Deoxyribose-5-phosphate Aldolase as a Catalyst in Asymmetric Aldol Condensation

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Abstract: This paper describes the substrate specificity and synthetic utility of deoxyribose-5-phosphate aldolase (DERA, EC 4.1.2.4). Eight donors and 20 acceptors have been tested as substrates. In addition to acetaldehyde, propanal, acetone, and fluoroacetone have been used to condense with a number of acceptor aldehydes. Thirteen aldol products have been prepared and characterized. A new stereogenic center with 3(*S*) configuration is formed when acetaldehyde, fluoroacetone, or acetone is used as a donor substrate. With propanal, two new stereogenic centers are formed with 2(*R*) and 3(*S*) configurations. The acceptor substrates have very little structural requirements. The 2-hydroxyaldehydes appear to react the fastest, and the D-isomers are better substrates than the L-isomers. The stereospecificity is absolute regardless of the chirality of 2-hydroxyaldehydes. The aldol reactions thus follow the Cram-Felkin mode of attack for D-substrates and anti-Cram-Felkin mode of attack for L-substrates.

Introduction

Asymmetric aldol condensation is a topic of current interest in synthetic organic chemistry.[1] While considerable progress based on nonbiological methods has been made, these methods generally require low temperature and organic solvent to achieve high asymmetric induction. Enzyme-catalyzed aldol condensations, however, are often carried out in aqueous solution at neutral pH and room temperature.[2] The aldol products obtained in enzymatic reactions are usually unprotected and quite different from those obtained via nonenzymatic aldol reactions. Of more than 20 aldolases known so far, most exhibit relaxed acceptor specificity with a high degree of "absolute" stereoselectivity in the aldol reaction, i.e., the selectivity is completely controlled by the enzyme, not by the substrate. When a racemic aldehyde is used as an acceptor, often only one enantiomer is accepted, and the C-nucleophile often attacks only one of the two diastereotopic π-faces of the carbonyl group.

Among the aldolases proven to be useful in organic synthesis is 2-deoxyribose-5-phosphate aldolase (DERA, EC 4.1.2.4),[3] a 28 000 kD enzyme that reversibly catalyzes the condensation of acetaldehyde and D-glyceraldehyde 3-phosphate (D-G3P) to form 2-deoxyribose-5-phosphate (DRP, see **1b**, Scheme I). In *Escherichia coli*, DERA is associated with thymidine phosphorylase, purine nucleoside phosphorylase, and phosphopentomutase in the *deo* regulon.[4] This enzymatic reaction proceeds through a Schiff base intermediate[5] and is the only aldolase which accepts two aldehydes in the condensation reaction, while other aldolases require a ketone and an aldehyde.

Preliminary data from our laboratory has established that in addition to the donor substrate acetaldehyde and the wide variety of acceptors, DERA accepts at least two ketones as donor substrates,[3] acetone and fluoroacetone, albeit at slower rates. The addition of arsenate to D-glyceraldehyde does not, however, increase the reaction significantly as was observed with FDP aldolase.[6] This two-dimensional variability in substrate specificity

Table I. Purification of DERA[a] from 72-g Cells (Wet Weight)

step	vol. (mL)	units	mg/mL	sp ac (U/mg)	%
lysate	272	33 700	169	0.73	100
strept sulf	280	36 000	148	0.87	107
am sulf	75	25 900	273	1.3	77
dialysate	112	40 900	200	1.83	121
(1/10 further purified)					
mono Q	58	3840	0.4	166	114
phen seph	100	3600	1.9	189[b]	107

[a] Containing 259 amino acids with a molecular weight of 28 000 kD (see ref 7). [b] k_{cat} = 156 s^{-1}, K_m for DRP = 0.193 mM.

Table II. Relative Rates of DERA-Catalyzed Reactions Uisng D-G3P As an Acceptor[a]

donor	V_{rel}	donor	V_{rel}
CH_3CHO	100	$ClCH_2CHO$	~0
$(CH_3)_2CO$	0.7	$HOCH_2CHO$	~0
CH_3COCH_2F	0.6	CH_3COCH_2OH	~0
CH_3CH_2CHO	0.4	CH_3COCN	~0

[a] See Experimental Section for details.

