NaH–oil dispersion. The resulting suspension was stirred at 23 °C for 2 h, at which point 8 mL of CH_2Cl_2 and 3 mL of 15% NH_4Cl solution were added. The aqueous layer was separated and extracted with CH_2Cl_2 (2×). The combined extracts were dried (Na_2SO_4), filtered, and concentrated to afford 33 mg of a pale yellow solid. This crude material was crystallized from CCl_4 to yield white crystals: 24 mg (95%); mp 128–129.5 °C; ^1H NMR ($CDCl_3$) δ 7.3 (m, 10 H, aromatic), 4.84 (m, 1 H, H_3), 4.53, 4.52 (AB, J_{AB} = 12 Hz, 2 H, benzylic), 4.13 (dd, J = 2.2, 4.4 Hz, 1 H, H_4), 4.05 (br m, 1 H, H_5), 3.73 (t, J = 5.9 Hz, 2 H, H_1), 2.1 (m, 2 H, H_2), 1.70 (d, J = 4 Hz, 1 H, OH), 1.15 (d, J = 6.6 Hz, 3 H, H_6); IR (CH_2Cl_2) 3200–3700 (OH), 3020, 2920, 1745, 1595, 1495 cm^{-1}; high-resolution mass spectrum, calcd for $C_{20}H_{23}NO_4$ m/e 341.162 71, found m/e 341.163 89.

Correlation of Urethane 7a (X = OH) with *xylo*-Triacetate 3. A solution of 19 mg (0.053 mmol) of **7a** (X = OH) in 5 mL of THF was treated with 6 mg (0.16 mmol) of $LiAlH_4$, and the resulting suspension was heated to reflux for 5 h. The reaction was quenched by the addition of 2 mL of H_2O which was followed by 2 mL of 1 N NaOH. The resulting precipitate was removed by filtration through a Celite pad and was washed with several portions of ether. The aqueous phase was separated from the filtrate and was extracted with CH_2Cl_2 (5×). The combined organic phases were concentrated in vacuo to afford 30 mg of crude material which was purified by flash chromatography (15 g of silica gel; EtOAc as the eluent) to yield 8 mg (63%) of the *xylo* triol. This material was acylated by the usual procedure (see preparation of **2**) to afford **3** in quantitative yield.

Correlation of 2 with 6b via *arabino*-Hexane-1,3,4,5-tetraol Tetraacetate (27). A solution of 20.3 mg (0.055 mmol) of **2** in 7 mL of reagent grade MeOH was hydrogenated over 10.1 mg of 5% Pd/C under an atmosphere of H_2. The reaction mixture was stirred for 4 h, filtered, and concentrated in vacuo. The crude product (8.8 mg, 65%) was purified by chromatography on a 0.5-mm silica gel plate with 3:1 ether–hexane as the eluent, giving 7.7 mg (55%) of the desired primary alcohol. This material was then acylated according to the conditions described previously (Ac_2O, pyridine, Et_2O) to give 7.5 mg (78%) of **27** following chromatographic purification (0.25-mm silica gel preparative plate, 2:1 ether–hexane).

Tetraacetate **27** prepared in this manner was identical with a sample prepared from carbonate **6b**. Thus, 37 mg (0.21 mmol) of **6b** was treated with NaOMe in MeOH, and the crude triol was acylated with acetic anhydride and pyridine in Et_2O according to the procedure described previously for the synthesis of **2** from **5a** and **6a**. The triacetate (35 mg) was isolated in 60% overall yield by chromatography (0.5-mm silica gel plate, 3:1 ether–hexane). A portion of this product (26 mg, 0.096 mmol) was dissolved in 20 mL of MeOH and cooled to −78 °C. A stream of dry O_3/O_2 was passed through the solution until it developed a deep blue color. The solution was then purged with O_2 to remove excess O_3 and was quenched with 3 mL of Me_2S. The reaction mixture was then allowed to warm to room temperature and was stirred for 19 h. To this mixture was then added 10.8 mg (3 equiv) of $NaBH_4$. The solution was stirred for 1 h and then was diluted with 11 mL of 0.1 N HCl. The mixture was extracted with CH_2Cl_2 (4×), and the extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was chromatographed (0.5-mm silica gel plate, 3:1 ether–hexane) to give 19.8 mg of crude primary alcohol. This intermediate was acylated as described above to give **27**: 14.5 mg (45%); ^1H NMR ($CDCl_3$) δ 5.3 (dt, J = 3.4, 6.4 Hz, 1 H, H_3), 5.1 (dd, J = 7.5, 3.4 Hz, 1 H, H_4), 4.95 (dt, J = 7.5, 6.4 Hz, 1 H, H_5), 4.05 (t, J = 6.4 Hz, 2 H, H_1), 2.11 (s, 3 H, acetate), 2.03 (s, 3 H, acetate), 2.02 (s, 3 H, acetate), 2.00 (s, 3 H, acetate), 1.84 (m, 2 H, H_2), 1.17 (d, J = 6.4 Hz, 3 H, H_6); IR (CH_2Cl_2) 2960, 1740, 1368, 1228, 1042, 677 cm^{-1}; mass spectrum, m/e 303 ($M^+ - CH_3$).

Correlation of 3 with 28 via *xylo*-Hexane-1,3,4,5-tetraol Tetraacetate (29). *Xylo* triacetate **3** and *xylo* triol **28**[3b] were transformed into *xylo* tetraacetate **29** by using procedures exactly analogous to those described above for the synthesis of *arabino* tetraacetate **27**. Data for **29**: ^1H NMR ($CDCl_3$) δ 5.24 (td, J = 8.0, 4.6 Hz, 1 H, H_3), 5.10 (m, 2 H, H_5 and H_4), 4.07 (t, J = 6.3 Hz, 2 H, H_1), 2.12 (s, 3 H, acetate), 2.09 (s, 3 H, acetate), 2.06 (s, 3 H, acetate), 2.05 (s, 3 H, acetate), 1.88 (td, J = 6.3, 8.0 Hz, 2 H, H_2), 1.24 (d, J = 6.0 Hz, 3 H, H_6); IR (CH_2Cl_2) 2920, 1732, 1424, 1327, 1230 cm^{-1}; mass spectrum, m/e 303 ($M^+ - CH_3$).

Acknowledgment. This research has been supported by grants from the National Cancer Institute (Grant No. CA-29847 and Training Grant No. T32-CA-09258). We are grateful to Dr. C. Costello for measurement of high-resolution mass spectra and to the MIT Undergraduate Research Opportunities Program for partial support of M.D.

Total Synthesis of Carbohydrates. 3. Efficient, Enantioselective Syntheses of 2,6-Dideoxyhexoses

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Received April 5, 1983

Highly diastereoselective syntheses of five 2,6-dideoxyhexoses are described. The syntheses of (+)-olivose (**1**), (+)-digitoxose (**3**), (+)-oliose (**4**) and (+)-cymarose (**5**) are short (four to seven steps), relatively efficient (14–22%), and enantioselective. These syntheses feature the kinetic resolution–enantioselective epoxidation of racemic allylic alcohols **13** and **17** and the highly regioselective ring-opening reactions of erythro epoxy alcohols (+)-**14**, (−)-**14**, and (+)-**18**. Syntheses of racemic **1** and boivinose (**2**) are also described.

Considerable effort has been devoted to the synthesis of carbohydrates from noncarbohydrate precursors in recent years.[3] Rare monosaccharides are important structural components of numerous antibiotics,[4] and functionalized monosaccharides continue to be of interest as intermediates in natural products synthesis.[5] In the preceding paper[6a] we outlined a general strategy for the syn-

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(2) NCI Trainee (Grant No. T32-CA-09258).

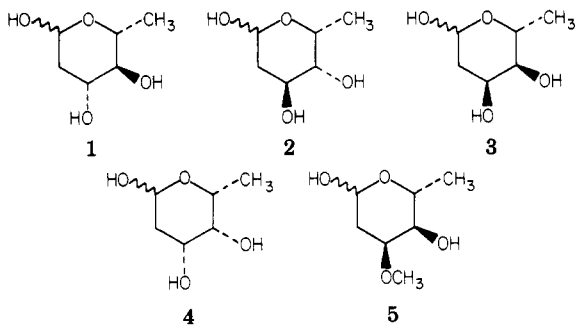
(3) For leading references, see the literature cited in footnote 3 of the preceding paper.[6a]

(4) (a) Horton, D.; Wander, J. D. In "The Carbohydrates", 2nd ed.; Academic Press: New York, 1980, Vol. 1B, p 643. (b) Williams, N. R.; Wander, J. D. *Ibid.*, p 761. (c) Butterworth, R. F.; Hanessian, S. *Adv. Carbohydr. Chem. Biochem.* **1971**, *26*, 279.

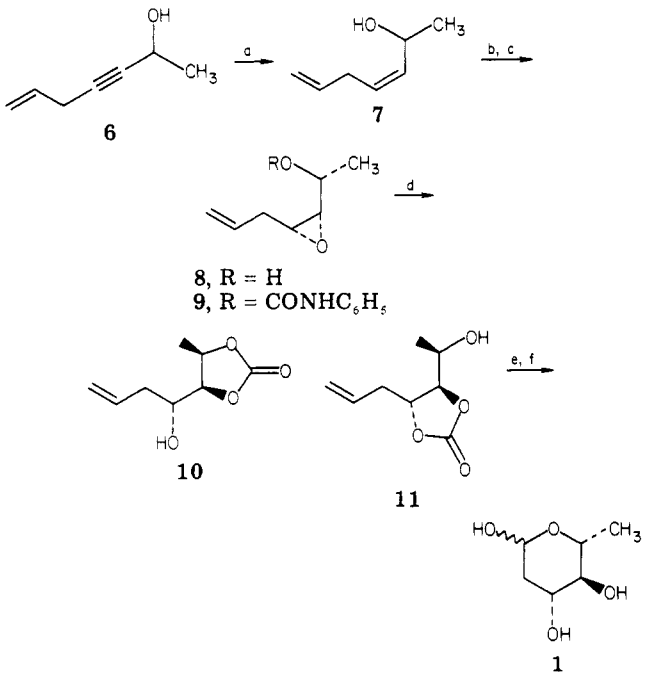
(5) (a) Fraser-Reid, B.; Anderson, R. C. *Prog. Chem. Org. Nat. Prod.* **1980**, *39*, 1. Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159.

