Reactions of *p*-Toluenesulfonates with Lithium Triethylborohydride. Visible and Hidden Rearrangements

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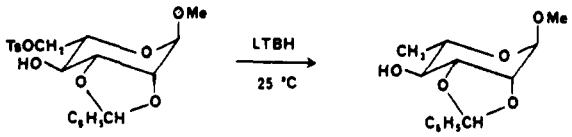
The reaction of methyl 6-deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (**4**) with lithium triethylborohydride (LTBH) gives three primary products, all of which result from rearrangement. One of these, methyl 5-deoxy-3-*C*-(hydroxymethyl)-2-*O*-*p*-tolylsulfonyl-α-D-xylofuranoside (**7**), arises from ring contraction while the other two, methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*xylo*- (**5**) and -*ribo*-hexopyranosides (**9**), result from hydride migration and reduction of the resulting ketone, methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*erythro*-hexopyranosid-4-ulose (**8**). Photolysis of compounds **4**, **5**, and **9** removes the tosyl groups.

As a part of a program designed to generate analogues of the anticancer antibiotic mithramycin,[1] a readily available source of a 2,6-dideoxy-D-hexose was needed. Recently, Baer and Hanna[2] described a reaction in which methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside reacted with lithium triethylborohydride (LTBH) to give methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside in excellent yield (Scheme I). When this reaction, producing a 2-deoxy sugar, was linked with the facile displacement of primary tosyloxy groups by hydride with LTBH (eq 1),[3] the reaction sequence shown in Scheme II emerged as a possible route to methyl 2,6-dideoxy-α-D-*xylo*-hexopyranoside (**1**), an acceptable dideoxy hexose.



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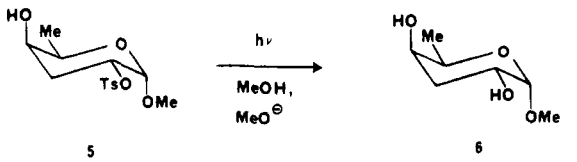
Results and Discussion

Reaction of methyl α-D-galactopyranoside (**2**) with *p*-toluenesulfonyl chloride at room temperature for 16 h resulted in formation of methyl 2,3,6-tri-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (**3**) in excellent yield. (The axial hydroxyl group at C_4 in the galactopyranose system reacts too slowly with tosyl chloride to form any tetratosylate under these conditions.[4]) Treatment of **3** with LTBH in tetrahydrofuran (THF) at 25 °C quantitatively produced methyl 6-deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (**4**). Reaction of the ditosylate **4** (or the tritosylate **3**) with LTBH in refluxing THF yielded a single major product as well as significant amounts of at least seven other materials. The ^1H NMR spectrum of the major product (Table I), which crystallized from the reaction mixture, was that of a dideoxy sugar; however, this compound was not the expected methyl 2,6-dideoxy-α-D-*xylo*-hexopyranoside (**1**) but rather methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexopyranoside (**5**). Compound **5** was formed in only 32% yield. The structure of **5** was determined by its analytical and NMR spectral data (Tables I and II) and by its photochemical conversion into methyl 3,6-dideoxy-α-D-*xylo*-hexopyranoside (**6**) (eq 2).



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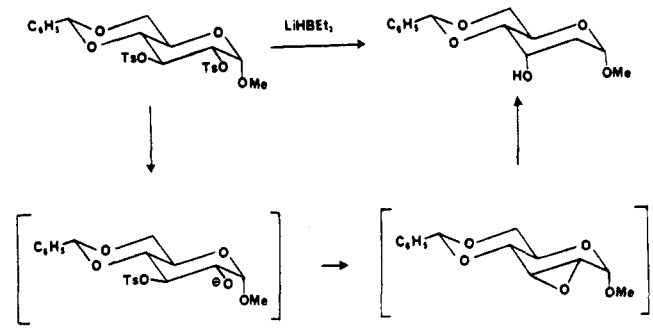
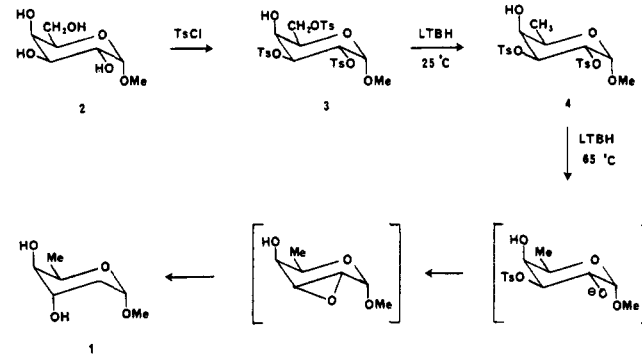
Scheme I