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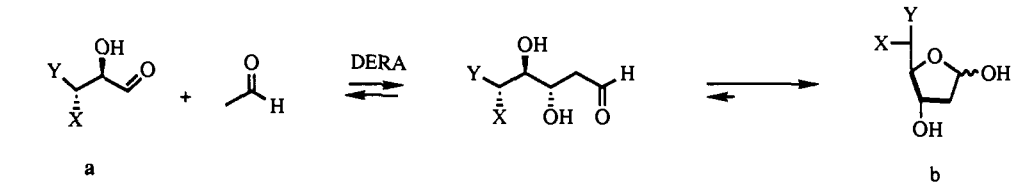
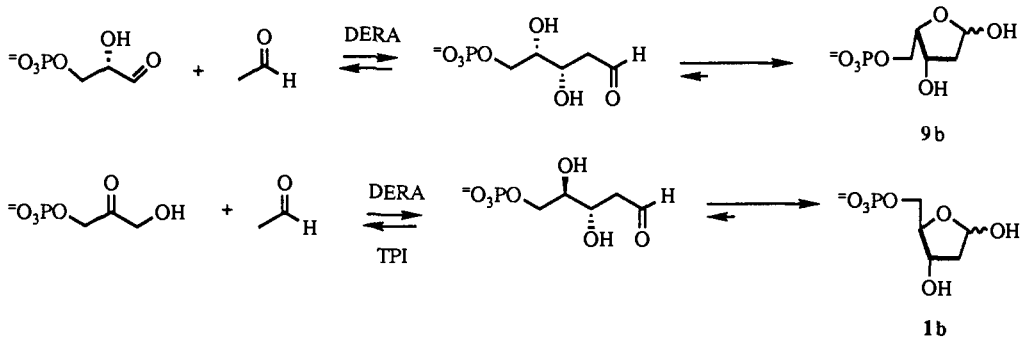
Scheme I. DERA-Catalyzed Syntheses of Aldoses by Using Acetaldehyde As a Donor



	X	Y
1	$OPO_3^=$	H
2	N_3	H
3	F	H
4	Cl	H
5	H	H
6	OH	H
7	OH	CH_2OH
8	CH_3	H



provides the means for the synthesis of an exceptional array of 2-deoxysugars. As such, DERA offers a convenient route toward a number of aldoses and ketoses. This report further details the substrate specificity of the recombinant DERA and the application of this enzyme to the synthesis of carbohydrate related compounds.

Results and Discussion

Preparation of DERA. The overexpression of *E. coli* DERA has been achieved as a part of the cloned *deo C* system described by Valentin-Hansen et al.[7] This plasmid, pVH17, was obtained and transformed into *E. coli* strain DH5α. A total of 6 L of DH5α/pVH17 was grown in LB broth at 37 °C with agitation. This culture provided about 40 000 units of DERA where 1 unit is that amount of enzyme required to cleave 1 μmol DRP per minute at 25 °C. DERA is readily purified to apparent homogeneity as judged by SDS polyacrylamide gel electrophoresis as outlined in Table I. For the purposes of synthesis, large quantities of DERA can rapidly be purified by ammonium sulfate fractionation and dialysis. Lyophilization of this product provides an enzyme preparation that may be stored for an indefinite time at 4 °C with no loss in activity.

Synthesis of Acceptor Substrates. The synthesis of the diethyl acetals of compounds **1a–5a** have previously been reported.[8] These are prepared chemoenzymatically with lipase resolution after ring opening and acylation of glycidaldehyde diethyl acetal or by ring opening of the chiral epoxide. 2-Hydroxybutanal was synthesized by the regioselective opening of glycidaldehyde diethyl acetal with Lipshutz's methyl cuprate, $(CH_3)_2CuCNLi_2$.[9] When ring opening was attempted with CH_3MgBr, a mixture of 2-hydroxybutanal diethyl acetal (38%) and 3-hydroxy-2-methylpropanal diethyl acetal (62%) was obtained. The preferential attack at the primary carbon with Lipshutz's methyl cuprate may be related to the relative softness of this reagent compared to methyl magnesium bromide.[10] Dihydroxyacetone phosphate,[11] DL-4-azido-3-hydroxybutanal,[12] and DL-2-acetamido-3-azidopropanal[13] were made as described previously.

Substrate Specificity. Like other aldolases, the specificity of DERA is most restricted for its substrate donors. The K_m for acetaldehyde is 1.7 ± 0.2 mM. Among the compounds tested as donors, propanal, acetone, and fluoroacetone proved to be substrates for DERA (Table II). Fluoroacetone reacts regioselectively at the nonsubstituted carbon as would be expected from the deactivating effect of fluorine for the formation of the enamine.[14] Acetol, chloroacetaldehyde, pyruvonitrile, and hy-

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(9) Lipshutz, B. H.; Kozlowski, J.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305.
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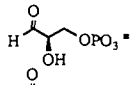
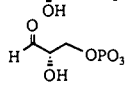
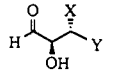
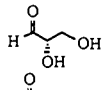
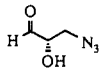
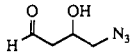
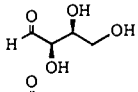
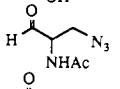
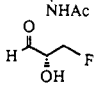
Table III. Relative Rates of DERA-Catalyzed Reactions Using Acetaldehyde As a Donor

