selectively reduced by bakers' yeast. Because of the versatility of sulfur-containing heterocycles, the compounds reported herein may prove to be useful optically active synthons in either ring expansion[10] or ring contraction[11] processes.

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Supplementary Material Available: X-ray crystallographic data for compounds **1** and **7** (15 pages). Ordering information is given on any current masthead page.

A. P. Kozikowski,* B. B. Mugrage
Department of Chemistry and Behavioral Neuroscience
1101 Chevron Science Center
University of Pittsburgh
Pittsburgh, Pennsylvania 15260
Received December 30, 1988

(5) X-ray structure data file for compound **1** are included in the supplemental data.

(6) (a) Agami, C.; Platzer, N.; Puchot, C.; Sevestre, H. *Tetrahedron* **1987**, *43*, 1091. (b) Agami, C.; Meynier, F.; Puchot, C.; Guilhem, J.; Pascard, C. *Tetrahedron* **1984**, *40*, 1031. (c) Agami, C.; Levisalles, J.; Puchot, C. *J. Chem. Soc., Chem. Commun.* **1985**, 441.

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(9) The X-ray structure data file for compound **7** are included in the supplemental data.

(10) (a) Vedejs, E.; Ried, J. G. *J. Am. Chem. Soc.* **1984**, *106*, 4617. (b) Vedejs, E.; Krafft, G. A. *Tetrahedron* **1982**, *38*, 2857.

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(12) All new compounds reported herein were characterized by IR, NMR, and high resolution mass spectral analysis.

Redox Glycosidation via Thionoester Intermediates

Summary: Several steroidal glycosides were prepared via esterification with aldonic acids, Lawesson thionation, lithium triethylborohydride mediated reductive methylation, and silver(I)-catalyzed ring closure.

Sir: The efficient construction of oligosaccharides remains a glittering prize for synthetic organic chemists. Although the Koenigs–Knorr reaction in its many disguises has been the subject of intense scrutiny[1–3] over nearly one century, experimentally simple approaches to iterative glycoside

(1) For reviews on glycosidation chemistry, see: Kennedy, J. F.; White, C. A. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. 5, p 755. Schaner, R. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 131.

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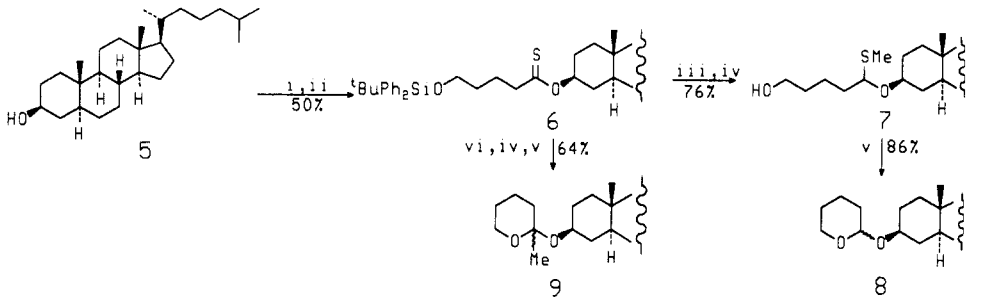
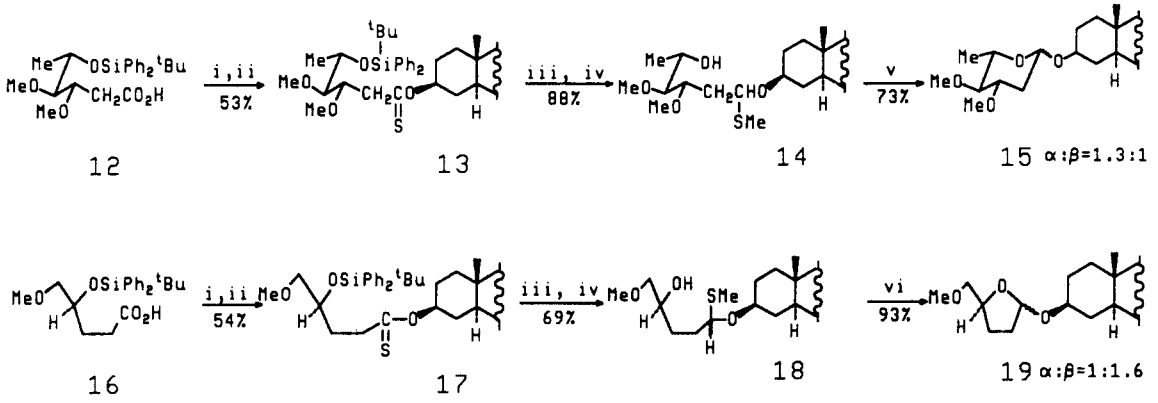
Scheme I[a]