0022-3263/83/1948-5093$01.50/0

Chart I



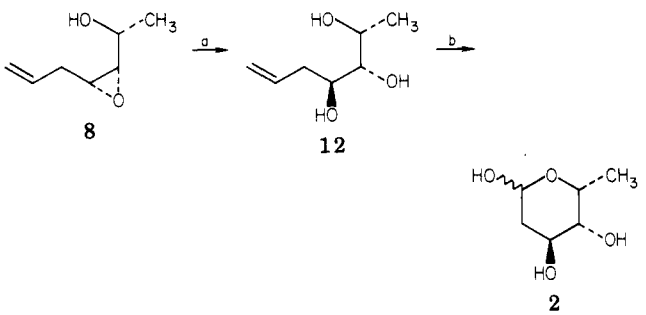
Scheme I[a]



[a] (a) excess Zn-Cu, CH_3OH, 120 °C, sealed tube (67–73%); (b) TBHP (1.1 equiv), $Ti(O\text{-}i\text{-}Pr)_4$ (1.0 equiv), CH_2Cl_2, −20 °C (80%); (c) C_6H_5NCO, pyridine, 23 °C (89%); (d) (i) $BF_3{\cdot}Et_2O$, Et_2O, −20 °C; (ii) 1 N H_2SO_4 workup (89%); (e) $NaOCH_3$, CH_3OH, 23 °C, 24 h (98%); (f) O_3, CH_3OH, −20 °C; Me_2S workup (85%).

thesis of the 2,3,4-triol system which occurs in a wide variety of polyhydroxylated natural products. We describe herein the application of this plan to the synthesis of five monosaccharides:[6b] 2,6-dideoxy-D-*arabino*-hexose (**1**, D-olivose),[7] 2,6-dideoxy-*xylo*-hexose (**2**, boivinose),[7f,i,8] 2,6-dideoxy-D-*ribo*-hexose (**3**, D-digitoxose),[7c,f,i,9] 2,6-dideoxy-D-*lyxo*-hexose (**4**, D-oliose),[7f,i,9a,10] and 2,6-dideoxy-3-*O*-methyl-D-*ribo*-hexose (**5**, D-cymarose)[7j,9e,11] (Chart I). The syntheses of (+)-**1**, (+)-**3**, (+)-**4**, and (+)-**5** range in length from four to seven steps and, generally, are shorter than classical syntheses which originate from the parent hexoses. Boivinose (**2**), however, was synthesized only as the racemate. The methods illustrated by these syntheses should be applicable to other problems in organic synthesis.[12]

Scheme II[a]



[a] (a) 20%, $HClO_4$, THF, 23 °C (65%); (b) O_3, CH_3OH, −20 °C; Me_2S workup (90%).

Results and Discussion

Syntheses of Racemic Olivose (1) and Boivinose (2). Our first synthesis of **1** (Scheme I) originated from propargyl alcohol **6**, which was prepared by treatment of 3-butyn-2-ol with excess allyl chloride and catalytic CuCl in aqueous methanol maintained between pH 7.5 and 8.5 (95% yield).[13] Reduction of **6** with Zn–Cu couple in methanol (sealed tube, 120 °C) afforded **7**, uncontaminated with the trans isomer or overreduced materials, in 67–73% yield.[14] Attempts to reduce **6** to **7** by use of H_2 and Lindlar catalyst resulted in partial (ca. 30%) saturation of the vinyl group. Epoxidation of **7** with *tert*-butyl hydroperoxide (TBHP) and titanium isopropoxide in CH_2Cl_2 at −20 °C afforded **8** with high threo selectivity (>19:1).[15] This intermediate was then transformed to phenylurethane **9** by treatment with phenyl isocyanate in pyridine. The overall yield of **9** from **7** was 70%. The solvolytic epoxide opening was best accomplished by treatment of **9** with $BF_3{\cdot}Et_2O$ in Et_2O at −20 °C, which, following hydrolysis of the intermediate iminocarbonate, afforded a 20:1 mixture of **10** and **11** (89% yield). Isomer **11** was the major product when this reaction was performed with $BF_3{\cdot}Et_2O$ in CH_2Cl_2 (95% yield).[6] Deacylation of such mixtures was accomplished by using $NaOCH_3$ in CH_3OH. The resulting racemic *arabino* triol was then transformed to deoxy-*arabino*-hexose **1** by ozonolysis in 80–85% overall yield from **10**/**11**.

Epoxide **8** also served as an intermediate in a synthesis of racemic boivinose (**2**; Scheme II). Thus, hydrolysis of **8** with 20% aqueous $HClO_4$ in THF afforded *xylo* triol **12** in 65% yield.[16] None of the isomeric α-opened *arabino*

(6) (a) Roush, W. R.; Brown, R. J.; DiMare, M. *J. Org. Chem.*, preceding paper in this issue. (b) Portions of this work were published in a preliminary communication: Roush, W. R.; Brown, R. J. *J. Org. Chem.* **1982**, *47*, 1371.

(7) (a) Durette, P. L. *Synthesis* **1980**, 1037. (b) Staněk, J., Jr.; Marek, M.; Jarý, J. *J. Carbohydr. Res.* **1978**, *64*, 315; (c) Haga, M.; Chonan, M.; Tejima, S. *Ibid.* **1971**, *16*, 486. (d) Blindenbacher, F.; Reichstein, T. *Helv. Chim. Acta* **1948**, *31*, 2061. (e) Vischer, E.; Reichstein, T. *Ibid.* **1944**, *27*, 1332. (f) Fronza, G.; Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G.; Zirotti, C. *Tetrahedron Lett.* **1982**, *23*, 4143 (L series); (g) Sztaricskai, F.; Pelyvas, I.; Bognar, R. *Ibid.* **1975**, 1111 (L series). (h) Iselin, B.; Reichstein, T. *Helv. Chim. Acta* **1944**, *27*, 1146 (L series). (i) Chmielewski, M. *Tetrahedron* **1979**, *35*, 2067 (racemic). (j) Yasuda, S.; Matsumoto, T. *Tetrahedron Lett.* **1969**, 4393 (racemic).

(8) (a) Bolliger, H. R.; Reichstein, T. *Helv. Chim. Acta* **1953**, *36*, 302. (b) Meyer, A. S.; Reichstein, T. *ibid.* **1946**, *29*, 139 (L series).

(9) (a) Cheung, T. M.; Horton, D.; Weckerle, W. *Carbohydr. Res.* **1977**, *58*, 139. (b) Bolliger, H. R.; Ulrich, P. *Helv. Chim. Acta* **1952**, *35*, 93. (c) Gut, M.; Prins, D. A. *Ibid.* **1947**, *30*, 1223. (d) Iselin, B.; Reichstein, T. *Ibid.* **1944**, *27*, 1203. (e) Brimacombe, J. S.; Hanna, R.; Saeed, M. S.; Tucker, L. C. N. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2583 (L series).

(10) (a) Brimacombe, J. S.; Portsmouth, D. *Carbohydr. Res.* **1965**, *1*, 128. (b) Brimacombe, J. S.; Portsmouth, D.; Stacey, M. *J. Chem. Soc.* **1964**, 5614. (c) Garegg, P. J.; Norberg, T. *Acta Chem. Scand., Ser. B.* **1975**, *B29*, 507. (d) Iselin, B.; Reichstein, T. *Helv. Chim. Acta* **1944**, *27*, 1200.

(11) (a) Bolliger, H. R.; Ulrich, P. *Helv. Chim. Acta* **1952**, *35*, 93. (b) Prins, D. A. *Ibid.* **1946**, *29*, 378.

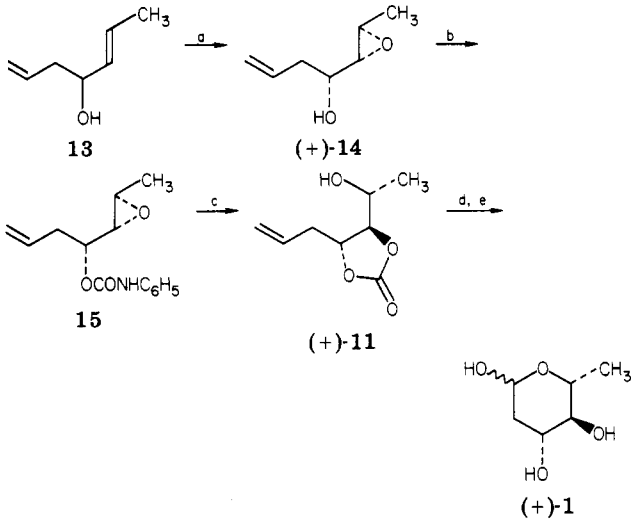
(12) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2.

(13) Kurtz, P. *Justus Liebigs Ann. Chem.* **1962**, *658*, 6.

(14) (a) Clarke, A. J.; Crombie, L. *Chem. Ind. (London)* **1957**, 143. (b) Crombie, L.; Jenkins, P. A.; Roblin, J. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1099. (c) Bergman, R. G. *J. Am. Chem. Soc.* **1969**, *91*, 7405.

(15) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

Scheme III[a]



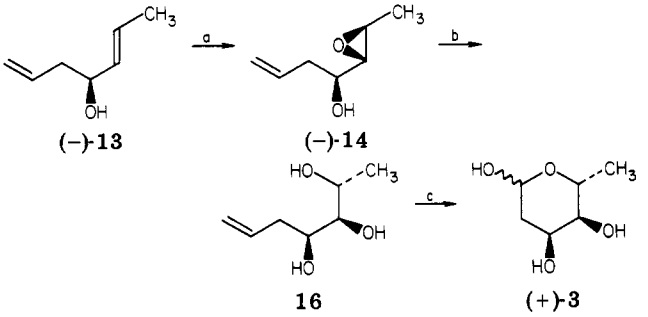
[a] (a) $Ti(O\text{-}i\text{-}Pr)_4$ (1.0 equiv), (−)-DIPT (1.5 equiv), TBHP (0.4 equiv), CH_2Cl_2, −20 °C; 27–33% of (+)-14 and 33–38% of (−)-13 were obtained; (b) C_6H_5NCO, pyridine, 23 °C, 71%; (c) Et_2AlCl, Et_2O, −20 °C; 1 N H_2SO_4 workup, 93–95%; (d) $NaOCH_3$, CH_3OH, 23 °C, 24 h, 98%; (e) O_3, CH_3OH, −20 °C; Me_2S workup, 85%.

triol was detected in this reaction mixture. Ozonolysis of **12** completed this five-step synthesis of racemic **2** (90% yield).

Enantioselective Syntheses of Olivose (1) and Digitoxose (3). We originally planned to synthesize optically active **1** by adopting modifications of the route summarized in Scheme I by which optically active **6** would be prepared by an enantioselective reduction of the corresponding propargyl ketone.[17] This approach, however, has been obviated by the development of the asymmetric epoxidation reaction by Sharpless and co-workers.[15,18] In particular, the kinetic resolution–enantioselective epoxidation procedure[15] appeared to offer a convenient route to chiral secondary epoxy allylic alcohols. It is important to note, however, that in order to synthesize a specific epoxy alcohol in good yield and with high optical purity by using this procedure, it is necessary that the relative rate ratio for epoxidation of the two allylic alcohol enantiomers be large (maximizes efficiency of the resolution) and that the epoxidation step be highly diastereoselective. Secondary *Z* allylic alcohols are not suitable intermediates on the basis of these criteria.[15] Consequently, we selected *E* allylic alcohol **13**[19] for use in the synthesis of (+)-**1** (Scheme III).

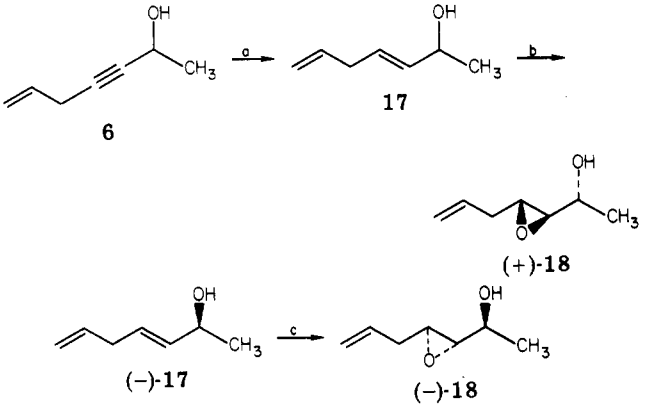
Treatment of racemic **13** with 1.0 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 1.5 equiv of (−)-diisopropyl tartrate ((−)-DIPT), and 0.4 equiv of TBHP in CH_2Cl_2 at −20 °C afforded, after chromatography and distillation of the individual fractions, erythro epoxide (+)-**14** (27–33% yield; 67–76% based on

Scheme IV[a]



[a] (a) 0.2 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 0.37 equiv of (+)-DET, 0.8 equiv of TBHP, CH_2Cl_2, −20 °C, 75%; (b) 3:1 Me_2SO–1 N H_2SO_4, 23 °C, 89% (c) O_3, CH_3OH, −20 °C (Me_2S workup), 79%.