Acceptor	X	Y	V_{rel}
			100[a]
			5[b]
	H	H	0.4
	OH	H	0.4
	F	H	0.4
	CH_3	H	0.3
	Cl	H	0.3
	N_3	H	0.3
	OH	CH_2OH	0.3
			0.3
			0.2
			0.2
			0.07
			0.03
			~0
			~0
			~0
			~0
			~0

[a] K_m = 0.7 mM. [b] K_m = 0.3 mM.

droxyacetaldehyde did not react at detectable rates. Presumably this is due to steric hindrance in the active site. Otherwise one would expect activation of the α hydrogens in these compounds by induction. The finding that DERA accepts fluoroacetone and acetone as nucleophilic substrates sets this enzyme apart in that no other aldolase has been reported to tolerate both aldehydes and ketones as donors. The synthetic route toward 1-methyl and 1-fluoromethyl sugars is as straightforward as their unmethylated counterparts.

A summation of the acceptor substrate specificity is compiled in Table III. This data clearly demonstrates the flexibility of DERA for the electrophilic component of the aldol condensation. There is little change in affinity for L-G3P versus D-G3P as is reflected in the Michaelis constants for these compounds—0.3 ± 0.1 and 0.7 ± 0.2 mM, respectively. The relative velocities for these compounds, however, do not reflect this equivalence in binding affinities since D-G3P is favored as a substrate by a factor of 20. It is therefore evident that in spite of the comparable binding, L-G3P must be oriented in the active site in such a fashion as to reduce the reactivity. This trend is also reflected in comparing the relative velocities of L- to D-3-azido-2-hydroxypropanal but not significantly for L-glyceraldehyde to D-glyceraldehyde. Improvement of the enantioselectivity may be achieved by limiting reaction times or by maintaining an excess of the racemic acceptor substrate. Deviation of functionality at C-3 from a hydroxy group to the halides and azide or removal of functionality altogether

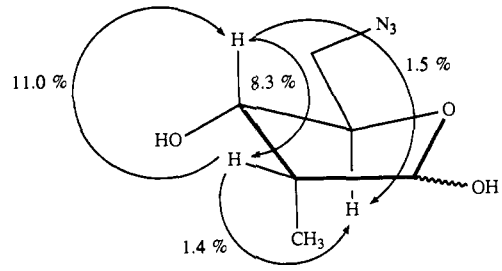


Figure 1. NOE of 5-azido-2(*R*)-methyl-2,5-dideoxy-D-ribofuranose (**12**).

has little effect on the activity of DERA, but these variants all fall well short of the activity of D-G3P, indicating the importance of the phosphate group. On the other hand, removal of functionality at C-2 diminishes the activity of DERA even though stereochemistry at this site does not appear to play a major role in determining this selectivity. This conclusion is drawn from the comparison of propanal and butanal to 2-methylpropanal and then upon realization that 2-methylpropanal is as competent a substrate as L-glyceraldehyde. There are limits to the substrates accepted by DERA. No products could be detected after 2 days by ^{1}H-NMR spectroscopy for the reaction of acetaldehyde with L-3-azido-2-hydroxypropanal, L-3-fluoro-2-hydroxypropanal, DL-4-azido-3-hydroxybutanal, or DL-2-acetamido-3-azidopropanal.

Stereochemistry. The DERAs from *Lactobacillus plantarum*[15] and *Salmonella typhimurium*[16] have been shown to have complete equilibration of the methyl group protons prior to release of acetaldehyde from the enzyme active site. While this equilibrium might be viewed as a lack in stereospecificity, current information favors a rapid rotation of the methyl group after formation of the enamine.[16] Like these enzymes, the *E. coli* DERA exchanges all of the methyl group protons as is observed by the deuterium incorporation in the ^{1}H-NMR spectrum after incubation of DERA with acetaldehyde in D_2O. In this experiment the quartets at 9.60 ppm (CH_3CHO) and 5.17 ppm ($CH_3CH(OH)_2$) turn into singlets. Incubation of the enzyme with propanal, however, results in the exchange of only one proton. This is reflected in the integration of the proton spectrum and the shift of the methyl triplet signals to doublets. Prolonged incubation of the enzyme with propanal results in no further incorporation of deuterium. Clearly, the *E. coli* DERA (as has also been shown for the *L. plantarum* DERA) reacts stereospecifically at the C-2 group. The absolute configuration of the product of the DERA catalyzed condensation of propanal and D-3-azido-2-hydroxypropanal was determined by NOE (Figure 1). The large NOEs of about 10% observed for the C-2 and C-3 protons indicate a cis orientation of these protons. In comparison, the trans protons at C-3 and C-4 have an NOE of only 1.5%. Furthermore, reductive amination and ring closure of **12** resulted in the synthesis of a six-member ring for which the large coupling constant of 12.4 Hz for the C-1 axial proton (this proton signal appears as an apparent triplet due to the almost identical coupling to the geminal C-1 proton) to the C-2 proton which obviously is in the axial position. Therefore, condensation of propanal with D-3-azido-2-hydroxypropanal generates (*R*) stereochemistry at C-2 of the product. It is not known whether DERA catalyzes this reaction with retention of stereochemistry at C-2 as with other aldolases or with inversion. While this fact has not been rigorously established, the stereochemical course for the reaction with propanal and analogy to other aldolases implies the stereoselective exchange of the *pro* (*S*) hydrogen from propanal by DERA.