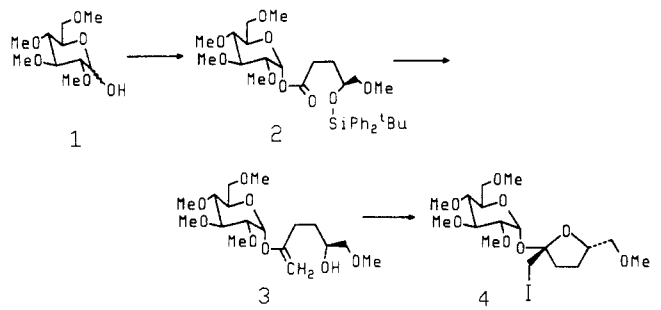
[a] Reagents: (i) acid **10**, DCC, 4-pyrrolidinopyridine, CH_2Cl_2; (ii) Lawesson's reagent (**11**), xylenes, reflux; (iii) $LiBHEt_3$, THF, −78 °C; MeI; (iv) Bu_4NF, THF; (v) $AgBF_4$, 2,4,6-collidine, CH_2Cl_2, 0 °C; (vi) MeLi (1.5 M in Et_2O), THF; MeI; −78 °C.

Scheme II[a]

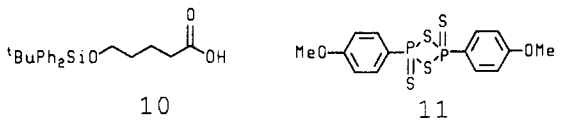


[a] Reagents: (i) DCC, 4-pyrrolidinopyridine, 5α-cholestan-3β-ol, CH_2Cl_2; (ii) Lawesson's reagent (**11**), xylenes, reflux; (iii) $LiBHEt_3$, THF, −78 °C; MeI; (iv) Bu_4NF, THF; (v) $AgBF_4$, 2,4,6-collidine, CH_2Cl_2, −10 °C; (vi) $AgBF_4$, 2,4,6-collidine, CH_2Cl_2, −20 °C.

construction remain elusive. Recently, we described a procedure whereby disaccharides were assembled via glycosyl aldonic esters, Tebbe methylenylation, and cyclization.[4] The process is exemplified by the transformation of **1** into **4** via **2** and **3**. Clearly this strategy, redox glycosidation, involves manipulation of a carboxylate carbon without cleavage of the masked glycosyl C–O bond. This methylenylation process, while of potential merit for ketose-based oligosaccharides,[5] is of no use in the elaboration of glycosides containing aldose units only. Although the hydride reduction of aldonic glycosyl esters may conceptually be employed in oligosaccharide synthesis, such an approach will be complicated by C–O fission of the intermediate hemiacetal. However, it is well-known that tetrahedral intermediates formed by the addition of nucleophiles to thionoesters are slow to fragment to expell the alkoxide substituent.[6] Thus, we sought to exploit the potential of thionoester chemistry for redox glycosidation.



Thionoester **6** was readily prepared from 5α-cholestan-3β-ol (**5**) via DCC mediated acylation[7] using **10**[8] followed by thionation using the Lawesson's reagent **11**.[9] Much to our delight, reductive methylation of **6** and deprotection proceeded without any C–O bond cleavage to produce the



(2) For recent examples of oligosaccharide syntheses, see: Lemieux, R. U. *Chem. Soc. Rev.* **1978**, *7*, 423. Spohr, U.; Lemieux, R. U. *Carbohydr. Res.* **1988**, *174*, 211. Paulsen, H.; Lorentzen, J. P. *Justus Liebigs Ann. Chem.* **1986**, 1586. Paulsen, H.; Tietz, H. *Carbohydr. Res.* **1985**, *144*, 205. Nakahara, Y.; Ogawa, T. *Tetrahedron Lett.* **1989**, *30*, 87. Nunomura, S.; Ogawa, T. *Ibid.* **1988**, *29*, 5681. Sato, S.; Ito, Y.; Ogawa, T. *Ibid.* **1988**, *29*, 5267.

(3) For recent examples of 2-deoxy glycoside syntheses including steroidal 2-deoxy glycosides, see: Jin, H.; Tsai, T. Y.; Wiesner, K. *Can. J. Chem.* **1983**, *61*, 2442. Treuss, R.; Schmidt, R. R. *Synthesis* **1988**, 694. Nicolaou, K. C.; Ladduwahetty, T.; Randall, J. L.; Chucholowski, A. *J. Am. Chem. Soc.* **1986**, *108*, 2466. Kahne, D.; Yang, D.; Lim, J. J.; Miller, R.; Pagnada, E. *Ibid.* **1988**, *110*, 8716. Jaurand, G.; Beau, J.-M.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1981**, 572. Crich, D.; Ritchie, T. J. *Ibid.* **1988**, 1461. Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1987**, *28*, 2723. Michalska, M.; Borowiecka, J. *J. Carbohydr. Chem.* **1983**, *2*, 99.