Scheme V[a]



[a] (a) $LiAlH_4$, THF, reflux, 4 h, 82–84%; (b) $Ti(O\text{-}i\text{-}Pr)_4$ (0.13 equiv), (−)-DIPT (0.2 equiv), TBHP (0.45 equiv), CH_2Cl_2, −20 °C; 40% of (+)-18 and 39% of (−)-17 were obtained; (c) $Ti(O\text{-}i\text{-}Pr)_4$ (0.13 equiv), (+)-DIPT (0.21 equiv), TBHP (0.8 equiv), CH_2Cl_2, −20 °C, 76%.

TBHP), kinetically resolved (−)-**13** (33–38% yield; 72% ee), and recovered (−)-DIPT. The optical purity of (+)-**14** was greater than 95% ee as determined by Mosher ester analysis.[20] Crystalline urethane **15** (mp 57–57.5 °C) was prepared from (+)-**14** in 71% yield and was transformed subsequently to carbonate (+)-**11** (93–95%) by treatment with Et_2AlCl in Et_2O at −20 °C. Less than 3% of the isomeric *ribo* δ-carbonate, resulting from attack of the urethane carbonyl oxygen at the epoxide β-position, was observed under these conditions.[6a] Carbonate (+)-**11** was then converted to (+)-**1** by using the two-step sequence developed in the synthesis of racemic **1**. The optically pure sugar so obtained was identical in all respects with an authentic sample prepared from D-glucose.[7a,b] The overall yield of **1** was 14–17% for this six-step synthesis from crotonaldehyde.

Allylic alcohol **13** also served as a precursor of (+)-digitoxose (**3**; Scheme IV). Thus, treatment of kinetically resolved (−)-**13** (72% ee), the enantiomer not used in the synthesis of (+)-olivose (Scheme III), with 0.2 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 0.37 equiv of (+)-diethyl tartrate ((+)-DET), and 0.8 equiv of TBHP in CH_2Cl_2 at −20 °C afforded erythro epoxide (−)-**14** (92% ee) in 75% yield. Epoxide (−)-**14** (>95% ee) was also prepared directly from racemic **13** by using (+)-DIPT as the chiral auxiliary (37% yield).[21]

(16) For a review of the regioselectivity of hydrolytic epoxide openings, see: Buchanan, J. G.; Sable, H. Z. *Sel. Org. Transform.* **1972**, *2*, 1.

(17) (a) Brinkmeyer, R. S.; Kapoor, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 8339. (b) Cohen, N.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1980**, *45*, 582. (c) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 867. (d) Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1982**, *47*, 1606. (e) Brown, H. C.; Jadhav, P. K.; Desai, M. C. *Ibid.* **1982**, *47*, 4583. (f) Vigneron, J. P.; Bloy, V. *Tetrahedron Lett.* **1980**, *21*, 1735. (g) Nishizawa, M.; Yamada, M.; Noyori, R. *Ibid.* **1981**, *21*, 247.

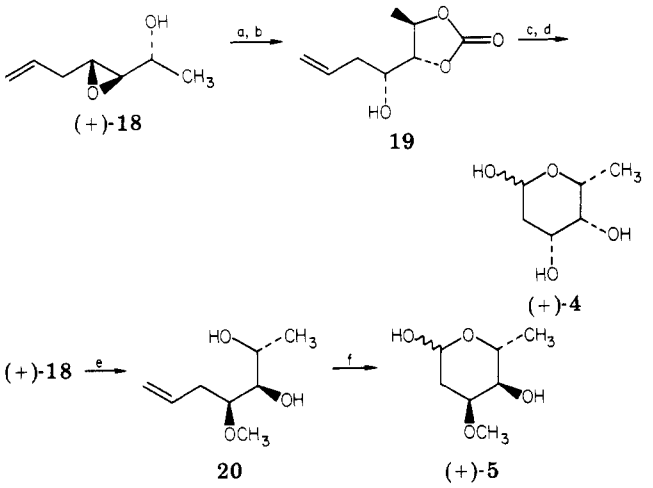
(18) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5975. (b) Rossiter, B. E.; Katsuki, T.; Sharpless, K.B. *Ibid.* **1981**, *103*, 464.

(19) Henze, H. R.; Allen, B. B.; Leslie, W. B. *J. Org. Chem.* **1942**, *7*, 326. For a related procedure see also: Hwa, J. C. H., Sims, H. "Organic Synthesis"; Wiley: New York, 1973; Collect. Vol. V, p 608.

(20) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(21) We thank Susannah M. Hagadorn for performing this experiment.

Scheme VI[a]



[a] (a) C_6H_5NCO, pyridine, 78%; (b) Et_2AlCl, Et_2O, −20 °C; 1 N H_2SO_4 workup, 99%; (c) NaOMe, MeOH, 95%; (d) O_3, MeOH, −20 °C; Me_2S workup, 82%; (e) CH_3OH, *p*-TsOH, reflux, 84%; (f) O_3, MeOH, −20 °C; Me_2S workup, 87%.

Hydrolysis of (−)-**14** with 3:1 Me_2SO–1 N H_2SO_4 afforded *ribo* triol **16** (89%), ozonolysis of which afforded (+)-digitoxose in 79% yield. The synthetic sugar, which was identical in all respects with a commercial sample, was thus obtained in 22% overall yield for the four-step synthesis from crotonaldehyde.

Enantioselective Syntheses of Oliose (4) and Cymarose (5). Each of these sugars was synthesized from *erythro*-epoxy alcohol (+)-**18**, which was prepared as outlined in Scheme V. Reduction of propargyl alcohol **6** with $LiAlH_4$ afforded **17** (82–84% yield) which was epoxidized by using 0.13 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 0.20 equiv of (−)-DIPT, and 0.45 equiv of TBHP in CH_2Cl_2 at −20 °C.[15] In this manner (+)-**18** and kinetically resolved (−)-**17** were obtained in 40% and 39% yields, respectively. The optical purity of each was 90% ee as determined by Mosher ester analysis. The Mosher ester prepared from (−)-**18** (92% ee) was most useful in confirming the optical purity of the (+)-enantiomer.

This synthesis of (+)-**18** illustrates the use of catalytic[18a] $Ti(O\text{-}i\text{-}Pr)_4$ in the kinetic resolution–enantioselective epoxidation procedure. We have observed that the isolated yields of epoxide and kinetically resolved (recovered) allylic alcohol are generally greater when the catalytic system is employed. This tendency is probably related to the difficulty of separating the tartrate ester from the product mixtures. For example, epoxidation of **17** with 1.0 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 1.5 equiv of (−)-DIPT, and 0.4 equiv of TBHP afforded 30% of (+)-**18** and 37% of (−)-**17**, whereas under the catalytic conditions described in Scheme V these compounds were obtained in 40% and 39% yields, respectively. Similar results were obtained with the epoxidations of **13** (see Experimental Section). One disadvantage to the catalytic epoxidation system, however, is that the optical purity of the epoxide produced is sometimes lower than when a stoichiometric reagent is employed.[15,18] This problem, though, is easily rectified by crystallization of intermediates, such as the derived phenyl urethanes, at a later stage of the synthesis.

Conversion of (+)-**18** to the crystalline phenylurethane (mp 55.5–56.0 °C) followed by treatment with Et_2AlCl in Et_2O afforded carbonate **19** in high yield (Scheme VI).[6a] This intermediate was transformed to D-oliose ((+)-**4**) by transesterification with NaOMe in MeOH and ozonolysis. The overall yield of **4** was 18–20% for this seven-step synthesis.

D-Cymarose ((+)-**5**) was synthesized by solvolysis of (+)-**18** in methanol followed by ozonolysis of the resulting diol **20** (Scheme VI). This methanolysis reaction was highly regioselective and afforded **20** in up to 84% yield. The overall yield of (+)-cymarose was 17–20% for the present five-step sequence.

Concluding Remarks

The use of acetylenic or olefinic starting materials in syntheses of carbohydrates has received much attention in previous decades.[22] Only with the development of highly enantioselective[15,18] and diastereoselective epoxidation procedures,[23] together with efficient methods for regioselective epoxide opening, however, has it become possible to synthesize monosaccharides stereoselectively by this strategy.[3,6,24] The present syntheses of (+)-**1**, (+)-**3**, (+)-**4**, and (+)-**5** are short (four to seven steps), relatively efficient (14–22%),[25] and easily adaptable to the preparation of the (−) enantiomers (by selection of the appropriate tartrate enantiomer for the epoxidation step). These methods and procedures will undoubtedly find application in other areas of natural product synthesis where triols or triol derivatives of the *arabino*, *ribo*, or *lyxo* configuration have, until now, been prepared or approached from carbohydrate chiral pool precursors.[5] We note, however, that *xylo* triol derivatives (e.g., boivinose, **2**) are not well suited for preparation by this method. The stereochemistry of this sugar requires the intermediacy of an epoxide prepared from a chiral secondary *Z* allylic alcohol,[6a] but, as we noted previously, *Z* allylic alcohols are not ideal substrates for the enantioselective epoxidation–kinetic resolution procedure.[26] For this reason we have described herein only a synthesis of racemic boivinose. Optically active *xylo* triol derivatives, therefore, might be better prepared by an alternative enantioselective synthesis[17] or by classical resolution of synthetic intermediates (e.g., resolution of **6** as a precursor of **12** or **2**).[27]

Epoxy alcohol intermediates such as **8** or (+)-**18** may also prove useful in synthesis of amino sugars. Thus, for example, treatment of (+)-**18** with benzyl amine in the presence of catalytic phenol at 145 °C afforded amino diol **21** (eq 1) in 91% yield.[28] Alternatively, azide **22** was obtained in 78% yield when (+)-**18** was treated with NaN_3

(22) For reviews, see: (a) Jones, J. K. N.; Szarek, W. A. In "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley-Interscience: New York, 1973; Vol. I, p 1. (b) Zamojski, A.; Banaszek, A.; Grynkiewicz, G. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 1.

(23) (a) Mihelich, E. D.; Daniels, K.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 769. (b) Mihelich, E. D. *Tetrahedron Lett.* **1979**, 4729. (c) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Ibid.* **1979**, 4733. (d) Tomioka, H.; Suzuki, T.; Oshima, K.; Nozaki, H. *Ibid.* **1982**, *23*, 3387. (e) Narula, A. S. *Ibid.* **1982**, *23*, 5579.

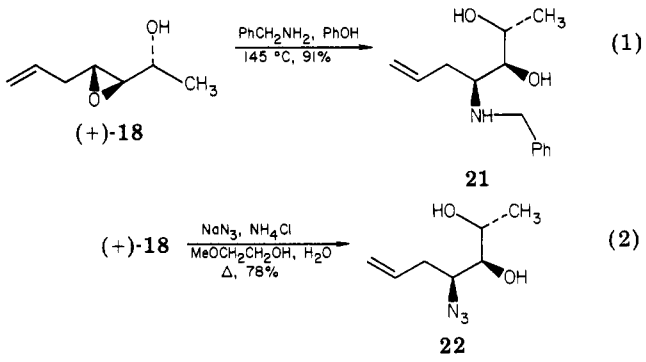
(24) For a brief review, see: Hoppe, D. *Nachr. Chem., Tech. Lab.* **1982**, *30*, 935.

(25) The maximum theoretical yield for these syntheses is 40–45%, the amount of TBHP employed in the kinetic resolution–enantioselective epoxidation step.