Synthesis of Deoxysugars. The use of DERA in the synthesis of deoxysugars provides a new route to a wide range of potentially biologically active compounds. In addition, the incorporation of isotope labels at almost any position of these compounds can be achieved with only minor adjustments of protocol. The natural product, DRP, was synthesized from D-G3P and acetaldehyde.

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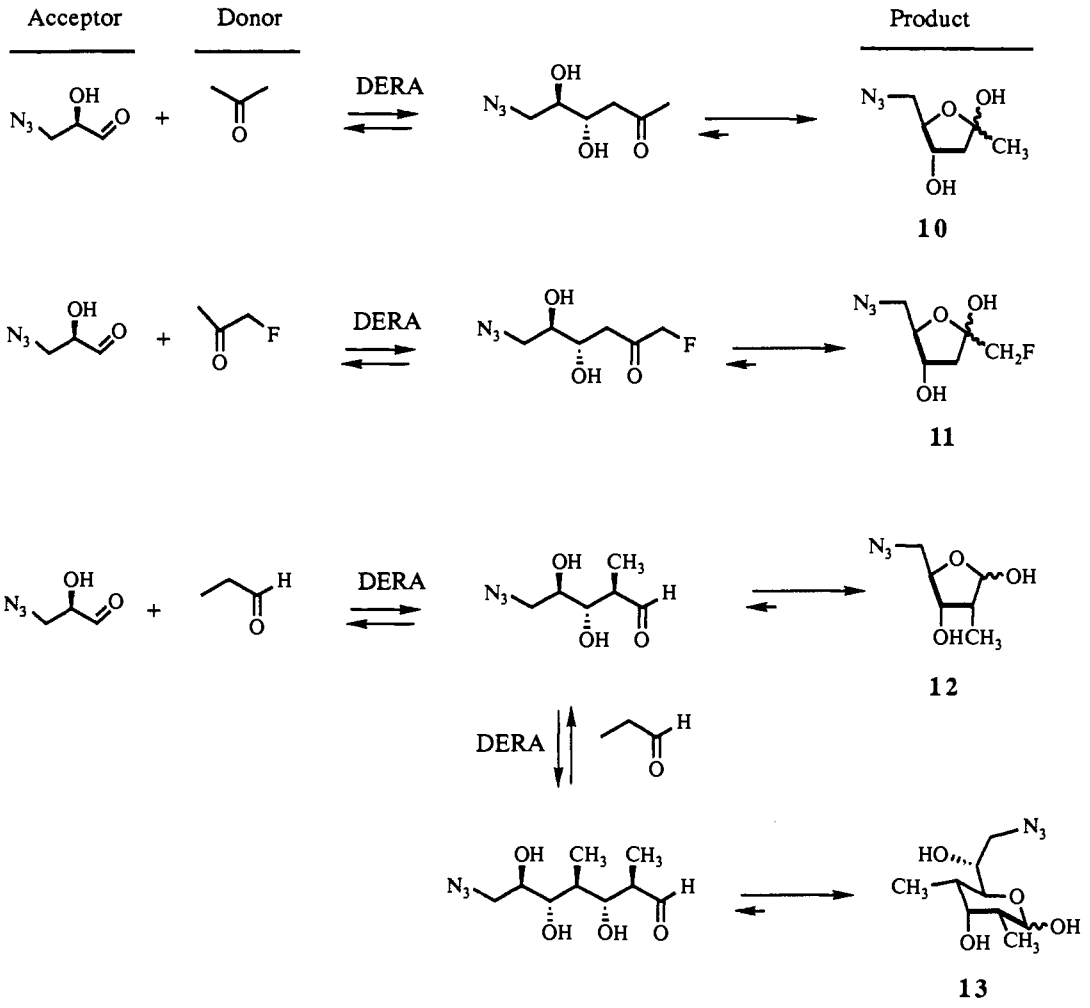
(16) Corina, D. L.; Wilson, D. C. *Biochem. J.* **1976**, *157*, 573.