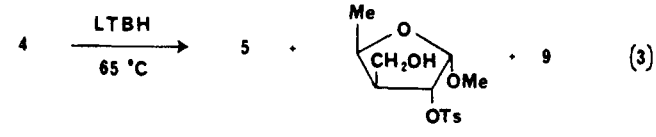


Scheme II



(Photochemical reaction selectively removes tosyl groups without causing other structural changes.[5]) The reaction of the ditosylate **4** clearly was quite different from that expected (Scheme II); consequently, in an effort to understand why this alternate pathway was selected, reaction of **4** with LTBH was investigated in greater detail.

Analysis of the mixtures from reactions of **4** for shorter time periods showed that only three products were formed directly from **4**. One of these was the previously isolated dideoxy sugar **5**, and another was the ring-contraction product, methyl 5-deoxy-3-*C*-(hydroxymethyl)-2-*O*-*p*-tolylsulfonyl-α-D-xylofuranoside (**7**) (eq 3). [The structure



(3)

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of **7** also was determined from its analytical and NMR spectral data (Tables I and II) and was supported by a shift reagent experiment and by spectral simulation.] The

(1) Binkley, R. W. *J. Carbohydr. Chem.* **1985**, *5*, 1.
(2) Baer, H. H.; Hanna, H. R. *Carbohydr. Res.* **1982**, *110*, 19.
(3) Equation 1 comes from ref 1. Reference 2 contains an additional example.
(4) Matsuhiro, B.; Zanlungo, A. B. *Carbohydr. Res.* **1980**, *81*, 330.
(5) Binkley, R. W. *Adv. Carbohydr. Chem. Biochem.* **1981**, *38*, 105.

0022-3263/85/1950-5646$01.50/0

Table I. ^{1}H NMR Spectral Data[a]

	compounds				
	4	5	7	8	9
H_1	4.81	4.58	4.61	4.84	4.46
($J_{1,2}$)		(3.7)	(4.4)	(3.2)	(3.4)
H_2		4.79	4.67	4.65	4.39
($J_{2,3}$)		(11.3)		(10.5)	(11.2)
($J_{2,3'2}$)		(5.9)		(6.4)	(6.0)
($J_{2,3}$)			(8.2)		
H_3	4.72		2.60		
($J_{3,4}$)	(3.0)		(8.4)		
(J_{3,CH_2})			(5.8)		
H_{3a}		2.07		2.83	2.09
($J_{3a,4}$)		(2.8)			(9.1)
H_{3e}		1.97		2.60	1.96
($J_{3e,4}$)					(4.2)
H_4	4.07	3.74	4.40		3.26
($J_{4,5}$)	(1.0)		(6.7)		(10.0)
H_5	3.95	3.91	1.22	4.10	3.26
($J_{5,6}$)	(6.6)	(6.6)		(6.7)	(6.6)
H_6	1.23	1.16		1.24	1.19
CH_3Ar	2.44	2.42	2.44	2.46	2.44
OCH_3	3.25	3.33	3.25	3.45	3.29
Ar	7.86	7.86	7.88	7.86	7.84
	7.75	7.75	7.77	7.75	7.74
	7.38	7.38	7.40	7.41	7.40
	7.28	7.28	7.28	7.30	7.29
CH_2OH		3.69			

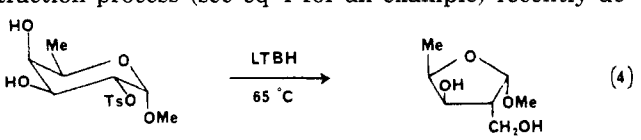
[a] Chemical shifts are in parts per million from Me_4Si. Coupling constants are in Hertz. All compounds were dissolved in $CDCl_3$.

