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Acyclic Stereoselection. 32. Synthesis and Characterization of the Diastereomeric (4*S*)-Pentane-1,2,3,4-tetrols[1]

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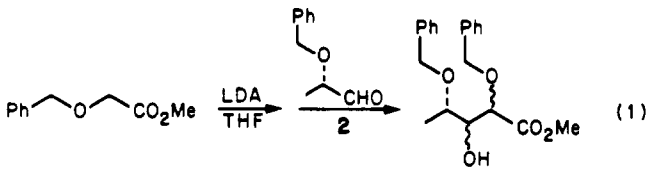
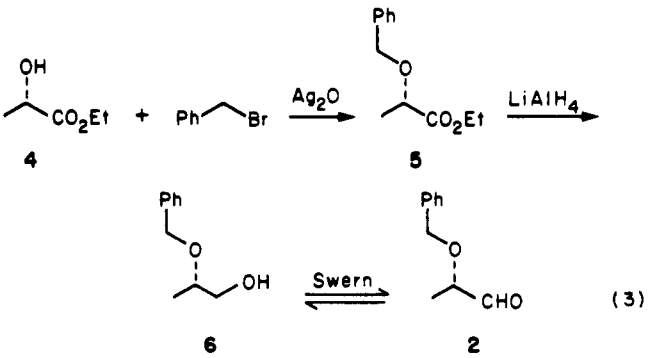
The stereochemistry of the reaction of the lithium enolate of ester **1** and ketene acetal **3** with aldehyde **2** has been investigated. The diastereomeric (4*S*)-pentane-1,2,3,4-tetrols and their corresponding tetraacetate esters have been prepared and characterized.

As part of a program to explore the use of stereoselective aldol methodology[3] for the de novo synthesis of carbohydrates,[4] we have examined the aldol reaction of methyl (benzyloxy)acetate (**1**) with (*S*)-2-(benzyloxy)propanal (**2**, eq 1) and the related Lewis acid mediated reactions of silyl ketene acetal **3** with **2** (eq 2). As part of this study, we have prepared the diastereomeric (4*S*)-pentane-1,2,3,4-tetrols and characterized the corresponding tetraacetate esters.[5]



Preparation of Materials. Ethyl (*S*)-lactate (**4**) was treated with benzyl bromide and silver oxide to obtain ester **5** (eq 3).[6] Immediate reduction of ester **5** with lithium aluminum hydride provides diol monoether **6** in 85% yield, and in an enantiomeric purity of ca. 100%. Oxidation of **6** by Swern's method[7] provides aldehyde **2** in 83% yield. Less than 8% racemization occurs in the Swern oxidation, as shown by reduction of **2** back to alcohol **6** ($LiAlH_4$), the enantiomeric purity of which was assayed by Mosher's method.[8] Alkylation of benzyl (*S*)-lactate with sodium hydride and benzyl bromide results in considerable racemization; ester **5** is obtained in an optical purity of only 50–75% ee.



Silyl ketene acetal was prepared as shown in eq 4. (Benzyloxy)acetic acid (**7**)[9] is treated with hexamethyldisilazane and trimethylsilyl chloride to obtain silyl ester

(1) For part 31, see: Heathcock, C. H.; Oare, D. A. *J. Am. Chem. Soc.*, submitted for publication.
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(3) (a) Heathcock, C. H. *Science (Washington, D.C.)* **1981**, *214*, 395. (b) Heathcock, C. H. "Comprehensive Carbanion Chemistry"; Buncel, E., Durst, T., Eds.; Elsevier: New York, 1984; Vol. 2. (c) Heathcock, C. H. "Asymmetric Syntheses"; Morrison, J. D., Ed., Academic Press: New York, 1984; Vol. 3.
(4) (a) Heathcock, C. H.; Montgomery, S. H. *Tetrahedron Lett.* **1983**, *24*, 4637. (b) Heathcock, C. H.; Montgomery, S. H. *Ibid.* **1985**, *26*, 1001.
(5) The traditional names of these four tetraols are 1-deoxy-D-ribitol, 1-deoxy-L-arabinitol, 1-deoxy-L-lyxitol, and 1-deoxy-D-xylitol (corresponding to tetraacetates **17–20**, respectively). Although the literature contains a number of references to these substances, there is a lack of spectral data with which to make effective comparisons.
(6) Abbot, S. J.; Jones, S. R.; Weinmen, S. A.; Bockoff, F. M.; McLafferty, F. W.; Knowles, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4323.
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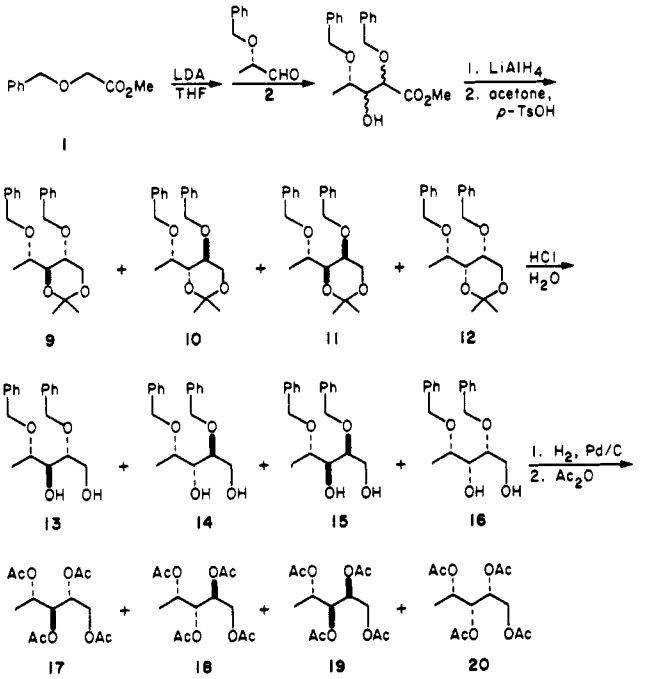
Table I. Diastereomer Ratios in Reactions of Ester 1 and Ketene Acetal 3 with Aldehyde 2 (Scheme I)