Scheme II. DERA-Catalyzed Syntheses of Aldoses and Ketoses by Using **2a** As an Acceptor



Similarly, the natural product could be synthesized by coupling the DERA reaction with triose phosphate isomerase (EC 5.3.1.1, TPI) (Scheme I). This would relieve the necessity for the addition of D-G3P by the in situ generation of this substrate from dihydroxyacetone phosphate. The 5-deoxy analogues of DRP recorded in Scheme I were synthesized in good isolated yields ranging from 76% for the azido analogue (**2b**) to 18% for the methyl analogue (**8b**). 5-Chloro-2,5-dideoxy-D-*erythro*-pentofuranose (**4b**) existed as a dimer in methanol as evidenced by the ^{1}H- and ^{13}C-NMR spectra. When this compound was dissolved in D_2O, it dissociated to a monomer. 2,5-Dideoxy-D-*erythro*-pentofuranose (**5b**) has previously been synthesized chemically as a fragment of the boron containing antibiotic boromycin, but these methods are multistepped and result in a mixture of products.[17] Condensation of acetaldehyde with D-glyceraldehyde or D-erythrose produced 2-deoxyribose and 2-deoxyribohexose, respectively. These reactions were carried out in phosphate buffer in order to facilitate the purification. These compounds both exist as mixture of the pyranose and furanose forms in water and thus give rise to quite complicated ^{1}H-NMR spectra as reported.[18] The previously unreported 2,5,6-trideoxy-D-*erythro*-hexofuranose (**8b**) was synthesized from 2-hydroxybutanal and acetaldehyde.

DERA was also used in the synthesis of novel azidosugars (Scheme II). The condensation of propanal with D-3-azido-2-hydroxypropanal resulted in the synthesis of 5-azido-2(*R*)-methyl-2,5-dideoxy-D-*ribo*-furanose (**12**, 20%) and 7-azido-2-(*R*),4(*S*)-dimethyl-2,4,7-trideoxy-D-glycero-D-*allo*-heptopyranose (**13**, 2.1%). The latter compound was formed from the condensation of propanal with the former. Upon successive hydrogenolysis with Pd/C as a catalyst, a new group of azasugars was made with high facial selectivity (Scheme III). This facial selectivity may be explained either by the potential hindrance by axial groups if hydrogen attack were not from the opposite face or hydrogen attack may only proceed from the face which would provide the development of a minimal amount of torsional strain during the course of the reaction. It is worth noting that fluorine was displaced by hydrogen similar to the case of the phosphate displacement reported previously.[13,19] This observation may indicate that the reaction proceeds through an allylic fluoride intermediate (**15a**) in which the fluorine is activated and is thus more susceptible to hydrogen displacement. These compounds, **14**, **15**, **16**, and **17**, bear structural resemblance to piperidine glycosidase inhibitors.[13,19] Compound **17** has been used as a building block in the synthesis of antihypertensive drugs.[20] These compounds may therefore find use as inhibitors of the enzymes associated with oligosaccharide, glycoprotein, or glycolipid processing.

Conclusion

In summary, DERA is capable of catalyzing the syntheses of a wide variety of compounds that may find use in asymmetric synthesis. By using this enzyme in a synthetic scheme, a new stereogenic center with 3(*S*) configuration is formed when ac-