Table II. ^{13}C NMR Spectral Data[a]

	compounds				
	4	5	7	8	9
C_1	97.63	96.93	99.40	96.28	96.01
C_2	77.47	73.45	79.26	74.35	75.38
C_3	73.89	32.23	44.26	40.38	33.23
C_4	71.52	69.18	72.87	203.63	70.59
C_5	65.39	65.54	16.35	70.14	68.30
C_6	15.75	15.99		14.22	16.70
CH_3Ar	21.59	21.64	21.42	21.67	21.67
CH_3O	55.46	55.31	54.71	56.02	55.06
C_6H_4	145.19	144.91	144.94	145.44	144.91
	145.04	134.00	134.00	133.56	134.00
	133.14	129.90	129.59	130.73	129.90
	133.01	127.84	127.83	127.84	127.84
	129.87				
	129.75				
	128.00				
	127.31				
CH_2OH			59.05		

[a] Chemical shifts are in parts per million from Me_4Si.

formation of 7 appeared to be analogous to the ring contraction process (see eq 4 for an example) recently de-



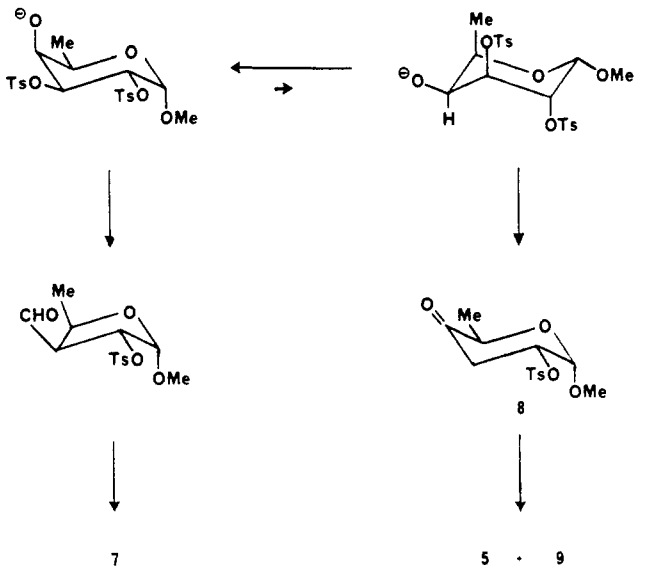
(4)

scribed by Baer and co-workers.[6] The third primary product was detectable only in small quantities in reactions run to partial completion; it clearly was unstable under the reaction conditions. This product (designated A) could not be obtained in sufficient quantities and purity from these reactions for identification but was identified as a result of a later experiment (vide infra).

The results from reaction of 4 for different time periods suggested that the ring-contraction product 7 also was not

(6) Baer, H. H.; Astles, D. J.; Chin, H.-C.; Siemsen, L. *Can. J Chem.* **1985**, *63*, 432.

Scheme III



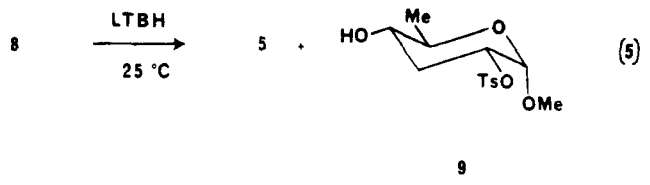
stable under the reaction conditions, and, indeed, it was not. Compound 7 reacted with LTBH in refluxing THF to produce a complex mixture of compounds which by TLC and ^{13}C NMR analysis appeared to contain most of products (except for 5 and A) originally derived from reaction of the ditosylate 4. Because these additional products were not formed directly from 4, their structures were not pertinent to understanding its reactivity and, therefore, were not investigated. It is worth noting, however, that the instability of 7 is almost certainly attributable to the presence of a tosyloxy group in the molecule since structurally similar (but tosyloxy lacking) ring-contraction products are stable under the reaction conditions.[6]