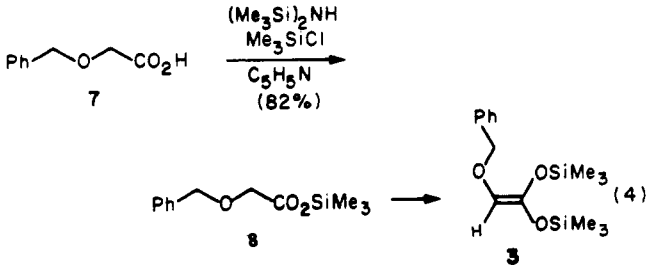
entry	Lewis acid[a]	yield, %[b]	product distribution[c]				diastereoselection	
			9	10	11	12	C-2,C-3	C-3,C-4
1	BF_3·OEt_2	34	23	39	17	21	62:38	40:60
2	$SnCl_4$	43	11	57	17	15	68:32	28:72
3	$TiCl_4$	58	10	52	24	14	62:38	34:66
4	$MgBr_2$	28	0	19	1	80	19:81	1:99
5	$ZnCl_2$	26	0	68	1	31	68:32	1:99
6	$ZnCl_2$[d]	54	0	61	0	39	61:39	0:100
7	$ZnCl_2$[e]	46	11	45	16	28	56:44	27:73
8	$Eu(fod)_3$	36	0	80	8	12	80:20	8:92
9	$Eu(fod)_3$[f]	53	0	80	11	9	80:20	11:89
10	1 Li enolate	36	36	21	38	5	57:43	74:26

[a] Aldehyde 2 was treated with 1.1 equiv of Lewis acid and 1.1 equiv of silyl ketene acetal 3 in CH_2Cl_2 (see general procedure in the Experimental Section). [b] Isolated yield of diols 9–12 based on aldehyde 2. [c] The ratios of diols were determined from the ^{13}C NMR spectra of the corresponding tetraacetates 17–20 or HPLC analysis (hexane–ethyl acetate, 20:1) of the corresponding 1,3-acetonides 9–12. [d] Soluble $ZnCl_2$–ether complex was used (ref 10). [e] THF was used instead of CH_2Cl_2. [f] Two equivalents of $Eu(fod)_3$ were used.

Scheme I



8. Further silylation of the lithium enolate with trimethylsilyl chloride affords ketene acetal 3 in 58% overall yield.



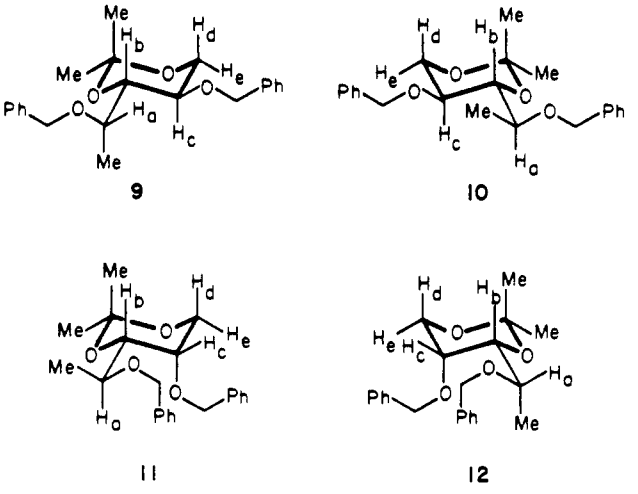
Characterization of Diastereomeric Products. In order to evaluate the stereochemistry of eq 1 and 2, it was necessary to prepare and identify the diastereomeric pentane-1,2,3,4-tetraols. This was accomplished as shown in Scheme I. Reaction of the lithium enolate of ester 1 with aldehyde 2 gives a mixture of all four diastereomeric aldols (Table I, entry 10). The product of this reaction was reduced with lithium aluminum hydride to a mixture of tetraol dibenzyl ethers, which was treated with *p*-toluenesulfonic acid in acetone to obtain the corresponding acetonides. These materials (9–12) were separated by chromatography on silica gel.

Table II. ^1H NMR Parameters for Acetonides 9–12

	compound				
	9	10	11	12	21
	Chemical Shifts, δ				
H_a	3.74	3.86	3.94	3.83	4.47
H_b	3.91	3.58	3.68	3.72	3.64
H_c	3.50	3.78	3.57	3.23	4.22
H_d	3.71	3.68	3.86[a]	3.90[a]	3.83
H_e	3.90	3.92	4.03[a]	4.11[a]	4.04
	Coupling Constants, Hz				
$J_{a,b}$	2.0	2.4	8.9	8.1	9.2
$J_{b,c}$	9.0	8.9	1.8	1.8	9.4
$J_{c,d}$	7.5	6.7	1.9	2.0	9.7
$J_{c,e}$	5.0	4.5	1.9	2.0	5.3
$J_{d,e}$	11.2	11.0	12.9	13.1	10.7

[a] In compounds 11 and 12, the chemical shifts for H_d and H_e are uncertain, since $J_{c,d}$ and $J_{c,e}$ are equal.