(26) The relative rate ratio for epoxidation of the two enantiomers of a *Z* allylic alcohol is ≤20, and product formation from the fast reacting enantiomer is not, in general, highly diastereoselective.[15] Although a two-step sequence involving a Sharpless kinetic resolution followed by an epoxidation reaction with an achiral reagent is feasible, one should note that for a relative ratio of 20 the kinetic resolution must proceed to 65–70% conversion in order to prepare >95% ee *Z* allylic alcohol. Moreover, the efficiency of the resolution also appears to decrease as a function of the steric environment of the *Z* allylic alcohol.

(27) (a) Pirkle, W. H.; Boeder, C. W. *J. Org. Chem.* **1978**, *43*, 1950. (b) Pirkle, W. H.; Hauske, J. R. *Ibid.* **1977**, *42*, 2781. (c) Pirkle, W. H.; Hauske, J. R. *Ibid.* **1977**, *42*, 1839.

(28) (a) Shtacher, G.; Rubinstein, R.; Somani, P. *J. Med. Chem.* **1978**, *21*, 678. (b) Colclough, T.; Cunneen, J. I.; Moore, C. G. *Tetrahedron* **1961**, *15*, 187. (c) See also: Tucker, H. *J. Org. Chem.* **1979**, *44*, 2943.



in the presence of NH_4Cl[29] (eq 2). Diols **21** and **22** were the only isomers detected in these transformations. The cyclohexyl ketals of the *lyxo*, *xylo*, and *arabino* isomers of **22** have previously been transformed to 2,3,6-trideoxy-3-aminohexose derivatives.[30] Additional studies on the synthesis of amino sugars will be reported in due course.

Experimental Section

For general experimental details please refer to the Experimental Section of the preceding paper.[6a]

Hept-1-en-4-yn-6-ol (6).[13] A 1000-mL three-necked flask equipped with a magnetic stirrer, two dropping funnels, and a reflux condenser was charged under a nitrogen atmosphere with a solution of 2.0 g (20 mmol) of CuCl dissolved in 320 mL of saturated aqueous NaCl containing 2 mL of concentrated HCl. 3-Butyn-2-ol (19.7 g, 22 mL, 280 mmol) was then added. From one dropping funnel was added dropwise 40% NaOH solution until the pH, monitored by a pH meter, reached 8.5. The resulting suspension containing a bright yellow-orange precipitate was heated to 70–75 °C, and then a solution of allyl chloride (40 mL, 490 mmol) in 40 mL of methanol was added dropwise over a 1.5 h interval. Sufficient NaOH solution was added periodically to maintain the pH between 7.5 and 8.5. After the addition was complete and the uptake of NaOH ceased, an aliquot was worked up (as below) and analyzed by ^1H NMR which indicated that the reaction was ca. 50% complete. A fresh portion of CuCl (1.0 g) was added, followed by additional allyl chloride (approximately 40 mL) and NaOH until the orange precipitate no longer formed upon further addition of base. The resulting dark orange solution was cooled and acidified to pH 1 by the addition of concentrated HCl. The organic phase was separated and the aqueous layer extracted with CH_2Cl_2 (4 × 75 mL). The combined organic extracts were dried (Na_2SO_4), filtered, concentrated, and distilled to give 28.2 g of pure **6**, bp 114–115 °C (80–85 mmHg) [lit.[13] bp 73 °C (15 mmHg)]. Redistillation of the forerun resulted in the recovery of an additional 1.1 g of **6**: total yield 29.3 g (95%); ^1H NMR ($CDCl_3$) δ 5.7–5.9 (m, 1 H, H_2), 5.3 (dd, J = 1.8, 16.9 Hz, 1 H, H_{1E}), 5.1 (dd, J = 1.8, 10.3 Hz, 1 H, H_{1Z}), 4.55 (br q, J = 6 Hz, 1 H, H_6), 3.0 (dd, J = 1.5, 5.1 Hz, 2 H, H_3), 2.07 (br, 1 H, OH), 1.45 (d, J = 6.6 Hz, 3 H, H_7); IR (neat) 3100–3700 (OH), 3080, 2980, 2240, 1640, 1150, 1070 cm^{-1}; mass spectrum, m/e 110 (parent ion).

(*Z*)-Hepta-1,4-dien-6-ol (7). A solution of 1.28 g (11.6 mmol) of **6** in 15 mL of absolute MeOH was transferred to a resealable tube under N_2 and treated with the zinc–copper couple[14] prepared from 370 mg of $CuSO_4$ and 5.54 g of Zn dust in 11 mL of H_2O. The reaction vessel was purged with Ar, sealed, and heated to 120 °C for 11 h. Analysis of the reaction mixture by GC [10-ft, 5% SE-30 column, 130–140 °C temperature program (10 °C/min ramp rate); t_R 0.9 (**7**), 1.1 min (**6**)] indicated that the reduction had proceeded to approximately 50% conversion. A second batch of Zn/Cu couple (as above) was added, and the reaction mixture was heated at 100–120 °C until all **6** had been consumed (40 h in this run). The spent reagent was then removed by filtration. The filtrate was diluted with 50 mL of CH_2Cl_2 and washed with 10 mL of saturated aqueous NH_4Cl, which was back-extracted with CH_2Cl_2 (2×). The combined extracts were dried (Na_2SO_4), filtered, concentrated, and distilled (Kugelrohr, 100 °C, 80 mmHg) to afford pure **7**: 958 mg (73%); ^1H NMR ($CDCl_3$) δ 5.7–5.9 (m, 1 H, H_2), 5.4–5.6 (m, 2 H, H_4 and H_5), 5.0–5.1 (m, 2 H, H_1) 4.63 (dq, J = 7.4, 6.2 Hz, 1 H, H_6) 2.85 (br t, 2 H, J = 6 Hz, H_3), 1.83 (br, 1 H, OH), 1.24 (d, J = 6.2 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 136.5, 135.0, 127.6, 115.1, 63.7, 31.7, 23.8; IR (neat) 3100–3700 (OH), 3080, 3010, 1635, 910 cm^{-1}; mass spectrum, m/e 112 (parent ion); high-resolution mass spectrum, calcd for $C_7H_{12}O$ m/e 112.088 81, found m/e 112.090 31.

***lyxo*-4,5-Epoxyhept-1-en-6-ol (8).** To a solution of 1.15 g (10 mmol) of **7** in 100 mL of dry CH_2Cl_2 under argon cooled in a dry ice/CCl_4 bath were added 3 mL (10 mmol) of titanium tetraisopropoxide and 2.2 mL of 5 M *tert*-butyl hydroperoxide (11 mmol) in CH_2Cl_2.[31] This mixture was stirred for 30 min and then placed in a −20 °C freezer for 18 h. The solution was diluted with 100 mL of acetone and 3 mL of H_2O. The resulting mixture was stirred at room temperature for 1 h and then the resulting precipitate was removed by filtration through a pad of Celite. The solvents were removed in vacuo and the crude product distilled (Kugelrohr, 100 °C, 25 mmHg) to give pure **8**: 1.02 g (80%); ^1H NMR ($CDCl_3$) δ 5.8 (m, 1 H, H_2), 5.1 (m, 2 H, H_1), 3.65 (br quintet, J = 6.3 Hz, 1 H, H_6), 3.10 (dt, J = 4.4, 8.8 Hz, 1 H, H_4), 2.90 (dd, J = 4.4, 8.3 Hz, 1 H, H_5), 2.59 (br, 1 H, OH) 2.3 (m, 2 H, H_3), 1.22 (d, J = 6.3 Hz, H_7); ^{13}C NMR ($CDCl_3$) δ 133.4, 117.3, 66.0, 61.5, 56.0, 32.6, 19.5; IR (neat) 3100–3700, 3080, 2972, 1640, 990, 915, 820 cm^{-1}; mass spectrum, m/e 128 (parent ion). Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.43; H, 9.36.

***arabino*-Hept-1-ene-4,5,6-triol.** Conversion of epoxy alcohol **8** to urethane **9** (89%; mp 55.5–56 °C (EtOAc/hexane)) and then to carbonates **10** and/or **11** (89–95% yield) was performed as described in the preceding paper.[6a]

A solution of 346 mg (2.01 mmol) of a mixture of racemic carbonates **10** and **11** (combined from a number of solvolytic ring openings of **9**) in 20 mL of 0.2 N NaOMe in MeOH was stirred at room temperature for 5 h. The solution was then passed through a column containing 14 cm^3 (wet volume) of Dowex 50W-X8 H^+ ion-exchange resin which had been pretreated with methanol. A total of 100 mL of MeOH was used to ensure that the triol had eluted from the column. Concentration of the eluate in vacuo afforded 288 mg (98%) of triol as a pale yellow oil: ^1H NMR ($CDCl_3$, D_2O exchanged) δ 5.82 (m, 1 H, H_2), 5.2 (m, 2 H, H_1), 3.95 (m, 2 H, H_4 and H_6), 3.34 (dd, J = 2.6, 4.0 Hz, 1 H, H_5), 2.4 (m, 2 H, H_3), 1.26 (d, J = 6.6 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 134.5, 117.8, 75.4, 70.1, 69.5, 38.0, 18.8; IR (CH_2Cl_2) 3100–3700 (br, OH), 3040, 2920, 1640, 1245, 1060, 990, 915 cm^{-1}; mass spectrum, m/e 146 (parent ion); high-resolution mass spectrum calcd for $C_7H_{12}O_2$ ($M^+ - H_2O$) m/e 128.083 43, found m/e 128.083 72.

By an analogous procedure, 667 mg of (+)-**11** (prepared as described subsequently) was transformed to 560 mg (99% yield) of (+)-*arabino* triol ($[\alpha]^{22}_D$ +5.5° (*c* 4.7, CH_2Cl_2)), the spectroscopic properties of which are identical in all respects with the data summarized above for the racemic material.

2,6-Dideoxy-D-*arabino*-hexose (Olivose, (+)-1). A solution of 560 mg (3.84 mmol) of the (+)-*arabino* triol described above in 50 mL of absolute methanol was cooled to −20 °C (dry ice, CCl_4) and treated with a stream of O_3 in O_2 until the triol was consumed (TLC analysis). The solution was purged with O_2 to remove excess O_3 before 5 mL of Me_2S was added. The solution was warmed to room temperature and stirred for 18 h. All volatile components were then removed in vacuo to give 711 mg of crude sugar. This material was chromatographed (130 g of silica gel, 10% EtOH in CH_2Cl_2) to give 485 mg (85%) of pure (+)-**1**, $[\alpha]^{22}_D$ +19.4° (*c* 2.9, H_2O, equilibrated). An authentic sample of (+)-**1** prepared from D-glucose[7a,b] had $[\alpha]^{25}_D$ +19.5° (*c* 1.6, H_2O, equilibrated). Rotations of +20° and −18.2° have been reported for the D and L enantiomers, respectively:[4c] ^1H NMR (D_2O; 60:40 mixture of

(29) (a) Guthrie, R. D.; Murphy, D. *J. Chem. Soc.* **1963**, 5288. (b) Behrens, C. H.; Masamune, S.; Sharpless, K. B., unpublished results. We thank Professor Sharpless for suggesting these reaction conditions. (c) The yield of **22** was much lower (30%) when the Prinzbach conditions were employed (NaN_3, $MgCl_2$, MeOH, reflux): Schwesinger, R.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 989.

(30) Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G. *Tetrahedron Lett.* **1981**, *22*, 4017.

(31) TBHP solutions were prepared and titrated according to the procedure of: Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.