The 3,6-dideoxy sugar 5 decomposed only slowly when subjected to LTBH in refluxing THF; thus, even though 5 is the major isolated product from reaction of 4, the major reaction pathway appears to lead to the unstable ring-contraction product 7. A proposed mechanism for the formation of 7 is given in Scheme III. This mechanism suggests that the deprotonated hydroxyl group is converted to an aldehyde with simultaneous migration of the C_4–C_5 bond and departure of the tosyloxy group attached to C_3. The aldehyde generated by this process is quickly reduced to compound 7 under the reaction conditions. Such a mechanism explains the exclusive loss of the C_3 tosyloxy group during ring contraction because this process depends upon both the vicinal positioning of the hydroxyl and tosyloxy groups and on the trans antiparallel arrangement of the C_4–C_5 and the C_3–O bonds.

Although a reasonable explanation now existed for formation of 7, questions remained about the process for conversion of the ditosylate 4 into the 3,6-dideoxy sugar 5. Did 5 result from a simple S_N2 displacement or was the reaction more complex? Why did displacement of the C_2 tosyloxy group not occur? In an effort to answer these questions by determining which proton in 5 had come from the hydride reagent, compound 4 was treated with lithium triethylborodeuteride (LTBD) in refluxing THF. When the 3,6-dideoxy sugar was isolated, the deuterium in this product was not bonded to C_3 but rather to C_4. Although this result was surprising, it did, upon reflection, provide satisfying answers to the questions that had been raised. Simply put, the 3,6-dideoxy sugar 5 was (like the ring-contraction product 7) also the result of rearrangement (hydride migration). This rearrangement, which requires the intermediacy of the ketone 8 (Scheme III), was un-

detectable until deuterium had been introduced into the molecule. It is interesting that Hansske and Robins[7] also have observed hydride migration upon reaction of ribonucleoside monotosylates with LTBH.

As a final experiment, the ketone **8**, a proposed intermediate in the conversion of **4** into **5**, was synthesized and reacted with LTBH at 25 °C. Compound **5** was formed in 60% yield along with methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranoside (**9**) in 35% yield (eq 5).



(5)

(Only compound **5** was isolated if the reaction mixture was refluxed for 30 min prior to isolation.) Comparison of the ^1H and ^{13}C NMR spectra of **9** with those obtained from compound A showed that these materials were identical; thus, all the primary products from the reaction of the ditosylate **4** with LTBH in refluxing THF were found to be products of rearrangement. Formation of each compound (**5**, **7**, and **9**), therefore, depends upon vicinal hydroxy and tosyloxy groups; consequently, only the C_3 tosyloxy group in the ditosylate **4** can participate in these rearrangements.

Experimental Section

^1H and ^{13}C NMR spectra were obtained from a Varian FT-80A spectrometer and are given in Tables I and II, respectively. Spectral simulation was done by using Varian Associates SIMEQ spin-simulation program.

Synthesis of Methyl 2,3,6-Tri-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (3). *p*-Toluenesulfonyl chloride (17.4 g, 0.0894 mol) was dissolved in 50 mL of pyridine, and to this stirred solution was added 3.81 g (0.0179 mol) of methyl α-D-galactopyranoside (**2**). This solution was stirred at 25 °C for 20 h. Water (5 mL) was added, and stirring was continued for an additional hour. Toluene (150 mL) then was added to the solution, and after being stirred for 15 min, the solution was filtered through a 5 × 2 cm layer of 230–400 mesh silica gel. The residue in the flask was washed with two 75-mL portions of toluene. These washings also were filtered through the silica gel, and all filtrates were combined and evaporated under reduced pressure. The residue was redissolved in 100 mL of toluene and the solvent again distilled under reduced pressure. Final traces of toluene were removed under vacuum by using a mechanical pump to give 11.2 g (0.0171 mol, 95%) of methyl 2,3,6-tri-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (**3**). This material was crystallized from methanol, mp 140–141 °C (lit.[4] 142–143 °C), and had ^1H and ^{13}C NMR spectra identical with those reported in the literature.[4]