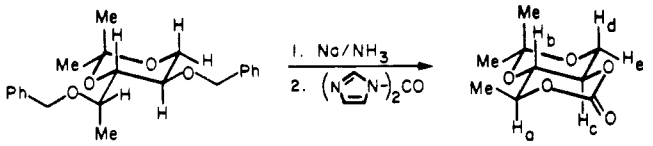
Chart I



The relative configurations at carbons 2 and 3 were determined by interpretation of the high field ^1H NMR spectra of acetonides 9–12 and the corresponding 1,1-dideuterio analogues, which were prepared by repeating the foregoing process with lithium aluminum deuteride. In interpreting the spectra of dioxolanes 9–12, it was assumed that the bulky (benzyloxy)ethyl substituent is equatorial in each case. The observed coupling constants reveal that isomers 9 and 10 have the C-2,C-3 anti configuration.[11] In

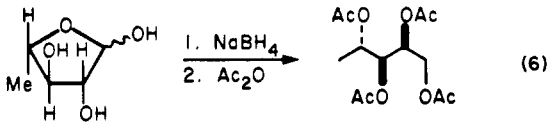
(11) For a definition of the syn/anti convention, see: Masamune, S.; Ali, Sk. A.; Snitman, D. L., Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* 1980, *19*, 557.

order to assign the C-3,C-4 relative configuration to these isomers, **9** was converted to cyclic carbonate **21** as shown in eq 5. The chemical shifts and coupling constants ob-



9 **21** (5)

served for **21** are included in Table II, and indicate that this isomer has the C-3,C-4 anti configuration. In order to distinguish the C-2,C-3 syn isomers **11** and **12**, we converted the commercially available 5-deoxy-L-arabinose (**22**)[12] to tetraacetate **19** (eq 6). Full spectral assignments are shown in Chart I and Table II.



22 **19** (6)

To provide reference substances for future investigations, acetonides **9–12** were deprotected and the resulting dibenzyl ethers (**13–16**) were hydrogenolized. Acetylation of the resulting tetraols provided tetraacetates **17–20** (Scheme I). Spectral data for compounds **17–20** are recorded in the Experimental Section.

Stereochemistry of Additions to Aldehyde 2. It is evident from Table I (entry 10) that aldol addition of the lithium enolate of ester **1** with aldehyde **2** occurs with poor stereoselectivity. The net simple diastereoselection is only 57/43 and the net diastereofacial preference of **2** is 74/26.[13]

The Lewis acid mediated reactions of ketene acetal **3** with **2** show several interesting effects. Not surprisingly, $BF_3{\cdot}OEt_2$ shows essentially no selectivity. However, the relatively low diastereofacial selectivity seen with $TiCl_4$ and $SnCl_4$ is surprising, in light of the high chelation-controlled selectivity usually observed with aldehyde **2** and these Lewis acids.[14,15] On the other hand, $MgBr_2$ and $ZnCl_2$ both show almost complete chelation-controlled diastereofacial preference. Curiously, the simple diastereoselection of the latter two reactions is opposite in sense. However, due to poor solubility of these Lewis acids in dichloromethane, yields are low. Mayr's "soluble" $ZnCl_2$[10] gives an improved yield, but with some loss of stereoselectivity. Stereoselectivity with $ZnCl_2$ essentially disappears when the reaction is carried out in THF instead of dichloromethane. The best stereoselectivity, from a preparative viewpoint, is observed with $Eu(fod)_3$.[16] However, it is necessary to employ 2 equiv of this relatively expensive catalyst in order to obtain an acceptable yield of product.

(12) 5-Deoxy-L-arabinose is available from Sigma Chemical Company, P. O. Box 14508, St. Louis, MO 63178 (catalog no. D9264).

(13) For definitions of the terms "simple diastereoselection" and "diastereofacial preference" see ref 3c.

(14) (a) Reetz, M. T.; Jung, A. *J. Am. Chem. Soc.* **1983**, *105*, 4833. (b) Reetz, M. T.; Kesseler, K.; Jung, A. *Tetrahedron Lett.* **1984**, *25*, 729. (c) Reetz, M. T.; Kesseler, K. *J. Chem. Soc., Chem. Commun.* **1984**, 1079. (d) Reetz, M. T.; Kesseler, K. *Angew Chem., Int. Ed. Engl.* **1984**, *23*, 556.

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(16) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 3716.

Experimental Section[17]

Trimethylsilyl (Benzyloxy)acetate (8). To a stirring solution of 33.2 g (0.200 mol) of (benzyloxy)acetic acid[9] in 120 mL of pyridine at 25 °C was added slowly 29.2 mL (0.140 mol) of hexamethyldisilazane. The reaction was slightly exothermic; a slurry was formed and redissolved during the course of addition of hexamethyldisilazane. The resulting solution was stirred for 40 min and 8.47 mL (66.7 mmol) of chlorotrimethylsilane was added at 25 °C. A white precipitate was formed. After stirring at 25 °C for 2 h, the mixture was filtered under nitrogen, pyridine was removed with a rotary evaporator, and the residue was distilled with a short path still to afford 39.2 g (82%) of colorless **8**: bp 107 °C (1.2 mm); IR (neat) 2960, 1740, 1500, 1258, 1218, 1124, 848 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.26 (s, 9 H), 3.97 (s, 2 H), 4.55 (s, 2 H), 7.27 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ −0.43, 67.7, 72.9, 127.7, 127.8, 128.2, 137.1, 170.4. Calcd for $C_{12}H_{18}O_3Si$: C, 60.47; H, 7.61. Found: C, 60.09; H, 7.68.