(4) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Gasiecki, A. F.; Howell, A. R.; Russell, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 1392.

(5) For example, see: *"Sialic Acids, Chemistry, Metabolism and Function"*; Schauer, R., Ed.; Springer-Verlag: New York, 1982.

(6) For the pioneering studies in the area, see: Narasimhan, L.; Sanitra, R.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1978**, 719. For a recent example, see: Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Veale, C. A.; Furst, G. T. *J. Am. Chem. Soc.* **1987**, *109*, 2504.

(7) (a) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, *19*, 4475. (b) Neiser, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522. (c) Zeigler, F. E.; Burger, G. D. *Synth. Commun.* **1979**, *9*, 539.

(8) (a) Barrett, A. G. M.; Dhanak, D. *Tetrahedron Lett.* **1987**, *28*, 3327. (b) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Dhanak, D.; Gasiecki, A. F.; Howell, A. R.; Lee, A. C.; Russell, M. A. *J. Org. Chem.*, in press.

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thioacetal **7**. This intermediate was readily cyclized using silver tetrafluoroborate to provide the model glycoside **8**.[10,11] Additionally, reaction of **6** with methyllithium and methyl iodide, deprotection, and cyclization gave the 2-methyl-2-tetrahydropyranyl derivative **9** (Scheme I). Although, these reactions give rise to trivial model glycosides they none the less demonstrate the possibility of a thio acyl approach to redox glycosidation.

The chemistry was extended to the preparation of the 2-deoxyrhamnopyranoside and 2,3-dideoxyribofuranoside derivatives **15** and **19** (Scheme II). Again, DCC-mediated acylation of 5α-cholestan-3β-ol with **12** and **16**,[8] Lawesson thionation, reductive methylation, and deprotection gave the thioacetals **14** and **18**. Both intermediates were obtained as mixtures of diastereoisomers [**14** (1.5:1), **18** (2:1)]. Subsequent cyclizations gave the pyranoside **15** (α:β = 1.3:1) and the furanoside **19** (α:β = 1:1.6).[12]

In a typical experimental procedure, $LiBEt_3H$ in THF (1.0 M; 0.48 mL) was added to **6** (90 mg) in dry THF (2 mL) under N_2 at −78 °C, and the mixture was stirred for 30 min. Dry MeI (0.2 mL) was added, and stirring was continued at 0 °C for another 15 min, before the mixture was diluted with Et_2O (30 mL) and extracted with water. The ether was dried ($MgSO_4$) and evaporated, and the crude product was isolated by chromatography on silica gel (R_f 0.5; hexanes–Et_2O, 99:1). The crude product was dissolved in THF (1 mL), $^nBu_4NF$ in THF (1.0 M; 0.5 mL) was added, and the mixture was stirred for 1.5 h. Evaporation and chromatography on silica gave **7** (48 mg, 76%). To a solution of **7** (18 mg) and 2,4,6-collidine (15 mg) in dry CH_2Cl_2 (0.5 mL) at 0 °C under N_2 was added $AgBF_4$ (16 mg), and the mixture was stirred for 2 h. Evaporation and chromatography gave **8** (14 mg, 86%).

These results clearly demonstrate that aldonic acid thionoesters are useful intermediates for redox glycosidation. The application of the chemistry to more complex systems including benzyl-protected saccharides and a mechanistic study of the thioacetal ring closure are currently under investigation.

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Anthony G. M. Barrett*
Barend C. B. Bezuidenhoudt, Amy R. Howell
Albert C. Lee

Department of Chemistry
Northwestern University
Evanston, Illinois 60208

Mark A. Russell*

G. D. Searle and Company
4901 Searle Parkway
Skokie, Illinois 60077

Received December 28, 1988

(10) All new compounds were fully authenticated by spectral data and microanalysis or high-resolution mass ion measurement.

(11) For an alternative preparation of **8** see: Kielczewski, M.; Paryzek, Z. *Zesz. Nauk. Uniw Imienia Adama Mickiewicza Poznaniu, Mat., Fiz, Chem.* **1967**, 131; *Chem. Abstr.* **1968**, *69*, 87305z.

(12) The anomeric stereochemistry for α-**15** and β-**15** were derived from the chemical shifts and coupling constants in the ^1H NMR spectra (δ 5.00, J = 3.2 Hz and δ 4.53, J = 9.8, 1.8 Hz, respectively) of the appropriate protons. The stereochemistries of α-**19** and β-**19** were assigned based on NOE experiments and by an X-ray crystallographic study of β-**19**.