α- and β-pyranose structures) β anomer δ 4.67 (dd, J = 2.2, 9.7 Hz, 1 H, H_1), 3.42 (ddd, J = 5.3, 9.3, 11.9 Hz, 1 H, H_3), 3.17 (dq, J = 9.3, 6.2 Hz, 1 H, H_5), 2.81 (t, J = 9.3 Hz, 1 H, H_4), 2.01 (ddd, J = 2.2, 5.3, 11.9 Hz, 1 H, H_{2e}), 1.26 (dt, J = 11.9, 9.7 Hz, 1 H, H_{2a}), 1.04 (d, J = 6.2 Hz, 3 H, H_6); α anomer 5.07 (br d, J = 4 Hz, 1 H, H_1), 3.6 (m, 2 H, H_3 and H_5), 2.86 (t, J = 9.3 Hz, 1 H, H_4), 1.88 (ddd, J = 1.3, 5.3, 13.3 Hz, 1 H, H_{2e}), 1.46 (ddd, J = 4.0, 11.9, 13.3 Hz, 1 H, H_{2a}), 1.02 (d, J = 6.2 Hz, 3 H, H_6); ^{13}C NMR (D_2O) β anomer δ 93.9, 77.0, 68.5 (2 C), 40.6, 17.8; α anomer δ 91.8, 77.7, 72.5, 71.0, 38.4, 17.8.

Racemic **1**, prepared by ozonolysis of the racemic triol in 89% yield, crystallized when stored at 0 °C for several months; mp 125.5–127 °C. We have been unsuccessful in all attempts to induce the optically active sugar to crystallize. The spectroscopic properties and TLC behavior of the racemic sugar were identical with the data summarized above for the optically pure sugar.

***xylo*-1-Heptene-4,5,6-triol (12).** A solution of 178 mg (1.39 mmol) of epoxy alcohol **8** in 4 mL of THF was treated with 1 mL of 20% aqueous perchloric acid at room temperature. All of **8** was consumed after 18 h. The solution was then diluted with 20 mL of methanol and passed through a column containing approximately 10 cm^3 (wet volume) of Dowex 1-X8 ion-exchange resin, which had been pretreated with 5 N NaOH. The resin was washed with 100 mL of methanol to ensure complete elution of the product. All volatile components of the mixture were removed in vacuo to give 244 mg of a thick syrup. This material was chromatographed on 110 g of silica gel with 4:1 EtOAc–hexane as the eluent (25-mL fractions). Fractions 8–30 were combined and evaporated to yield pure **12**: 133 mg (65%); ^{1}H NMR ($CDCl_3$–D_2O exchange) δ 5.65–5.8 (m, 1 H, H_2), 5.0–5.1 (m, 2 H, H_1), 3.8 (dq, J = 4.4, 6.6 Hz, 1 H, H_6), 3.63 (dt, J = 2.2, 6.6 Hz, 1 H, H_4), 3.14 (dd, J = 2.2, 4.4 Hz, 1 H, H_5), 2.27 (br t, J = 6.6 Hz, 2 H, H_3), 1.14 (d, J = 6.6 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 134.6, 117.8, 75.9, 72.5, 69.5, 38.7, 19.8; IR (CH_2Cl_2) 3100–3700 (br, OH), 3080, 2920, 1640, 1380, 1060, 995, 920 cm^{-1}; mass spectrum, m/e 146 (parent ion).

2,6-Dideoxy-*xylo*-hexose (Racemic Boivinose, 2). A solution of 175 mg (1.2 mmol) of racemic **12** in 5 mL of methanol was ozonized by using the procedure described for preparation of (+)-**1**. The crude product was purified by flash chromatography (40 g silica gel, 20% EtOH in CH_2Cl_2) to give 160 mg (90%) of racemic boivinose as a syrup: R_f 0.2 (in EtOAc); ^{1}H NMR (Me_2SO-d_6, D_2O exchanged) ~80% β-pyranose anomer (the remainder being a mixture of the α and the furanose anomers) δ 4.75 (dd, J = 2.5, 9.8 Hz, 1 H, H_1), 3.74 (br q, J = 6.2 Hz, 1 H, H_5), 3.7 (m, 1 H, H_3), 2.95 (m, fine coupling, 1 H, H_4), 1.58 (ddd, J = 3.1, 9.8, 13.2 Hz, 1 H, H_{2a}), 1.42 (dt, J = 13.2, 3.1 Hz, 1 H, H_{2e}), 1.02 (d, J = 6.2 Hz, 3 H, H_6); ^{13}C NMR (D_2O) δ 92.6, 69.9 (2 C), 69.3, 34.7, 16.7. These ^{13}C NMR data are in good agreement with literature values for racemic boivinose.[7i]

(*E*)-1,5-Heptadien-4-ol (13).[19] A 2-L three-necked flask equipped with a mechanical stirrer, reflux condenser, and two 500-mL dropping funnels was charged with 50 g (2 mol) of Mg turnings, 130 mL of anhydrous ether, and a few I_2 crystals. A solution of 58 mL (670 mmol) of allyl bromide in 650 mL of anhydrous Et_2O was transferred to the addition funnels. A small portion of this solution was added to the reaction vessel to initiate the Grignard formation. The remainder of the allyl bromide solution was added dropwise at a rate such that gentle reflux was maintained. The solution was heated to reflux for an additional hour. The heating bath was removed, and then 40 mL (490 mmol) of distilled crotonaldehyde was added dropwise over 1 h. After being stirred for an additional hour, the reaction mixture was poured through a glass wool plug into 800 mL of ice–water. Magnesium salts were dissolved by the careful addition of 160 mL of 9 N H_2SO_4. The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (4 × 100 mL). The combined organic extracts were dried (Na_2SO_4), filtered, concentrated in vacuo, and distilled to give **13**: 47.6 g; bp 71 °C (25 mmHg). An additional 3.0 g of product was obtained by redistillation of the forerun, bringing the total yield of **13** to 50.6 g (92%): ^{1}H NMR ($CDCl_3$) δ 5.6–5.9 (m, 2 H, H_6 and H_2), 5.49 (dd, J = 7, 16.4 Hz, 1 H, H_3), 5.1 (m, 2 H, H_7), 4.08 (q, J = 6.5 Hz, H_4), 2.2 (m, 2 H, H_5), 1.71 (br, 1 H, OH), 1.67 (d, J = 6.3 Hz, H_1); IR (neat) 3100–3600 (br, OH), 3080, 2910, 1675, 1640, 1440, 1030, 960, 910 cm^{-1}; mass spectrum, m/e 112 (parent ion).

(+)-*lyxo*-5,6-Epoxyhept-1-en-4-ol ((+)-14): Kinetic Resolution of Racemic 13. A solution of 30 mL (100 mmol) of titanium tetraisopropoxide and 31.5 mL (150 mmol) of D-(–)-diisopropyl tartrate in 1 L of dry CH_2Cl_2 was cooled to –20 °C (CCl_4, dry ice bath) under argon. The resulting pale yellow solution was stirred for 15 min, and then 11.2 g (100 mmol) of racemic **13** and 8.5 mL of 4.96 M *tert*-butyl hydroperoxide in CH_2Cl_2 (42 mmol)[31] were added. The reaction vessel was then stored in a –20 °C freezer for 18 h, after which the reaction mixture was poured into a prechilled (–20 °C) mixture of 30 mL of H_2O in 1000 mL of acetone. The resulting precipitate was removed by filtration through a pad of Celite, and the solvents were evaporated in vacuo to yield 46.5 g of crude product. This mixture was separated by chromatography using a Waters Prep 500 liquid chromatograph (four equal-sized portions, one silica gel cartridge, 3:7 EtOAc–hexane as the eluent). Allylic alcohol (–)-**13** elutes first (t_R = 12 min, 100 mL/min), followed by DIPT (t_R = 18 min) and epoxide (+)-**14** (t_R = 23 min). Similar fractions were combined, evaporated, and distilled (Kugelrohr) to give 3.38 g (30%) of (–)-**13** [bp 68 °C (25 mmHg); $[\alpha]^{25}_D$ –8.9° (c 9.4, CH_2Cl_2),[32] 72% ee by Mosher ester analysis], 3.50 g (27%) of (+)-**14** [bp 90 °C (25 mmHg); $[\alpha]^{23}_D$ +3.0° (c 7.2, CH_2Cl_2); >95% ee by Mosher ester analysis],[33] and 25 g of recovered DIPT (71%).

A simplified workup procedure was developed for the kinetic resolution of racemic **13** to produce (–)-**14**.[21] (The two-phase hydrolytic procedure recommended by Sharpless[18a] for removal of the tartrate ester or a modification using NaOH in saturated NaCl solution leads to partial (ca. 10%) epoxide rearrangement of **14**.) Thus, 9.95 g (88.8 mmol) of **13** was epoxidized by using 8.9 mmol of Ti(O-*i*-Pr)$_4$, 14.3 mmol of L-(+)-diisopropyl tartrate, and 37.3 mmol of TBHP (0.42 equiv; 6.3 mL of 5.93 M TBHP solution)[31] in 500 mL of CH_2Cl_2 (–20 °C, 43 h). Ether (200 mL) and 5–10 mL of saturated Na_2SO_4 solution were then added at 25 °C, and the mixture was stirred vigorously for 2 h at room temperature. The white precipitate was removed by filtration through a pad of Celite, and the solvents were evaporated in vacuo. The residue was dissolved in 50 mL of ether, washed with saturated Na_2SO_3–NaCl solution, dried ($MgSO_4$), filtered, and again concentrated in vacuo. The crude product was distilled through a short-path apparatus (25 mmHg, 90–110 °C) to give 7.8 g of a mixture of (+)-**13** and (–)-**14**, contaminated with a small amount of (+)-DIPT. The pot residue (ca. 10 mL) was Kugelrohr distilled (115 °C, 25 mmHg) to give 2.9 g of essentially pure (–)-**14**, leaving (+)-DIPT in the distillation pot. The mixed fraction was separated by chromatography (CH_2Cl_2–Et_2O, 16:1, 500 g of silica gel). Similar fractions were combined (the above distilled epoxide was combined with the chromatographically homogeneous fractions), concentrated, and redistilled (Kugelrohr) to give 4.17 g (37%) of (–)-**14** [$[\alpha]^{20}_D$ –2.8° (c 4.9, CH_2Cl_2), >95% ee by Mosher ester analysis] and 4.58 g (46%) of kinetically resolved (+)-**13** [$[\alpha]^{20}_D$ +10.3° (c 3.1, CH_2Cl_2), $[\alpha]^{20}_D$ +12.3° (c 2.8, $CHCl_3$), 68% ee by Mosher ester analysis].[32]

Data for (+)-**14**: ^{1}H NMR ($CDCl_3$) δ 5.8 (m, 1 H, H_2), 5.1 (m, 2 H, H_1), 3.7 (br m, 1 H, H_4), 3.0 (dq, J = 2.5, 5.5 Hz, 1 H, H_6), 2.66 (dd, J = 2.5, 4.4 Hz, 1 H, H_5), 2.44 (br, 1 H, OH), 2.3 (m, 2 H, H_3), 1.24 (d, J = 5.5 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 133.5, 117.0, 68.5, 61.1, 51.4, 37.9, 16.7; IR (neat) 3100–3700 (br, OH), 3070, 2990, 1640, 1430, 1375, 995, 910 cm^{-1}; mass spectrum, m/e 128 (parent ion). Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.37; H, 9.65.

General Procedure for Mosher Ester Analyses.[20] A solution of 10–20 mg of the alcohol in 50 μL of CCl_4 and 10–20 μL

(32) Duveen, D.; Kenyon, J. *Bull. Soc. Chim. Fr.* **1938**, *5*, 704 (series 5). These authors report $[\alpha]^{19}_D$ –18.3° (c 5.0, $CHCl_3$) for resolved (–)-**13**.