2-(Benzyloxy)-1,1-bis(trimethylsiloxy)ethene (3). To a solution of 15.4 mL (11.1 g, 0.110 mol) of diisopropylamine in 110 mL of dry THF at 0 °C was added 65.5 mL (0.110 mol) of a 1.68 M solution of *n*-butyllithium in hexane. The resulting solution was stirred for 20 min and then cooled to −78 °C. To this solution was added slowly a solution of 23.8 g (0.100 mol) of ester **1** in 40 mL of dry THF. The mixture was stirred for an additional 40 min and chlorotrimethylsilane (14.0 mL, 12.0 g, 0.110 mol) was added at −78 °C. The reaction mixture was allowed to warm to 0 °C and was stirred for 40 min. After removal of THF under reduced pressure 100 mL of petroleum ether was added. A white precipitate that formed was removed by filtration and the filtrate was concentrated with a rotary evaporator. Distillation of the residue under reduced pressure gave 22.0 g (71%) of colorless **3**: bp 106 °C (0.9 mm); IR (neat) 2960, 1705, 1322, 1250, 1222, 1148, 1130, 842 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.10 (s, 9 H), 0.15 (s, 9 H), 4.50 (s, 2 H), 5.21 (s, 1 H), 7.20 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ −0.16, 0.47, 74.4, 112.6, 127.5, 127.8, 128.1, 137.8, 144.9. Anal. Calcd for $C_{15}H_{26}O_3Si_2$: C, 58.02; H, 8.44. Found: C, 57.88; H, 8.36.

(*S*)-2-*O*-Benzylpropane-1,2-diol (6). In a 250-mL round-bottomed flask equipped with a mechanical stirrer and a reflux condenser was placed a solution of 13.2 g (0.112 mol) of ethyl (*S*)-lactate and 19.9 mL (28.6 g, 0.167 mol) of benzyl bromide in 60 mL of dry ether. To this solution was added 26.0 g (0.122 mol) of freshly prepared silver(I) oxide over a period of 30 min at a rate so as to maintain a gentle reflux. After the addition was completed, the mixture was heated at reflux for a further 30 min. At that time, TLC of the mixture showed a new UV-active spot (R_f 0.45, hexane–ethyl acetate, 5:1) corresponding to ethyl 2-*O*-benzyl-(*S*)-lactate (**5**). The solid material was removed with filtration and triturated with ether. The solvent was removed from the combined ethereal solution with a rotary evaporator. The residue was used without further purification.

To a stirred suspension of 3.80 g (0.100 mol) of $LiAlH_4$ in 150 mL of dry ether at 0 °C was added a solution of the crude ester **5** in 50 mL of dry ether over a period of 40 min. After being stirred at 0 °C for 40 min, the reaction mixture was quenched at 0 °C by addition of 3.8 mL of water, 3.8 mL of 15% aqueous sodium hydroxide, and 11.4 mL of water. The mixture was filtered and the solid was washed three times with 20 mL of ether. The combined ethereal washes were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Purification by column chromatography (hexane–ethyl acetate, 5:1) on silica gel gave 15.8 g (85%) of colorless liquid **6**: bp 95 °C (1.0 mm); IR (neat) 3425, 2868, 1452, 1060, 730, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (d, J = 6, 3 H), 2.00 (dd, J = 4,6, 1 H), 3.35–3.70 (m, 3 H), 4.37 (d, J = 11, 1 H), 4.62 (d, J = 11, 1 H), 7.25 (m, 5 H); $[\alpha]_D$ +45.86 ($CHCl_3$, *c* 6.4).

(*S*)-2-(Benzyloxy)propanal (2). In a 500-mL three-necked flask equipped with two dropping funnels and magnetic stirring bar was placed 1.92 mL (2.79 g, 22.0 mmol) of oxalyl chloride and

(17) ^1H NMR spectra were determined at 200, 250, or 300 MHz. ^{13}C NMR spectra were measured at 50.31 or 62.89 MHz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Significant ^1H NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant(s), number of protons. For other general experimental details, see ref 15b.

100 mL of dry dichloromethane. The solution was cooled to −60 to −70 °C and a solution of 3.12 mL (3.44 g, 44.0 mmol) of dimethyl sulfoxide in 20 mL of dry dichloromethane was added. During the course of the addition, exothermic gas evolution was observed and the reaction temperature was kept below −50 °C. After 20 min, a solution of 3.32 g (20.0 mmol) of alcohol **6** in 20 mL of dry dichloromethane was added over a period of 5 min. Stirring was continued while 13.9 mL (10.1 g, 0.100 mol) of triethylamine was added, keeping the temperature below −40 °C. After being stirred at −50 °C for 5 min and 25 °C for 10 min, the reaction mixture was poured into water and the separated aqueous layer was extracted three times with dichloromethane. The combined extracts were washed two times with brine, dried over anhydrous magnesium sulfate, and concentrated with a rotary evaporator. The residue was purified by column chromatography (hexane–ethyl acetate, 20:1 to 10:1) on silica gel with dry ice cooling to afford 2.71 g (83%) of aldehyde **2** as a colorless liquid: IR (neat) 2860, 1740, 1455, 1088, 730, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (d, J = 7, 3 H), 3.82 (dq, J = 1,7, 1 H), 4.59 (s, 2 H), 7.28 (m, 5 H), 9.60 (d, J = 1, 1 H); $[\alpha]_D$ = −52.2 ($CHCl_3$, c 6.5).