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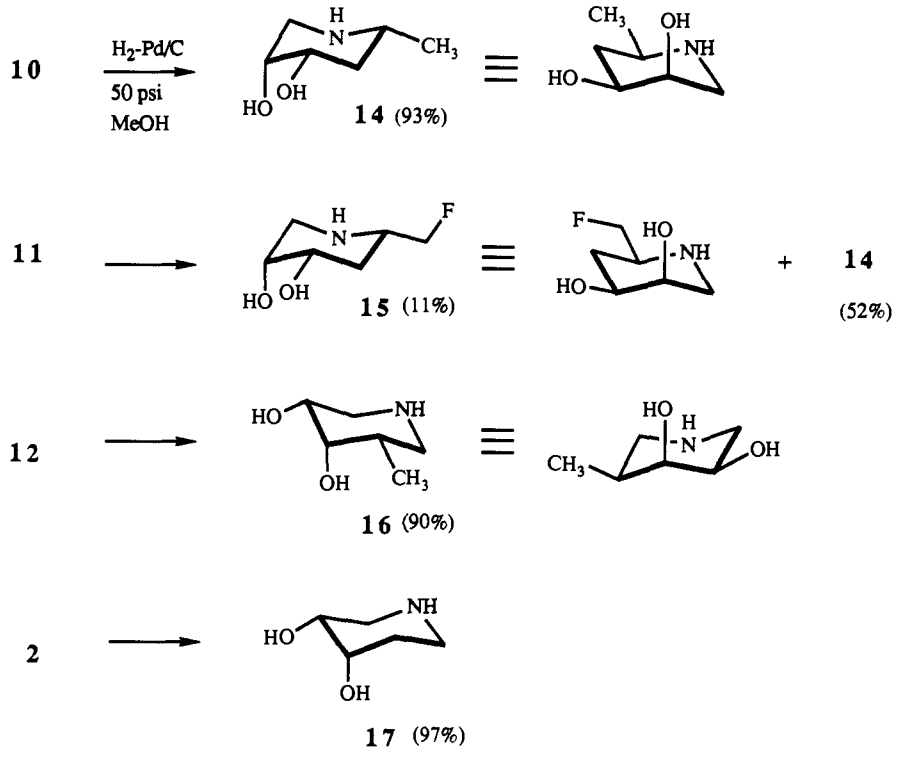
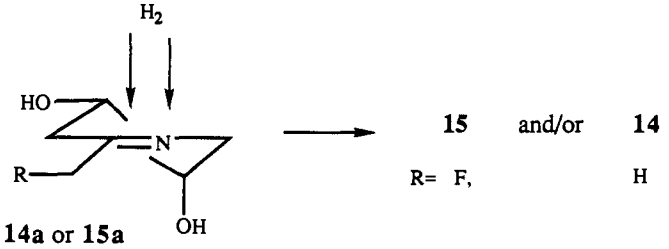
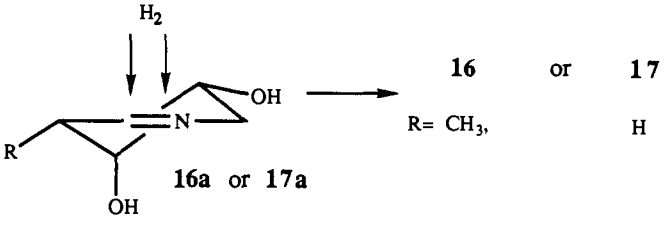
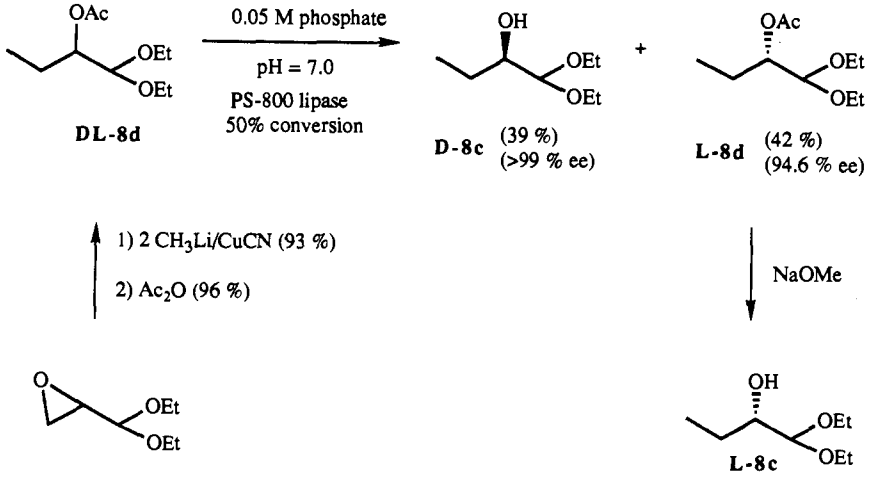
Scheme III. Syntheses of Azasugars by Pd/C-Catalyzed Reductive Amination

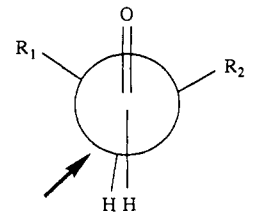






Scheme IV. Synthesis and PS-800 Lipase-Catalyzed Hydrolysis of **8d**





Cram-Felkin mode of attack for good substrates (R_2 = OH).

Anti-Cram-Felkin attack for weak substrates (R_1 = OH).

Figure 2. DERA-catalyzed aldol condensation with 2-hydroxyaldehydes.

etaldehyde, fluoroacetone, or acetone is used as a donor substrate. With propanal, two new stereogenic centers are formed with 2(*R*) and 3(*S*) configurations. The acceptor substrates have very little structural requirements. The 2-hydroxyaldehydes appear to react the fastest, and the D-isomers are better substrates than the L-isomers. The stereospecificity is absolute regardless of the chirality of 2-hydroxyaldehydes. The aldol reactions thus follow the Cram–Felkin mode[21] of attack for D-substrates and anti-Cram–Felkin mode for L-substrates (Figure 2). The wide range of substrates accepted by this enzyme clearly marks DERA as a useful catalyst for asymmetric aldol condensations.

Experimental Section

Materials and Methods. UV–visible spectroscopy was performed on a Beckman DU-70 spectrophotometer thermostated at 25 °C. The Bruecker Ac-250, Am-300, and AMX-500 NMR spectrometers were used for 250-, 300-, 500-MHz spectra, respectively. High-resolution mass spectra (HRMS) were obtained on a VG ZAB-VSE or a VG 70 SE mass spectrometer under electron impact (EI) or fast atom bombardment (FAB) conditions. Gas chromatography was studied with a Hewlett Packard 5890 instrument using an Alltech NON PAKD capillary column with 5 μm RSL160 coating (30 m × 0.54 mm, catalog no. 16843). Fast protein liquid chromatography was performed on a Pharmacia FPLC system with columns purchased from Pharmacia. Lipase PS-800 was purchased from Amano. All other chemicals for these studies were purchased from either Aldrich or Sigma. The extinction coefficient for NADH was taken as 6.22×10^3 M^{-1} cm^{-1}.