(33) The kinetic resolution–epoxidation sequence is highly erythro selective (≥19:1). Erythro epoxides **14** and **18** isolated by chromatography as described in the experimental procedures were usually contaminated with up to 5% of the respective threo epoxide isomers. These mixtures can be separated by chromatography using 10:1 CH_2Cl_2–Et_2O as the eluent [R_f *erythro*-**14**, 0.36; R_f *threo*-**14**, 0.29; R_f *erythro*-**18**, 0.43; R_f *threo*-**18**, 0.35 (two developments in each case)]. All optical rotations and Mosher ester analyses were performed on isomerically pure epoxides obtained in this manner. This separation was not routinely performed, however, for preparative scale experiments. In the *arabino*- and *lyxo*-hexose series this separation was accomplished by crystallization at the stage of the phenylurethanes.

(34) Colonge, J.; Varagnat, A. *Bull. Soc. Chim. Fr.* **1964**, 561.

of pyridine was treated with 1.2 equiv of the acid chloride of (−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid ((−)-MTPA-Cl). After 12 h at room temperature the reaction was quenched with 1 mL of water and the mixture extracted with 20 mL of ether. The organic extract was washed with dilute HCl and saturated $NaHCO_3$. The sample was dried (Na_2SO_4), filtered, and concentrated in vacuo. The NMR analysis was performed on the crude esters. Diastereomeric ratios were calculated from integrations of signals in the 250- or 270-MHz ^1H spectra. Tabulated below are the relevant signals of the MTPA esters used in the diastereomer analyses.

MTPA ester of racemic 13: ^1H NMR ($CDCl_3$) δ 3.53 (s, with fine coupling, OCH_3), 1.70 (dd, J = 1.5, 6.3 Hz, 3 H, H_7, for the S isomer), 1.66 (dd, J = 1.5, 6.3 H, 3 H, H_7, for the R isomer); the signal for H_4 of both isomers is obscured by H_1 in the vinyl group.

MTPA ester of (+)-14: δ 4.96 (ddd, J = 4.4, 5.9, 7.9 Hz, 1 H, H_4), 3.53 (s, with fine coupling, OCH_3), 2.93 (d of q, J = 2.0, 5.4 Hz, 1 H, H_6), 2.64 (dd, J = 2.0, 6 Hz, 1 H, H_5), 1.21 (d, J = 5.4 Hz, 3 H, H_7).

MTPA ester of (−)-14: δ 3.52 (s, with fine coupling, OCH_3), 3.00 (d of q, J = 2.9, 5.4 Hz, 1 H, H_6), 2.78 (dd, J = 2.0, 5.0 Hz, 1 H, H_5), 1.26 (d, J = 5.4 Hz, 3 H, H_7); the signal for H_4 is obscured by H_1.

MTPA ester of racemic 17: δ 3.52 (s, with fine coupling, OCH_3), 1.39 (d, J = 6.4 Hz, 3 H, H_7 of R isomer), 1.32 (d, J = 6.2 Hz, 3 H, H_7 of S isomer); the resonances for H_6 of both isomers are obscured by olefinic signals.

MTPA ester of (+)-18: δ 3.54 (s, with fine coupling, OCH_3), 2.91 (dt, J = 2.0, 5.4 Hz, 1 H, H_4), 2.74 (dd, J = 2.0, 5.2 Hz, 1 H, H_5), 1.39 (d, J = 6.6 Hz, 3 H, H_7); the signal for H_6 overlaps with H_1.

MTPA ester of (−)-18: δ 3.53 (s, with fine coupling, OCH_3), 3.00 (dt, J = 2.0, 5.4 Hz, 1 H, H_4), 2.85 (dd, J = 2.0, 5.0 Hz, 1 H, H_5), 1.31 (d, J = 6.6 Hz, 3 H, H_7); the signal for H_6 overlaps with H_1.

(−)-*lyxo*-5,6-Epoxyhept-1-en-4-ol ((−)-14): Kinetic Resolution of Partially Resolved (−)-13. A solution of 1.5 mL (5.0 mmol) of Ti(O-i-Pr_4) and 1.3 mL (7.5 mmol) of (+)-diethyl tartrate in 200 mL of dry CH_2Cl_2 was cooled to −20 °C. The pale yellow solution was stirred for 15 min, and then 2.24 g (20 mmol) of 72% ee (−)-13 and 3.2 mL of 4.96 M TBHP in CH_2Cl_2 (15.8 mmol, 0.80 equiv)[31] were added. The reaction mixture was stored in a −20 °C freezer for 52 h and then was worked up by using the procedure described above for the preparation of (+)-14. The crude product (3.3 g) was distilled in vacuo to give 2.55 g of volatile products ((−)-14 and residual 13) and 1.48 g of recovered DET (94%). The mixture containing (−)-14 was purified by flash chromatography (170 g silica gel, 2:1 hexane–ether, 25-mL fractions). Fractions 18–30 afforded 393 mg (17%) of recovered 13 and fractions 31–70 afforded 1.91 g (75%) of chromatographically homogeneous (−)-14 (92% ee by Mosher ester analysis).

***lyxo*-5,6-Epoxy-4-[(*N*-phenylcarbamoyl)oxy]hept-1-ene (15).** A solution of 4.7 g (36.7 mmol) of (+)-14 (containing ~5% of the threo epoxide isomer)[33] in 40 mL of pyridine and 200 mL of dry CH_2Cl_2 was treated with 5 mL (47 mmol) of phenyl isocyanate at 23 °C. Starting material was still present after 20 h by TLC analysis, so an additional portion of phenyl isocyanate (4 mL) was added. Ten hours later all volatile components were removed in vacuo, and the residue was dissolved in 50 mL of acetone and 14 mL of water. The solution was again evaporated, dissolved in $CHCl_3$, and filtered to remove insoluble diphenylurea. The crude product was then chromatographed (200 g of silica gel, 1:1 hexane–ether) to give 9.1 g of urethanes. Crystallization of this material from ether–hexane afforded pure 15: 6.55 g (72%); mp 57–57.5 °C; $[\alpha]^{23}_D$ +24° (c = 1.08, CH_2Cl_2). Spectroscopic and combustion analytical data for this compound are reported in the preceding paper.[6a]

Additional quantities of 15 can be obtained by chromatography of the mother liquors from the above crystallization. For example, recrystallized 15 was obtained in 71% yield from a 4-mmol-scale experiment. Careful chromatography to remove the *threo*-epoxyurethane isomer (R_f 0.56 vs. R_f 0.62 for 15 in 1:1 hexane–ether) afforded an additional 18% of 15 for a total yield of 89%.

***arabino*-Hept-1-ene-4,5,6-triol 4,5-Carbonate ((+)-11).** A solution of 5.30 g (21.5 mmol) of (+)-15 in 350 mL of dry Et_2O was cooled to −20 °C (CCl_4, dry ice bath) and treated with 24 mL of 1 M diethylaluminum chloride in hexane. Starting material was completely consumed after 45 min (TLC analysis). The mixture was warmed to 23 °C, and 200 mL of 1 N H_2SO_4 was added. The resulting two-phase mixture was stirred vigorously for 2 h, and then the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (5 × 70 mL). The combined extracts were dried (Na_2SO_4), filtered, concentrated in vacuo, and chromatographed (300 g of silica gel, 1:1 ether–hexane) to give pure (+)-11: 3.43 g (93%); $[\alpha]^{23}_D$ +59.4° (c 8.8, CH_2Cl_2). Spectroscopic and combustion analytical data for this compound are reported in the preceding paper.[6a]

***ribo*-Hept-1-ene-4,5,6-triol (16).** A solution of 644 mg (5.03 mmol) of (−)-14 in 30 mL of Me_2SO was treated with 10 mL of 1 N H_2SO_4 for 20 h at 23 °C. The solution was diluted with 40 mL of methanol and filtered through a column of 40 cm^3 (wet volume) of Dowex 1-X8 ion-exchange resin (pretreated with 5 N NaOH and washed with methanol). An additional 100 mL of methanol was used to ensure that all of 16 had been removed from the column. The filtrate was concentrated in vacuo (high vacuum used to remove Me_2SO) to give 1 g of crude product. This material was purified by flash chromatography (170 g of silica gel, 3:1 EtOAc–hexane, R_f 0.08 with 1:1 EtOAc–hexane as the eluent) to give 16 as a white solid: 660 mg (89%); mp 54–55 °C; $[\alpha]^{22}_D$ −19.3° (c 5.15, acetone) [lit.[7f] for (+)-16, $[\alpha]^{20}_D$ +20.1° (c 1, EtOH)]; ^1H NMR ($CDCl_3$, D_2O exchange) δ 5.85 (m, 1 H, H_2), 5.2 (m, 2 H, H_1), 3.95 (quintet, J = 6.4 Hz, 1 H, H_6), 3.69 (dt, J = 2.9, 6.4 Hz, 1 H, H_4), 3.44 (t, J = 6.4 Hz, 1 H, H_5), 2.57 (dm, J = 14.2 Hz with fine splitting, 1 H, H_3), 2.2 (ddd, J = 6.3, 8.8, 14.2 Hz, 1 H, $H_{3'}$), 1.25 (d, J = 6.4 Hz, 3 H, H_7); IR (CH_2Cl_2) 3100–3600 (br, OH), 3080, 2960, 1640, 1050, 990, 920 cm^{-1}; high-resolution mass spectrum (no parent ion observed), calcd for $C_7H_{12}O_2$ (M − H_2O) m/e 128.083 72, found m/e 128.084 65.

2,6-Dideoxy-D-*ribo*-hexose (Digitoxose, (+)-3). A solution of 317 mg (2.17 mmol) of *ribo* triol 16 in 50 mL of methanol was ozonized by using the procedure described for preparation of (+)-1. The crude product was purified by flash chromatography (200 g of silica gel, 10% EtOH in CH_2Cl_2) to yield 254 mg (79%) of pure, crystalline digitoxose. After recrystallization from EtOAc and drying over P_2O_5 the sample had the following: mp 102–103 °C; $[\alpha]^{22}_D$ +48.8° (c 1.3, H_2O, equilibrated). An authentic sample obtained from commercial sources had the following: mp 105–106 °C; $[\alpha]^{25}_D$ +47.3° (c 1.3, H_2O). The following values have previously been reported for natural digitoxose:[35] mp 110 °C and $[\alpha]^{20}_D$ +46.3°; mp 108–110 °C and $[\alpha]^{19}_D$ +50.2°; mp 105–108 °C and $[\alpha]^{22}_D$ +47.8°. Spectroscopic data: ^1H NMR (D_2O; a 2:1 mixture of pyranose α and β epimers plus minor amounts of furanose epimers) β-anomer δ 4.91 (dd, J = 2.5, 9.8 Hz, 1 H, H_1), 3.9 (m, 1 H, H_3), 3.64 (dq, J = 9.8, 6.1 Hz, 1 H, H_5), 3.12 (dd, J = 3.1, 9.8 Hz, 1 H, H_4), 1.86 (ddd, J = 2.5, 3.6, 13.5 Hz, 1 H, H_{2e}), 1.53 (ddd, J = 3.1, 9.8, 13.5 Hz, 1 H, H_{2a}), 1.03 (d, J = 6.1 Hz, 3 H, H_6); α anomer δ 4.97 (t, J = 3 Hz, 1 H, H_1), 3.9 (m, 1 H, H_3), 3.6 (m, 1 H, H_5), 3.19 (dd, J = 3.1, 8.5 Hz, 1 H, H_4), 1.9 (m, 1 H, H_{2a}), 1.69 (d, fine coupling, J = 14 Hz, 1 H, H_{2e}), 0.98 (d, J = 7.3 Hz, 3 H, H_6); ^{13}C NMR (D_2O) β anomer δ 92.1, 73.1, 70.1, 68.2, 39.2, 18.2; α anomer δ 91.6, 72.7, 70.9, 65.6, 39.6, 17.8.