Preparation of 2,4-Bis(benzyloxy)-1,3-pentanediol Acetonides (9–12). To a solution of 11.2 mL (8.09 g, 80.0 mmol) of diisopropylamine in 350 mL of dry THF at 0 °C was added 48.5 mL (80.0 mmol) of a 1.65 M solution of n-butyllithium in hexane. The resulting solution was stirred for 20 min and then cooled to −78 °C. A solution of 13.5 g (75.0 mmol) of methyl 2-(benzyloxy)acetate (**1**) in 100 mL of dry THF was added over a period of 30 min and the mixture was stirred for an additional 40 min. A solution of 4.10 g (25.0 mmol) of 2-(benzyloxy)propanal (**2**) in 50 mL of dry THF was added slowly at −78 °C. After stirring at −78 °C for 50 min, the mixture was poured into saturated NH_4Cl solution (400 mL) and separated. The aqueous layer was extracted with ether (3 × 30 mL) and the combined extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated with a rotary evaporator.

A solution of the crude β-hydroxy esters in 50 mL of ether was added slowly at 0 °C to a stirred suspension of 4.56 g (0.120 mol) of $LiAlH_4$ in 200 mL of ether. After stirring at 0 °C for 40 min, the reaction was quenched by addition of 4.56 mL of water, 4.56 mL of 15% NaOH solution, and 13.7 mL of water. The resulting mixture was stirred at 25 °C for an additional 1 h and filtered. The filtrate was concentrated with a rotary evaporator and purified by column chromatography (hexane–ethyl acetate, 2:1) on silica gel. The yield of the mixture of 2,4-bis(benzyloxy)-1,3-pentanediols (**13–16**) was 31% (2.45 g, based on aldehyde **2**). As it was difficult to separate the four diastereomers, the mixture of the diols was transformed into acetonides.

A mixture of 2.45 g (7.75 mmol) of 2,4-bis(benzyloxy)-1,3-pentanediols (**13–16**) in 150 mL of acetone, 150 mL of benzene, and a catalytic amount of p-TsOH (0.15 g, 0.78 mmol) was placed in a 500-mL round-bottomed flask equipped with a Soxhlet extraction apparatus containing 50 g of 4Å molecular sieves and stirring bar. The mixture was heated at reflux for 8 h. TLC analysis (hexane–ethyl acetate, 15:1, 2 elutions) of the mixture showed five UV active bands, R_f 0.40 (acetonide **9**), R_f 0.36 (acetonide **10**), R_f 0.34 (acetonide **11**), R_f 0.26 (acetonide **12**), and mesityl oxide. The reaction mixture was poured into 100 mL of 2 N NaOH solution and separated. The aqueous layer was extracted with ether (2 × 40 mL). The separated organic layers were washed with brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated with a rotary evaporator. The crude product was separated by column chromatography (hexane–ethyl acetate, 20:1) on silica gel to give 0.83 g (30%) of acetonide **9**, 0.48 g (17%) of acetonide **10**, 0.87 g (32%) of acetonide **11**, and 0.11 g (4%) of acetonide **12**.

Acetonide 9: IR (neat) 2998, 1498, 1456, 1380, 1222, 1095, 905, 730, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (d, J = 6.6, 3 H), 1.39 (s, 3 H), 1.47 (s, 3 H), 3.50 (ddd, J = 5.0, 7.5, 9.0, 1 H), 3.71 (dd, J = 7.5, 11.2, 1 H), 3.74 (dq, J = 2.0, 6.6, 1 H), 3.90 (dd, J = 5.0, 11.2, 1 H), 3.91 (dd, J = 2.0, 9.0, 1 H), 4.43 (d, J = 11.6, 1 H), 4.54 (d, J = 11.6, 1 H), 4.63 (s, 2 H), 7.20–7.41 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 14.8, 20.0, 27.7, 62.2, 70.9, 71.5, 74.1, 74.2, 98.9, 127.3, 127.6, 127.7, 127.8, 128.2, 128.3, 137.7, 138.8. Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.96; H, 7.85.

Acetonide 10: IR (neat) 2998, 2874, 1498, 1456, 1372, 1224, 1092, 1070, 868, 732, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (d, J = 6.5, 3 H), 1.41 (s, 3 H), 1.42 (s, 3 H), 3.58 (dd, J = 2.4, 9.0, 1 H), 3.68 (dd, J = 6.7, 11.0, 1 H), 3.78 (ddd, J = 4.5, 6.7, 9.0, 1 H), 3.86 (dq, J = 2.4, 6.5, 1 H), 3.92 (dd, J = 4.5, 11.0, 1 H), 4.23 (d, J = 11.3, 1 H), 4.38 (d, J = 11.3, 1 H), 4.39 (d, J = 12.1, 1 H), 4.68 (d, J = 12.1, 1 H), 7.14–7.40 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 15.0, 20.2, 27.4, 62.6, 70.9, 71.6, 71.8, 75.1, 99.3, 127.4, 127.7, 127.8, 128.0, 128.2, 128.3, 138.0, 138.7. Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.15; H, 8.03.