Preparation of Enzyme. All steps were carried out at 4 °C with the exception of FPLC which was performed at room temperature. A total of 6 L of *E. coli* DH5α containing pVH17 was grown at 37 °C with agitation. The cells were cooled to 4 °C and harvested by centrifugation at 8 K for 20 min. The cells (about 72 g) were resuspended in 200 mL of buffer containing 100 mM TRIS pH 7.6 and 2 mM EDTA (buffer A). The cells were lysed in a French Pressure apparatus (Aminco, Inc.) and centrifuged at 16 000 × g for 30 min. The supernatant fluid was decanted and made 1% with streptomycin sulfate with stirring over a period of 20 min. The resulting solution was centrifuged as before. The supernatant fluid cut with ammonium sulfate (40–60%), and the resulting pellet was resuspended in buffer A. This solution was dialyzed extensively against buffer A. One tenth of this solution was used for further purification, while the remaining solution was lyophilized and stored at −70 °C. Further purification was achieved by FPLC with a MonoQ 10/10 anion exchange column. The sample was eluted with a gradient of 50 mM NaCl in buffer A. The enzymatically active fractions were pooled and applied to a phenyl sepharose FPLC column in buffer A containing 40 mM NaCl. Under these conditions, the remaining contaminating proteins stick to phenyl sepharose, while DERA elutes in the void volume.

Enzymatic Assays. DERA was routinely assayed with a coupled enzymatic system where 2 mM DRP, 0.3 mM NADH, and an enzyme mixture of glycerolphosphate dehydrogenase and triose phosphate dehydrogenase (TPI) was incubated in 50 mM triethanolamine buffer, pH 7.5 at 25 °C. The assay was initiated upon addition of DERA, and the decrease in absorbance at 340 nm was monitored. One unit of enzymatic activity is defined as that amount of enzyme required to liberate 1 μmol G3P/min at 25 °C. Protein concentrations were measured spectrophotometrically at 280 nm.

Substrate Specificity. Aldol donor substrate specificity was assayed by monitoring the consumption of D-G3P. Incubation mixtures contained 100 mM D-G3P, 200 mM acceptor, 1 mM EDTA, and 5 units DERA in 100 mM triethanolamine buffer, pH 7.5. Aliquots (0.1 mL) of this mixture were removed at 0, 30 and 60 min and quenched by addition of 40 μL of 60% perchloric acid and incubated on ice for 10 min. This solution was neutralized with 134 μL of 2 M NaOH and 826 μL of 1 M triethanolamine buffer, pH 7.0.[6] A 25-μL aliquot of this neutralized solution was introduced into an assay mixture containing glycerophosphate dehydrogenase and 0.3 mM NADH in 50 mM triethanolamine buffer, pH 7.5. The decrease in absorbance at 340 nm, which corresponds to the consumption of D-G3P, was monitored. The overall decrease in D-G3P in the intial incubation mixture was taken to be equivalent to the incorporation of the test substrate into product. Similarly, this method was used to determine the kinetic constants for D-G3P in the presence of 40 mM acetaldehyde. Acceptor substrates were analyzed spectrophotometrically by the consumption of acetaldehyde and acceptor by oxidation of these compounds with yeast aldehyde dehydrogenase (AlDH).[22] Incubation mixtures contained 200 mM acetaldehyde and 100 mM acceptor in 100 mM triethanolamine buffer, pH 7.3 containing 1 mM EDTA and 5 units of DERA. Aliquots were removed and neutralized as described above and assayed for remaining acetaldehyde and acceptor with AlDH in 100 mM pyrophosphate buffer, pH 9.0 containing 0.3 mM NAD^+. The increase in absorbance at 340 nm was monitored to indicate the amount of remaining acetaldehyde and acceptor substrate in the incubation mixture. Product formation was taken to be one-half of the total NADH generated with AlDH. The consumption of acetaldehyde was used for the determination of the kinetic constants for L-G3P in the presence of different constant concentrations of acetaldehyde ranging from 0.5 to 2.0 mM using yeast alcohol dehydrogenase and 0.3 mM NADH. The initial concentrations of L-G3P were determined as described.[23] Aliquots of these incubation mixtures were quenched as described above, and the reduction of acetaldehyde was deemed equivalent to the oxidation of NADH as determined spectrophotometrically at 340 nm. Alternatively, a gas chromatographic assay was used for the analysis of some of these acceptor aldehydes. This method involved extraction of aliquots of the incubation mixture with equal volumes of ether. Aliquots of this ether were then injected onto the GC capillary column using a temperature gradient from 37 °C to 100 °C at a rate of 5 °C/min. The integrated peak areas were compared to a calibration curve of standard acetaldehyde and standard acceptor solutions in water extracted with ether as described above. In this manner, the consumption of the substrates could be followed directly.