Synthesis of Methyl 6-Deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (4). Compound **3** (12.53 g, 0.02399 mol) was dissolved in 50 mL of tetrahydrofuran, and the resulting solution was purged with nitrogen. As the nitrogen purge continued, 75 mL of a 1.0 M solution of lithium triethylborohydride (LTBH) in THF was added slowly to the stirred solution. After 2.0 h, 5 mL of methanol was added in a dropwise manner. The solution then was cooled in a ice bath and rapidly stirred as 75 mL of 30% hydrogen peroxide was introduced with **caution. The hydrogen peroxide solution must be added dropwise with rapid stirring because the resulting reaction is extremely exothermic. Particularly during the early stages of addition of hydrogen peroxide, the rate of addition must be very slow and carefully monitored.** After peroxide addition was complete, the mixture was vigorously shaken with 300 mL of chloroform, and the layers were separated. The aqueous layer was extracted twice more with 100-mL portions of chloroform, and the chloroform extracts were combined and passed through a 2 × 5 cm layer of 230–400 mesh silica gel. The colorless solution was evaporated under reduced pressure to give 11.73 g (0.024 mol, 100% yield) of methyl 6-deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (**4**). This material was identical with that obtained by treating methyl 6-deoxy-α-D-galactopyranoside with *p*-toluenesulfonyl chloride according to the procedure used for synthesis of **3**. The ^1H and ^{13}C NMR spectra for compound **4** are given in Tables I and II.

Photolysis of Methyl 6-Deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (4). Compound **4** (0.454 g, 0.933 mmol) and 0.30 g (7.5 mmol) of sodium hydroxide were placed in a quartz Rayonet photochemical reaction vessel, dissolved in 125 mL of methanol, purged with nitrogen for 1 h, and irradiated for 2 h in a Rayonet photochemical reactor using 254-nm lamps. After 2 h, the photolysis was stopped, 3 g of Amberlite IR-120H acidic ion-exchange resin was added, and the mixture was stirred until it became neutral. The resin was filtered and the solvent concentrated to give 0.129 g (0.793 mmol, 85%) of methyl 6-deoxy-α-D-galactopyranoside, mp 156–158 °C, identical (mixture mp and ^1H and ^{13}C NMR spectra) with an authentic sample prepared from 6-deoxy-D-galactose (D-fucose).[8]

Reaction of Methyl 6-Deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (4) with Lithium Triethylborohydride (LTBH). Compound **4** (8.30 g, 0.0170 mol) was dissolved in 20 mL of tetrahydrofuran, and the solution was purged with nitrogen. The nitrogen purge was continued while 120 mL of a 1.0 M solution of LTBH in THF was added. The reaction mixture was stirred at room temperature for 30 min and then refluxed for 30 min. The reaction mixture was then cooled in an ice bath, and 5 mL of methanol was added in a dropwise manner with stirring. To the rapidly stirred, cooled reaction mixture, 50 mL of 30% hydrogen peroxide was added very slowly. After addition of the hydrogen peroxide, the solution was extracted with three 300-mL portions of chloroform. The chloroform extracts were passed through a 2 × 5 cm layer of 230–400 mesh silica gel and then concentrated to a colorless liquid. This material crystallized upon standing and was recrystallized from chloroform–hexane (1:4) to give 1.506 g (4.76 mmol, 28%) of methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexopyranoside (**5**), mp 136–137 °C. Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37. Found: C, 53.14; H, 6.32. The ^1H and ^{13}C NMR spectra are given in Tables I and II, respectively, and the photochemical conversion of **5** into the known methyl 3,6-dideoxy-α-D-*xylo*-hexopyranoside (**6**) is described below.