Acetonide 11: IR (neat) 2998, 2872, 1455, 1368, 1200, 1098, 850, 730, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (d, J = 6.0, 3 H), 1.43 (s, 3 H), 1.44 (s, 3 H), 3.57 (ddd, J = 1.8, 1.9, 1.9, 1 H), 3.68 (dd, J = 1.8, 8.9, 1 H), 3.86 (dd, J = 1.9, 12.9, 1 H), 3.94 (dq, J = 8.9, 6.0, 1 H), 4.03 (dd, J = 1.9, 12.9, 1 H), 4.32 (d, J = 11.2, 1 H), 4.50 (d, J = 12.0, 1 H), 4.61 (d, J = 11.2, 1 H), 4.68 (d, J = 12.0, 1 H), 7.20–7.42 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 16.1, 18.8, 29.1, 61.6, 69.2, 70.8, 71.0, 72.8, 74.8, 98.6, 127.4, 127.6, 127.7, 127.9, 128.2, 138.4, 138.5. Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.89; H, 8.05.

Acetonide 12: IR (neat) 3002, 2895, 1462, 1392, 1215, 1100, 864, 750, 716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (d, J = 7.1, 3 H), 1.46 (s, 3 H), 1.49 (s, 3 H), 3.23 (ddd, J = 1.8, 2.0, 2.0, 1 H), 3.72 (dd, J = 1.8, 8.1, 1 H), 3.83 (dq, J = 8.1, 7.1, 1 H), 3.90 (dd, J = 2.0, 13.1, 1 H), 4.11 (dd, J = 2.0, 13.1, 1 H), 4.42 (d, J = 12.0, 1 H), 4.61 (d, J = 11.7, 1 H), 4.75 (d, J = 12.0, 1 H), 4.77 (d, J = 11.7, 1 H), 7.22–7.45 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 16.0, 18.9, 29.1, 60.7, 69.8, 70.2, 73.0, 75.2, 76.7, 98.5, 127.1, 127.4, 127.6, 128.0, 128.2, 137.6, 139.4. Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.99; H, 7.92.

2,4-Bis(benzyloxy) 1,3-Diols (13–16). A mixture of 0.36 g (1.0 mmol) of acetonide, 20 mL of THF, and 20 mL of 1 N HCl solution was stirred at 25 °C for 3 h. The resulting mixture was poured into 15 mL of water and extracted with ethyl acetate (4 × 15 mL). The combined extracts were dried over $MgSO_4$ and concentrated with a rotary evaporator. Purification of the crude diol by preparative TLC (hexane–ethyl acetate, 1:1) afforded the diol in about 90% yield (ca. 0.28 g).

Diol 13: IR (neat) 3450, 2880, 1500, 1458, 1090, 735, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (d, J = 6.3, 3 H), 2.56 (bs, 1 H), 2.64 (bs, 1 H), 3.51–3.58 (m, 1 H), 3.70–3.78 (m, 1 H), 3.78–3.92 (m, 2 H), 3.98 (bt, J = 4.9, 1 H), 4.48 (d, J = 6.9, 1 H), 4.52 (d, J = 6.9, 1 H), 4.60 (d, J = 8.1, 1 H), 4.64 (d, J = 8.1, 1 H), 7.24–7.41 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 61.0, 70.7, 71.5, 73.1, 75.0, 78.1, 127.6, 127.7, 127.9, 128.3, 128.4, 137.7, 138.1. Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 71.88; H, 7.58.

Diol 14: IR (neat) 3450, 2945, 2885, 1500, 1458, 1090, 1062, 736, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (d, J = 6.3, 3 H), 2.45 (bs, 1 H), 2.60 (bs, 1 H), 3.47–3.60 (m, 2 H), 3.75–3.90 (m, 3 H), 4.30 (d, J = 11.5, 1 H), 4.36 (d, J = 11.5, 1 H), 4.57 (d, J = 11.6, 1 H), 4.62 (d, J = 11.6, 1 H), 7.22–7.40 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 16.0, 61.5, 70.6, 71.8, 72.8, 75.0, 78.5, 127.7, 127.8, 127.9, 128.4, 137.9, 138.1.

Diol 15: IR (neat) 3440, 2980, 1460, 1110, 750, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (d, J = 5.5, 3 H), 2.43 (bs, 1 H), 2.72 (bs, 1 H), 3.48–3.66 (m, 2 H), 3.66–3.90 (m, 3 H), 4.31 (d, J = 11.2, 1 H), 4.49 (d, J = 11.9, 1 H), 4.59 (d, J = 11.9, 1 H), 4.64 (d, J = 11.2, 1 H), 7.22–7.40 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 15.8, 63.0, 70.5, 72.7, 74.9, 75.4, 77.6, 127.7, 127.9, 128.4, 128.5, 138.1, 138.2.

Diol 16: IR (neat) 3450, 2952, 2900, 1504, 1462, 1080, 748, 716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, J = 6.0, 3 H), 2.62 (bs, 1 H), 2.88 (bs, 1 H), 3.53–3.62 (m, 1 H), 3.62–3.94 (m, 4 H), 4.44 (d, J = 11.5, 1 H), 4.56 (d, J = 11.6, 1 H), 4.67 (d, J = 11.5, 1 H), 4.73 (d, J = 11.6, 1 H), 7.20–7.43 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 15.1, 61.7, 71.0, 72.0, 74.9, 75.7, 77.9, 127.9, 127.9, 128.0, 128.5, 137.9.