(*E*)-Hepta-1,4-dien-6-ol (17). To a 0 °C suspension of 12 g (310 mmol) of $LiAlH_4$ in 275 mL of THF was added dropwise a solution of 11.0 g (100 mmol) of racemic 6 over a 30-min period. The resulting mixture was then heated to reflux for 4.5 h.[34] The mixture was then cooled to 0 °C and the reaction terminated by the careful, dropwise addition of 50 mL of H_2O. The pale gray suspension was allowed to warm to 23 °C, and then 30 mL of 1 N NaOH was added slowly, with stirring, to give a grainy, white precipitate. The suspension was filtered through a pad of Celite and washed with five 50-mL portions of Et_2O. The filtrate and washes were dried ($MgSO_4$), filtered, concentrated in vacuo, and distilled to give pure 17: 9.1 g (82%); bp 78 °C (25 mmHg); ^1H NMR ($CDCl_3$) δ 5.7–5.85 (m, 1 H, H_2), 5.4–5.7 (m, 2 H, H_4 and H_5), 4.9–5.05 (m, 2 H, H_1), 4.23 (br quintet, J = 6.4 Hz, 1 H, H_6), 2.73 (br t, J = 6 Hz, 2 H, H_3), 1.94 (br, 1 H, OH), 1.21 (d, J = 6.4 Hz, 3 H, H_7); IR (neat) 3100–3700 (br, OH), 3070, 2960, 1640,

(35) (a) Elderfield, R. C. *Adv. Carbohydr. Chem.* **1945**, *1*, 147. (b) Horton, D.; Cheung, T. M.; Weckerle, W. *Methods Carbohydr. Chem.* **1980**, *8*, 195. (c) See also, ref 11a.

1055, 965, 910 cm^{-1}; mass spectrum, m/e 112 (parent ion). Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.85; H, 11.00.

(+)-*arabino*-4,5-Epoxyhept-1-en-6-ol ((+)-18). Kinetic Resolution of 17. A solution of 1.6 mL (7.5 mmol) of (-)-DIPT and 1.5 mL (5 mmol) of $Ti(O\text{-}i\text{-}Pr)_4$ in 50 mL of dry CH_2Cl_2 was cooled to -20 °C and stirred for 10 min before a solution of 4.39 g (39.2 mmol) of racemic **17** in 200 mL of dry CH_2Cl_2 was added. Finally, 5.0 mL of 3.34 M TBHP in CH_2Cl_2 (16.7 mmol, 0.43 equiv)[31] was added. The reaction mixture was stored at -20 °C for 5 days and then was worked up by being poured into a precooled (-20 °C) solution of 5 mL of H_2O in 300 mL of acetone. The resulting precipitate was removed by filtration through a pad of Celite, and the solvents were removed in vacuo to give 6 g of crude product. This material was purified by flash chromatography (300 g of silica gel, 7:3 hexane–EtOAc, 50-mL fractions). Fractions 13–21 contained dienol and DIPT and were concentrated to give 2.5 g of material which was distilled (Kugelrohr, 90 °C, 25 mmHg) to give 1.71 g (39%) of (-)-**17** [$[\alpha]^{31}_D$ -7.2° (*c* 12.1, CH_2Cl_2), 90% ee by Mosher ester analysis], with 524 mg (29%) of DIPT remaining in the pot. Fractions 22–50, which contained epoxy alcohol and DIPT, afforded 3.2 g of material which was dissolved in 75 mL of ether and 75 mL of saturated brine. This mixture was vigorously stirred, cooled to 0 °C, and treated with 15 mL of 15% NaOH solution. Two hours later the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried (Na_2SO_4), filtered, concentrated, and distilled (Kugelrohr, 95 °C, 25 mmHg) to give (+)-**18**:[33] 2.03 g (40%); $[\alpha]^{30}_D$ +2.8° (*c* 12.5, CH_2Cl_2), 90% ee by Mosher ester analysis; ^1H NMR ($CDCl_3$) δ 5.75 (m, 1 H, H_2), 5.1 (m, 2 H, H_1), 3.87 (br m, J = 3 Hz, 1 H, H_6), 3.01 (dt, J = 2.3, 5.5 Hz, 1 H, H_4), 2.73 (t, J = 2.3 Hz, 1 H, H_5), 2.5 (br d, J = 2.4 Hz, 1 H, OH), 2.27 (m, 2 H, H_3), 1.17 (d, J = 6.4 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 132.7, 117.1, 65.1, 61.1, 54.2, 35.4, 18.8; IR (neat) 3100–3700 (br, OH), 3080, 2980, 1640, 995, 915 cm^{-1}; mass spectrum, m/e 110 ($M^+ - H_2O$). Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.65; H, 9.52.

(-)-*arabino*-4,5-Epoxyhept-1-en-6-ol ((-)-18). Epoxidation of Partially Resolved (-)-17. By the usual procedure, 1.52 g (13.6 mmol) of 90% ee (-)-**17** was epoxidized by using 650 mg (2.8 mmol) of L-(+)-DIPT, 0.55 mL (1.85 mmol) of $Ti(O\text{-}i\text{-}Pr)_4$, and 3.2 mL of 3.34 M TBHP solution[31] in 80 mL of dry CH_2Cl_2 at -20 °C for 90 h. The crude product was dissolved in 60 mL of ether and treated with a mixture of 60 mL of saturated brine and 3 mL of 40% NaOH at 0 °C for 45 min with vigorous stirring to hydrolyze the tartrate ester. The aqueous phase was then extracted with CH_2Cl_2 (4 × 25 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the crude product (130 g of silica gel, 7:3 hexane–EtOAc) afforded 156 mg (10%) of recovered **17** and 1.92 g of (-)-**18**, which was distilled (Kugelrohr, 95 °C, 25 mmHg) to yield (-)-**18**: 1.32 g (76%); $[\alpha]^{30}_D$ -2.4° (*c* 12.6, CH_2Cl_2).[33] This sample was 92% optically pure as determined by the Mosher ester analysis.

***arabino*-4,5-Epoxy-6-[(*N*-phenylcarbamoyl)oxy]hept-1-ene (18a).** Epoxide (+)-**18** (1.84 g, 14.4 mmol, containing approximately 5% of the threo isomer)[33] was treated with phenyl isocyanate (33 mmol, added in two batches) in 15 mL of pyridine according to the procedure described for preparation of (+)-**15**. The crude product (5.8 g) was chromatographed on 120 g of silica gel with 2:1 hexane–ether as the eluent to give 3.54 g of chromatographically homogeneous phenylurethane. This sample was recrystallized from ether–hexane (two crops) to give pure **18a**: 2.81 g (79%); mp 55.5–56 °C; $[\alpha]^{22}_D$ +27° (*c* 4.25, CH_2Cl_2). Spectroscopic and combustion analytical data for this compound are recorded in the preceding paper.[6a] The mother liquors contained additional **18a** (R_f 0.62, 1:1 ether–hexane) along with the threo isomer (R_f 0.60 in the same solvent system).

***lyxo*-Hept-1-ene-4,5,6-triol 5,6-Carbonate (19).** A solution of 2.40 g (9.72 mmol) of urethane **18a** in 200 mL of Et_2O at -20 °C was treated with 12 mL of 1 M diethylaluminum chloride (12 mmol) in hexane. The reaction was judged complete by TLC analysis after 30 min. The solution was removed from the cooling bath, and 200 mL of 1 N H_2SO_4 was added. The initially formed precipitate redissolved after a few minutes, and the two-phase system was stirred vigorously for 2 h. The aqueous phase was then extracted with CH_2Cl_2 (5 × 50 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to yield 1.73 g of crude **19**. This material was purified by flash chromatography on 140 g of silica gel (3:7 hexane–EtOAc; 100-mL fractions) to give 1.66 g (99%) of pure **19** ($[\alpha]^{26}_D$ +37.9° (*c* 3.6, CH_2Cl_2) from fractions 4–9. Spectroscopic and combustion analytical data for this compound are reported in the preceding paper.[6a]

***lyxo*-Hept-1-ene-4,5,6-triol.** A solution of 622 mg (3.62 mmol) of **19** in 5 mL of 0.2 N NaOMe was heated to reflux for 48 h. The reaction mixture was then passed through 14 cm^3 (wet volume) of Dowex 50W-X8 H^+ ion-exchange resin. An additional 75 mL of methanol was used to ensure complete elution of the product. Concentration of the filtrate in vacuo afforded pure *lyxo* triol: 503 mg (95%); mp 45–46 °C; $[\alpha]^{20}_D$ +13.9° (*c* 1.0, EtOH); a value of $[\alpha]_D$ -1.4° (*c* 1, EtOH) has previously been reported[7f] for the L enantiomer; ^1H NMR ($CDCl_3$, D_2O exchanged) δ 5.8 (m, 1 H, H_2), 5.1 (m, 2 H, H_1), 4.0 (dq, J = 3, 6.4 Hz, 1 H, H_6), 3.73 (dt, J = 4.2, 8 Hz, 1 H, H_4), 3.26 (dd, J = 3, 4.2 Hz, 1 H, H_5), 2.28 (m, 2 H, H_3), 1.18 (d, J = 6.4 Hz, 3 H, H_7); IR (CH_2Cl_2) 3100–3700 (br, OH), 3050, 2990, 2940, 1640, 1250, 990, 920 cm^{-1}.

2,6-Dideoxy-D-*lyxo*-hexose ((+)-4, Oliose). A solution of 460 mg (3.15 mmol) of the above *lyxo* triol in 40 mL of MeOH was ozonized at -20 °C according to the procedure described for preparation of (+)-**1**. The crude product was chromatographed on 90 g of silica gel with 10% EtOH in CH_2Cl_2 as the eluent to give pure (+)-**4**: 380 mg (82%); R_f 0.15; $[\alpha]^{23}_D$ +48.8° (*c* 1, H_2O, equilibrated) [lit.[36a] $[\alpha]^{23}_D$ +46° (*c* 0.7, H_2O); lit.[36b] for the L enantiomer $[\alpha]^{23}_D$ -51.5° (*c* 1, H_2O, equil)]; ^1H NMR (D_2O; ~1:1 mixture of α/β-pyranose anomers) β anomer δ 4.58 (dd, J = 1.6, 9.8 Hz, 1 H, H_1), 3.64 (ddd, J = 3.0, 4.7, 12.0 Hz, 1 H, H_3), 3.44 (br q, J = 6.6 Hz, 1 H, H_5), 3.35 (s, with fine coupling, 1 H, H_4), 1.6 (m, 1 H, H_{2e}), 1.41 (dt, J = 12.0, 9.8 Hz, 1 H, H_{2a}), 1.01 (d, J = 6.6 Hz, 3 H, H_6); α anomer δ 5.12 (br s, 1 H, H_1), 3.90 (br q, J = 6.6 Hz, 1 H, H_5), 3.86 (ddd, J = 2.8, 6.4, 11.3 Hz, 1 H, H_3), 3.45 (br s, 1 H, H_4), 1.7 (m, 1 H, H_{2a}), 1.6 (m, 1 H, H_{2e}), 0.98 (d, J = 6.6 Hz, 3 H, H_6); ^{13}C NMR (D_2O) β anomer δ 94.3, 71.4, 70.2, 68.9, 35.4, 16.8; α anomer δ 92.0; 71.2, 67.3, 65.5, 32.4, 16.8.