The residue after crystallization of **5** was chromatographed on a 2.5 × 20 cm column of 230–400 mesh silica gel with ethyl acetate–hexane (1:3); 20-mL fractions were collected. Fractions 18–20 gave 215 mg (0.68 mmol) of compound **5**, mp 136–137 °C. The total yield of **5** was 32%. Fractions 21–30 gave 483 mg (1.53 mmol, 9% yield) of methyl 5-deoxy-3-*C*-(hydroxymethyl)-2-*O*-*p*-tolylsulfonyl-α-D-xylofuranoside (**7**), which did not crystallize. NMR spectra are given in Tables I and II. Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37. Found: C, 52.84; H, 6.47. In order to determine all the coupling constants in the ^1H NMR spectrum, it was necessary to obtain this spectrum in the presence of tris-(2,2,6,6-tetramethyl-3,5-heptanedioate)europium. This reagent caused substantial downfield shifts of H_2 and the hydroxymethyl protons. The chemical shift and coupling constant assignments were confirmed by spectral simulation.

Two reactions of the ditosylate **4** were conducted as described above except that the reflux times were 5 and 15 min. Isolation also was conducted as described above with the only difference being that unreacted **4** was isolated in fractions 15–17 in each instance. In the 5-min reaction 30% of the starting material (**4**) had reacted, and in the 15-min reaction 55% of **4** had reacted. The yields of **5**, based on reacted starting material, were 39% and 35%, respectively, while those of **7** were 26% and 18%, respectively. These reaction mixtures contained an additional product, designated A, which appeared to be formed directly from **4**. Compound A had a chromatographic mobility almost identical with that of **4** and was unstable under the reaction conditions;

(7) Hansske, F.; Robins, M. R. *J. Am. Chem. Soc.* **1983**, *105*, 6736. We thank a referee for pointing out this work.

(8) Binkley, R. W.; Goewey, G. S.; Johnston, J. C. *J. Org. Chem.* **1984**, *49*, 992.

therefore, it could not be obtained in a sufficiently pure form for identification from these reactions. This product (A) was subsequently identified by independent synthesis (vide infra). From the NMR spectra it was estimated to be present in 7% and 3% yields from the 5- and 15-min reactions, respectively.

An additional reaction of **4** was conducted as described above except that lithium triethylborodeuteride (LTBD) replaced LTBH. The results were the same except that deuterium was incorporated into compound **5** at C_4 and into compound **7** in the hydroxymethyl group.

Photolysis of 3,6-Dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexopyranoside (5). Compound **5** was photolyzed in the manner described above for the ditosylate **4**. This reaction converted 414 mg (1.31 mmol) of **4** into 191 mg (1.18 mmol, 90%) of methyl 3,6-dideoxy-α-D-*xylo*-hexopyranoside (**6**), identical in ^1H and ^{13}C NMR spectra with those reported for an independently synthesized sample.[9]

Oxidation of 3,6-Dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexopyranoside (5). Compound **5** (202 mg, 0.637 mmol) was dissolved in 10 mL of dry methylene chloride. To this stirred solution were added 100 mg (0.12 mmol) of sodium acetate and 540 mg (2.5 mmol) of pyridinium chlorochromate. The reaction mixture became dark after a few minutes. After 2 h, the reaction mixture was passed through a 5 × 10 cm column of silica gel by eluting with 1:1 ethyl ether–methylene chloride. This process removed the colored material. Concentration of the reaction mixture under reduced pressure gave 198 mg (0.62 mmol, 98%) of methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*erythro*-hexopyranosid-4-ulose (**8**), mp 84–85 °C. This material was identified by its ^1H and ^{13}C NMR spectra and by its subsequent reduction to **5**. Compound **8** was relatively unstable. It decomposed in solution in several hours.

Reaction of 3,6-Dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*erythro*-hexopyranosid-4-ulose (8) with LTBH. Compound **8** (198 mg, 0.62 mmol) was reacted with LTBH according to the procedure used for synthesis of **4** from **3**. After workup, compound **5** crystallized from the reaction mixture. The residue after crystallization was chromatographed on a 5 × 20 cm column of silica gel to give an additional quantity of **5**, bringing the total isolated yield to 126 mg (0.40 mmol, 60%). Also isolated was 64 mg (0.19 mmol, 35%) of a solid identified as methyl 3,6-dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranoside (**9**), mp 109–111 °C, on the basis of its NMR spectra and its photochemical deprotection to give methyl 3,6-dideoxy-α-D-*ribo*-hexopyranoside (**10**). Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37. Found: C, 52.87; H, 6.31.