Pentane-1,2,3,4-tetrol Tetraacetates (17–20). A mixture of 0.32 g (1.0 mmol) of diol, 48 mg of 10% Pd/C, and 0.2 drops of $HClO_4$ in 5 mL of ether and 5 mL of ethanol was stirred under hydrogen at 25 °C for 3 h. When hydrogen uptake ceased, 27 mg (0.20 mmol) of potassium carbonate was added to neutralize the acidic condition. The mixture was filtered and the filtrate was concentrated with a rotary evaporator. The 1,2,3,4-pentanetetrol was treated with 5.7 mL (6.1 g, 60 mmol) of acetic anhydride and 24 mL (23 g, 0.29 mol) of pyridine at 25 °C for 2 h. The mixture was poured into 0.5 N HCl solution (100 mL) and extracted with ethyl acetate (3 × 20 mL). The organic extracts were dried over $MgSO_4$ and concentrated with a rotary evaporator. Purification of the crude product by column chromatography

(hexane–ethyl acetate, 10:1) gave pure tetraacetate in 65–75% yield (0.20–0.23 g).

Tetraacetate 17: IR (neat) 3000, 1750, 1380, 1240, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (d, J = 6.5, 3 H), 2.06 (s, 6 H), 2.10 (s, 6 H), 4.10–4.21 (m, 1 H), 4.36 (dd, J = 1.6, 10, 1 H), 5.09 (dq, J = 4.2, 6.4, 1 H), 5.20–5.32 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.3, 20.6, 20.6, 20.8, 21.0, 62.0, 69.0, 70.0, 71.9, 169.6, 169.8, 169.9, 170.5. Anal. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.62. Found: C, 51.20; H, 6.66.

Tetraacetate 18: IR ($CHCl_3$) 3000, 1750, 1375, 1250, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, J = 6.5, 3 H), 2.05 (s, 3 H), 2.06 (s, 6 H), 2.15 (s, 3 H), 4.15 (dd, J = 4.4, 12.4, 1 H), 4.26 (dd, J = 2.1, 12.4, 1 H), 5.12–5.28 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 16.3, 20.6, 20.7, 20.8, 21.0, 61.9, 67.3, 68.5, 71.3, 169.8, 170.0, 170.2, 170.6. Anal. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.62. Found: C, 50.92; H, 6.56.

Tetraacetate 19: IR (neat) 3000, 1750, 1378, 1220, 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (d, J = 6.4, 3 H), 2.03 (s, 3 H), 2.06 (s, 3 H), 2.08 (s, 3 H), 2.14 (s, 3 H), 3.97 (dd, J = 6.0, 11.7, 1 H), 4.24 (dd, J = 5.0, 11.7, 1 H), 5.01 (dq, J = 7.4, 6.6, 1 H), 5.20–5.30 (m, 1 H), 5.35–5.45 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.1, 20.7, 21.0, 62.0, 67.0, 68.2, 72.0, 169.9, 170.0, 170.5. Anal. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.62. Found: C, 50.99; H, 6.62.

Tetraacetate 20: IR ($CHCl_3$) 3040, 1750, 1380, 1240, 1070, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, J = 6.4, 3 H), 2.06 (s, 3 H), 2.07 (s, 3 H), 2.10 (s, 3 H), 2.12 (s, 3 H), 3.94 (dd, J = 6.0, 12.0, 1 H), 4.35 (dd, J = 4.3, 12.0, 1 H), 5.02–5.17 (m, 1 H), 5.17–5.35 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.3, 20.6, 20.7, 20.8, 21.0, 62.0, 68.5, 69.3, 72.3, 170.0, 170.1, 170.4. Anal. Calcd for $C_{13}H_{20}O_8$; C, 51.31; H, 6.62. Found: C, 51.08; H, 6.66.

Tetraacetate **19** was also prepared from 5-deoxy-L-arabinose. A solution of 19 mg (0.5 mmol) of $NaBH_4$ in 2.5 mL of water was added at 25 °C to a solution of 120 mg (0.89 mmol) of 5-deoxy-L-arabinose[13] in 1.5 mL of water. Hydrogen gas evolution was observed immediately. The reaction mixture became faintly alkaline and was kept at 25 °C until a drop of it after acidification with acetic acid no longer reduced Fehling solution (2–3 h). The pH was brought to 5 with acetic acid to destroy the excess $NaBH_4$. The resulting mixture was evaporated to dryness under reduced pressure and the dry residue was shaken with 2.0 mL of acetic anhydride and 0.1 mL of sulfuric acid until most of the solid had dissolved and then the whole was warmed at 50 °C for 10 min. The reaction mixture was allowed to cool and poured into 10 mL of ice cold water with stirring. The mixture was extracted with ethyl acetate (4 × 5 mL) and the separated organic layer was washed with brine (5 mL), dried ($MgSO_4$), and concentrated with a rotary evaporator. Purification by preparative TLC (hexane–ethyl acetate, 2:1) gave 0.19 g (72%) of tetraacetate, identical by NMR spectroscopy with tetraacetate **19**.