***ribo*-4-Methoxyhept-1-ene-5,6-diol (20).** A solution of 44 mg (0.34 mmol) of pure (+)-**18** and 5 mg of *p*-toluenesulfonic acid monohydrate in 2 mL of absolute MeOH was heated to reflux for 24 h. The solvent was removed in vacuo, and the crude product was chromatographed on 30 g of silica gel (1% MeOH–CH_2Cl_2, 3-mL fractions). Fractions 65–105 afforded 46 mg (84%) of crystalline **20**, mp 54–55 °C.

A larger scale experiment using 698 mg (5.45 mmol) of (+)-**18** contaminated with approximately 5% of the threo epoxide isomer[33] afforded 543 mg (62%) of pure **20**. Fractions contaminated with products deriving from the threo epoxide were also obtained but were very difficult to separate efficiently by chromatography.

Data for **20**: $[\alpha]^{22}_D$ +37.0° (*c* 1.28, CH_2Cl_2); ^1H NMR ($CDCl_3$, D_2O exchange) δ 5.87 (m, 1 H, H_2), 5.0–5.2 (m, 2 H, H_1), 3.88 (dq, J = 3, 6 Hz, 1 H, H_6), 3.56 (t, J = 3 Hz, 1 H, H_5), 3.3 (m, 4 H, H_4 and OCH_3), 2.3–2.55 (m, 2 H, H_3), 1.20 (d, J = 6 Hz, 3 H, H_7); IR (CH_2Cl_2) 3200–3700, 3080, 2930, 1640, 1090, 915 cm^{-1}; mass spectrum, m/e 119 ($M^+ - C_3H_5$). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.19. Found: C, 60.13; H, 10.19.

2,6-Dideoxy-3-*O*-methyl-D-*ribo*-hexose ((+)-5, Cymarose). A solution of 522 mg (3.26 mmol) of methoxy diol **19** in 50 mL of methanol was ozonized at -20 °C by using the procedure described for preparation of (+)-**1**. Chromatography of the crude product on 130 g of silica gel (5% EtOH in CH_2Cl_2) afforded 470 mg (89%) of crystalline **5** (R_f 0.61, 10% EtOH–CH_2Cl_2). Recrystallization of this material from ether–pentane afforded colorless crystals: mp 84–85 °C (after being dried over P_2O_5); $[\alpha]^{20}_D$ +48.9° (*c* 0.7, H_2O, equilibrated), prepared from 90% ee **18** [lit.[11b] $[\alpha]^{14}_D$ +54.9° (*c* 0.58, H_2O)]; ^1H NMR ($CDCl_3$; ~1:1 mixture of α/β-pyranose epimers and smaller amounts of furanoses) β anomer δ 4.9 (br d, J = 8.5 Hz, 1 H, H_1), 3.9 (m, 1 H, H_3), 3.6 (m, 1 H, H_5), 3.37 (s, 3 H, OCH_3), 3.17 (dt, J = 3.4, 8 Hz, H_4), 2.26 (br d, J = 14 Hz, 1 H, H_{2e}), 1.47 (ddd, J = 2.6, 9.8, 14.1 Hz, 1 H, H_{2a}), 1.22 (d, J = 6.0 Hz, 3 H, H_6); α anomer δ 5.03 (br t, 1 H, H_1), 3.9 (m, 1 H, H_3), 3.6 (m, 1 H, H_5), 3.4 (m, 1 H, H_4), 3.30 (s, 3 H, OCH_3),

(36) (a) Berlin, Y. A.; Esipov, S. E.; Kolosov, M. N.; Shemyakin, M. M. *Tetrahedron Lett.* **1966**, 1431. (b) Horton, D.; Cheung, T.-M.; Weckerle, W. *Methods Carbohydr. Chem.* **1980**, *8*, 201.

2.1 (m, 1 H, H_{2a}), 1.70 (dt, J = 14.5, 1.7 Hz, 1 H, H_{2e}), 1.15 (d, J = 6.0 Hz, 3 H, H_6); ^{13}C NMR (D_2O) β anomer δ 88.0, 78.0, 73.1, 67.6, 57.8, 35.4, 18.3; α anomer δ 92.1, 81.7, 80.9, 68.2, 57.0, 39.0, 18.7.

***ribo*-4-(Benzylamino)hept-1-ene-5,6-diol (21).** A resealable Carius tube was charged with 490 mg (3.83 mmol) of (+)-18, 0.42 mL (3.85 mmol) of benzylamine, 32 mg (0.34 mmol) of phenol, and 0.9 mg (0.04 mmol) of BHT. The tube was purged with argon and heated to 145 °C for 86 h. The crude product was dissolved in CH_2Cl_2 and concentrated in vacuo to give 971 mg of crude product. Recrystallization of this sample from Et_2O–CCl_4 afforded 366 mg (mp 62–64 °C) of pure **21** as bulky plates. The mother liquors were chromatographed on 90 g of silica gel (4% MeOH in CH_2Cl_2) to afford an additional 448 mg (814 mg total, 91% yield) of crystalline **21**: $[\alpha]^{20}_D$ +27° (c 1.2, EtOH); ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 5.76 (m, 1 H, H_2), 5.13 (m, 2 H, H_1), 3.83, 3.75 (AB, J = 12.6 Hz, 2 H, benzylic), 3.76 (m, 1 H, H_6), 3.28 (t, J = 6.8 Hz, 1 H, H_5), 2.89 (dt, J = 4.1, 6.8 Hz, 1 H, H_4), 2.3–2.6 (m, 2 H, H_3), 1.24 (d, J = 6.2 Hz, 3 H, H_7); IR (CH_2Cl_2) 3100–3700 (br NH and OH), 3070, 3030, 2920, 1640, 1607, 1500, 1455, 1070, 995, 920 cm^{-1}; mass spectrum, m/e 236 (M^+ + 1). Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.58; H, 8.80; N, 5.95.

***ribo*-4-Azidohept-1-ene-5,6-diol (22).** A solution of 97 mg (0.76 mmol) of (+)-18, 275 mg (4.2 mmol) of NaN_3, and 90 mg (1.7 mmol) of NH_4Cl in 8 mL of 8:1 methoxyethanol–H_2O was heated to reflux for 6 h. The dark solution was then cooled, diluted with 3 mL of MeOH, and neutralized with saturated aqueous $NaHCO_3$ solution. Solvents were removed in vacuo, and the residue was dissolved in EtOAc and filtered through 20 g of silica gel. This procedure afforded 120 mg of crude **22** which was used directly in the next experiment. Pure **22** was obtained in 78% yield from a similar experiment following silica gel chromatography: mp 66–67 °C; $[\alpha]^{23}_D$ –62.5° (c 0.28, CH_2Cl_2); ^1H NMR ($CDCl_3$, D_2O exchange) δ 5.8 (m, 1 H, H_2), 5.19 (br d, J = 18 Hz, 1 H, H_{1Z}), 5.13 (br d, J = 10 Hz, 1 H, H_{1E}), 3.90 (dq, J = 4.1, 6.3 Hz, 1 H, H_6), 3.50 (dd, J = 4.1, 7.5 Hz, 1 H, H_5), 3.3 (m, 1 H, H_4), 2.5–2.7 (d with fine splitting, J = 14.6 Hz, H_3), 2.35 (dt, J = 14.6, 7.5 Hz, 1 H, $H_{3'}$), 1.15 (d, J = 6.3 Hz, 3 H, H_7); IR (CH_2Cl_2) 3100–3700 (br OH), 3080, 2980, 2920, 2100, 1640, 1380, 1065, 990, 920 cm^{-1}; mass spectrum, m/e 171 (parent ion). Anal. Calcd for $C_7H_{13}N_3O_2$: C, 49.11; H, 7.65; N, 24.54. Found: C, 49.10; H, 7.51; N, 24.42.

The crude azide from the preceding experiment was dissolved in 15 mL of CH_2Cl_2 and treated with 0.4 mL of pyridine and 1.6 mL of Ac_2O at room temperature for 16 h. Analysis of the crude product by 250-MHz ^1H NMR revealed that only one isomer was present. The crude product was purified by preparative TLC (0.5-mm silica gel plate, 2:1 hexane–Et_2O, two developments, R_f 0.7) to yield 105 mg (54% from **18**) of the azido diacetate: $[\alpha]^{19}_D$ +36.5° (c 3.52, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 5.72 (m, 1 H, H_2), 5.0–5.2 (m, 4 H, H_1, H_5, H_6), 3.43 (ddd, J = 4.3, 6.1, 9.2 Hz, H_4), 2.0–2.4 (m, 2 H, H_3), 2.04 (s, 3 H, acetate), 1.94 (s, 3 H, acetate), 1.19 (d, J = 6.2 Hz, 3 H, H_7); IR (CH_2Cl_2) 3080, 2940, 2110, 1740, 1640, 1370, 1225, 1020, 920 cm^{-1}; mass spectrum, m/e 256 (M^+ + 1).

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Rhodium(I)-Catalyzed Hydrosilylation of Styrene

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The investigation of Rh(I)-catalyzed hydrosilylation of styrene with trisubstituted silanes (R_3SiH, R = Et, *i*-Pr, Ph, OEt, and Cl) uncovered an unusual product dependence on the rhodium-to-silane ratio, a reflection of Rh concentration, and a novel, selective route to β-silyl-substituted *trans*-styrenes. At a ratio of 10^{-4}, the expected 1-silyl- and 2-silyl-substituted 1-phenylethanes were formed. At a ratio of 10^{-3}, however, a novel β-silyl-substituted *trans*-styrene was formed as a major product. In the intermediate range, both product types were formed. The results are rationalized on the basis of predominant intermediacy of monomeric Rh(III) complexes in the former and dimeric Rh complexes in the latter. The novel *trans*-styrenes are believed to be formed via a dihydridorhodium elimination process in which the dihydridorhodium hydrogenates styrene to give ethylbenzene as the coproduct.

Introduction

The chloroplatinic acid catalyzed addition of various chlorosilanes to styrene is well documented.[1] More recently, the reaction of trimethyl-, triethoxy-, and trichlorosilanes with styrene, catalyzed by Rh(I) complexes, was reported.[2] In both cases, a mixture of 1-silyl- and 2-silyl-substituted-1-phenylethanes was obtained. A recent review of the hydrosilylation reaction is available.[3]

In the present study, we investigated the rhodium-catalyzed hydrosilylation of styrene with trisubstituted silanes. The nature of the products was found to depend on the rhodium-to-silane ratio; under appropriate reaction conditions, β-silyl-substituted *trans*-styrenes were actually the major products of reaction.[4] While compounds of this type are known and can easily be prepared via hydrosilylation of phenylacetylene,[3,5] previous researchers failed to recognize the new reaction pathway that occurs during hydrosilylation of styrene.

Results

In the Rh(I)-catalyzed reaction of triethylsilane with styrene, under the reported conditions,[2] three silyl-containing products were obtained: 1-(triethylsilyl)-1-

(1) Musolf, M. C.; Speier, J. L. *J. Org. Chem.* **1964**, *29*, 2519.
(2) Rejhon, J.; Hetflejs, J. *Collect. Czech. Chem. Commun.* **1975**, *40*, 3680.
(3) Speier, J. L. In "Advances in Organometallic Chemistry", Academic Press: 1979; Vol. 17, p 407.
(4) A similar product has been reported by using a ruthenium carbonyl cluster as catalyst: Seki, Y.; Takeshita, K.; Kawamoto, K.; Murai, S.; Sonoda, N. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 928.
(5) Dickers, H. M.; Haszeldine, R. N.; Mather, A. P.; Parish, R. V. *J. Organomet. Chem.* **1978**, *161*, 91.

0022-3263/83/1948-5101$01.50/0