Photolysis of 3,6-Dideoxy-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranoside (9). Compound **9** was photolyzed in the manner described for photolysis of **4**. This reaction converted 64 mg (0.19 mmol) of **9** into 30 mg (0.18 mmol) of methyl 3,6-dideoxy-α-D-*ribo*-hexopyranoside (**10**), identical in ^1H and ^{13}C NMR spectra with those reported for an independently synthesized sample.[10]

Acknowledgment. I thank the Standard Oil Company (Ohio) for support of this work.

Registry No. **2**, 3396-99-4; **3**, 74052-05-4; **4**, 99310-36-8; **5**, 99310-37-9; **6**, 6109-60-0; **7**, 99310-38-0; **8**, 99310-39-1; **9**, 99310-40-4; **10**, 31899-66-8; LTBH, 22560-16-3; methyl 6-deoxy-α-D-galactopyranoside, 1128-40-1.

(9) Baer, H. H.; Astles, D. J. *Carbohydr. Res.* **1984**, *126*, 343.

(10) Klausener, A.; Runsink, J.; Scharf, H. D. *Liebigs Ann. Chem.* **1984**, 783.

A Chiral Synthesis of (+)-Lineatin, the Aggregation Pheromone of *Trypodendron lineatum* (Olivier), from D-Ribonolactone

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Lineatin, the aggregation pheromone of *Trypodendron lineatum* (Olivier), has been shown to be (+)-(1*R*,4*S*,5*R*,7*R*)-3,3,7-trimethyl-2,9-dioxatricyclo[3.3.1.$0^{4,7}$]nonane, (+)-**1**, by the first stereospecific chiral synthesis. D-Ribonolactone (**3**) was used to prepare (2*S*,3*R*)-2,3-(isopropylidenedioxy)-4-methyl-4-[[2-(trimethylsilyl)ethoxy]methoxy]pentanal (**12**). Condensation with the cyanophosphonate **7** provided two isomeric α,β-unsaturated nitriles, **13**. Catalytic hydrogenation furnished (3*RS*,5*R*,6*R*)-3-cyano-5,6-(isopropylidenedioxy)-7-methyl-7-[[2-(trimethylsilyl)ethoxy]methoxy]-1,1-dimethoxyoctane (**14**), which, upon acid-catalyzed hydrolysis, produced the diastereoisomeric mixture **17**. Blocking of the hemiacetal function of **17** with a *tert*-butyldimethylsilyl group, followed by reaction with methanesulfonyl chloride, produced the mixture **22**. Acid-catalyzed cyclization of the deprotected hemiacetal **23** yielded (1*R*,4*R*,5*R*,7*S*)-7-cyano-3,3-dimethyl-4-[(methylsulfonyl)oxy]-2,9-dioxabicyclo[3.3.1]nonane (**24**). Intramolecular nucleophilic ring closure provided (1*R*,4*S*,5*R*,7*S*)-7-cyano-3,3-dimethyl-2,9-dioxatricyclo[3.3.1.$0^{4,7}$]nonane (**25**). Conversion of the cyano group to a methyl group using diisobutylaluminum hydride, followed by Wolff–Kishner reduction, produced (+)-**1**. This 16-step synthetic route to (+)-lineatin clearly established the absolute configuration as 1*R*,4*S*,5*R*,7*R* and produced (+)-lineatin in 2.7% overall yield.

Lineatin (**1**), an aggregation pheromone from the frass of the female ambrosia beetle *Trypodendron lineatum* (Olivier),[1] has been shown to elicit powerful secondary attraction in laboratory and field trials.[2,3] The extensive damage to fallen and sawn timber, especially Douglas fir, caused by this beetle lends particular significance to the use of this semiochemical as a possible means for maintaining control of this pest.[4–6] Entomological investigations have demonstrated not only that (+)-**1** is the active

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