1,2,3,4-Pentanetetrol 1,3-Acetonide 2,4-Cyclic Carbonate (21). To a stirring solution of 0.21 g (0.58 mmol) of acetonide **9** in 15 mL of liquid NH_3 and 8 mL of THF at –78 °C was added 0.080 g (3.5 mmol) of sodium in portions. The color of the solution turned dark blue gradually. The resulting mixture was stirred at –23 °C (CCl_4–dry ice) for 1 h. The reaction was carefully quenched by addition of 0.37 g (7.0 mmol) of ammonium chloride. The mixture was evaporated to dryness under a stream of nitrogen. The solid residue was dissolved in 10 mL of water and extracted with ethyl acetate (3 × 10 mL). The combined extracts were dried over $MgSO_4$ and concentrated with a rotary evaporator. Purification by preparative TLC (hexane–ethyl acetate, 1:1) afforded 74 mg (72%) of 1,2,3,4-pentanetetraol 1,3-acetonide: ^1H NMR ($CDCl_3$) δ 1.27 (d, J = 6.2, 3 H), 1.37 (s, 3 H), 1.47 (s, 3 H), 2.60 (bs, 1 H), 3.41 (bs, 1 H), 3.41 (dd, J = 6.9, 8.5, 1 H), 3.62 (dd, J = 8.5, 10.7, 1 H), 3.72–3.83 (m, 1 H), 3.83–3.97 (m, 2 H).

A solution of 74 mg (0.42 mmol) of 1,2,3,4-pentanetetrol 1,3-acetonide and 0.14 g (0.84 mmol) of 1,1-carbonyldiimidazole in 10 mL of benzene was heated at reflux. After 3 h 0.14 g (0.84 mmol) of additional 1-carbonyldiimidazole was added and the mixture was heated at reflux for an additional 3 h. The mixture was allowed to cool to room temperature and poured into water (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 6 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated with a rotary evaporator. Purification of the crude product by preparative TLC (hexane–ethyl acetate, 2:1, R_f 0.31) afforded the desired cyclic carbonate in 22% (19 mg) yield: ^1H NMR ($CDCl_3$) δ 1.44 (d, J = 6.2, 3 H), 1.58 (s, 6 H), 3.64 (dd, J = 9.2, 9.4, 1 H), 3.83 (dd, J = 9.7, 10.7, 1 H), 4.04 (dd, J = 5.3, 10.7, 1 H), 4.22 (ddd, J = 5.3, 9.4, 9.7, 1 H), 4.47 (dq, J = 9.2, 6.2, 1 H).

General Procedure for Lewis Acid Mediated Additions of 3 to 2. To a stirring solution of 1.1 mmol of Lewis acid in 3 mL of dichloromethane at –78 °C was added slowly a solution of 0.16 g (1.0 mmol) of 2-(benzyloxy)propanal (**2**) in 0.5 mL of dichloromethane. The mixture was stirred at –78 °C for 10 min, a solution of 0.36 g (1.1 mmol) of 2-(benzyloxy)-1,1-bis(trimethylsiloxy)ethane (**3**) in 0.5 mL of dichloromethane was added, and the mixture was stirred at –78 °C for 1–4 h. Reaction was quenched by an addition of water (4 mL) and the mixture was warmed to 25 °C. The separated organic layer was extracted with ethyl acetate (2 × 5 mL) and chloroform (2 × 5 mL). The combined extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, and concentrated with a rotary evaporator.

To a suspension of 0.13 g (3.5 mmol) of $LiAlH_4$ in 14 mL of ether at 0 °C was added slowly a solution of a mixture of the aldol adducts in 3.5 mL of ether. The resulting mixture was stirred at 0 °C for 30 min and 25 °C for 1 h. After the usual workup of $LiAlH_4$ (N, N, 3N method),[18] the crude product was roughly purified by preparative TLC (hexane–ethyl acetate, 1:1). The resulting mixture of 2,4-bis(benzyloxy)-1,3-pentanediols (**13–16**) was transformed to 1,2,3,4-tetraacetoxypentanes (**17–20**) or 2,4-bis(benzyloxy)-1,3-pentanediol acetonides (**9–12**) by the method described previously.

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Registry No. **1**, 31600-43-8; **1** (Li enolate), 97416-53-0; **2**, 81445-44-5; **3**, 97416-40-5; **4**, 687-47-8; **5**, 54783-72-1; **6**, 33106-64-8; **7**, 30379-55-6; **8**, 97416-41-6; **9**, 97416-42-7; **10**, 97466-32-5; **11**, 97466-33-6; **12**, 97466-34-7; **13**, 97416-43-8; **14**, 97466-35-8; **15**, 97466-36-9; **16**, 97466-37-0; **17**, 7260-90-4; **18**, 96554-72-2; **19**, 90129-07-0; **20**, 7226-55-3; **21**, 97416-44-9; 2,4-di-*O*-benzyl-5-deoxy-L-ribonic acid methyl ester, 97416-45-0; 2,4-di-*O*-benzyl-5-deoxy-L-arabonic acid methyl ester, 97416-46-1; 2,4-di-*O*-benzyl-5-deoxy-L-lyxonic acid methyl ester, 97416-47-2; 2,4-di-*O*-benzyl-5-deoxy-L-xylonic acid methyl ester, 97416-48-3; 1-deoxy-D-ribitol, 13046-76-9; 1-deoxy-L-arabinitol, 92622-02-1; 1-deoxy-L-lyxitol, 97466-38-1; 1-deoxy-D-xylitol, 68832-17-7; 5-deoxy-L-arabinose, 13039-56-0; 1,2,3,4-pentanetetrol 1,3-acetonide, 83657-34-5; 2,4-di-*O*-benzyl-5-deoxy-L-ribonic acid, 97416-49-4; 2,4-di-*O*-benzyl-5-deoxy-L-arabonic acid, 97416-50-7; 2,4-di-*O*-benzyl-5-deoxy-L-lyxonic acid, 97416-51-8; 2,4-di-*O*-benzyl-5-deoxy-L-xylonic acid, 97416-52-9.

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