Synthesis of 2-deoxyribose-5-phosphate (1b): To a 50-mL solution containing 0.1 M DHAP, 0.3 M acetaldehyde, 0.1 M TEA buffer, pH 7.5, and 1 mM EDTA, 500 units of TPI and 200 units of DERA were added. The solution was stirred under N_2 at room temperature for 7 h. The pH was brought to 8.0 with 1 N NaOH. $BaCl_2$ (15 mmol) was added and stirred for 30 min before adding an equal volume of ethanol. The solution was refrigerated overnight and centrifuged to give a white solid. The solid material was washed with ethanol and dried in vacuo and treated with Dowex 50 (H^+ form) to give a clear solution. The overall yield was 78% as determined by enzymatic assay. This compound could also be synthesized from D-G3P as previously described.[3]

Synthesis of 5-azido-2,5-dideoxy-D-*erythro*-pentofuranose (2b): To a 10-mL solution containing 100 mM D-(*R*)-3-azido-2-hydroxypropanal (**2a**), 300 mM acetaldehyde, 100 mM triethanolamine buffer, pH 7.3, and 1 mM EDTA was added 400 units of DERA. The resulting solution was stirred in the dark for 2 days under N_2. The reaction was quenched by addition of 2 volumes of acetone. The mixture was then incubated in ice for 20 min and centrifuged to remove the precipitated enzyme. After removal of the solvent under reduced pressure, the residue was purified by silica gel chromatography (ethyl acetate/hexane, 2:1, R_f 0.12) to give the title compound (0.76 mmol, 76% yield): ^1H NMR ($CDCl_3$) of major anomer δ 2.0–2.3 (2 H, H-2), 2.95 (br s, 1 H, OH), 3.35 (ddd, J = 4.4, 4.9, 13.0, 2 H, H-5), 4.21 (br t, J = 6.4, 1 H, H-3), 4.38 (dt, J = 1.3, 4.7, 1 H, H-4), 4.48 (br s, 1 H, OH), 5.64 (app t, J = 4.1, 1 H, H-1); ^{13}C NMR ($CDCl_3$) δ 42.2, 42.7 (C-2), 53.2, 53.9 (C-5), 73.1, 74.1 (C-3), 85.0, 86.1 (C-4), 99.4, 99.9 (C-1); HRMS (M^+) calcd 159.0644, found 159.0683.

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Compounds **3b–8b** were synthesized as described for **2b** except that phosphate buffer (0.05 M, pH 7.3) was used instead of triethanolamine for the syntheses of **6b** and **7b**.

5-Fluoro-2,5-dideoxy-D-*erythro*-pentofuranose (3b): 33% yield; ^{1}H NMR (D_2O) of β form δ 2.2–2.05 (2 H, H-2), 4.04 (ddt, J = 3.2, 4.9, 23.8, 1 H, H-4), 4.44 (dt, J = 2.0, 4.5, 1 H, H-3), 4.53 (ddd, J = 3.4, 10.6, 47.0, 1 H, H-5), 4.57 (ddd, J = 3.4, 10.6, 47.0, 1 H, H-5), 5.62 (t, J = 4.3, 1 H, H-1); α form δ 1.88 (ddd, J = 2.8, 2.8, 14.2, 1 H, H-2), 2.40 (ddd, J = 6.7, 6.7, 14.2, 1 H, H-2), 4.25 (ddt, J = 2.8, 4.5, 25.6, 1 H, H-4), 4.32 (dt, J = 3.9, 7.0, 1 H, H-3), 4.5 (ddd, J = 4.8, 10.6, 47.0, 1 H, H-5), 4.56 (ddd, J = 2.9, 10.6, 47.0, 1 H, H-5), 5.57 (dd, J = 2.6, 6.2, 1 H, H-1); ^{13}C NMR (D_2O) δ 43.1, 43.2 (C-2), 72.3, 72.4 (C-3, $^3J_{CF}$ = 7.1), 85.2, 85.8 (C-5, $^1J_{CF}$ = 167.5), 85.7, 85.9 (C-4, $^2J_{CF}$ = 18.2), 100.4, 100.5 (C-1); HRMS (M – Na)$^+$ calcd 159.0433, found 159.0436.

5-Chloro-2,5-dideoxy-D-*erythro*-pentofuranose (4b): 37% yield; ^{1}H NMR (D_2O) of β form δ 2.16 (2 H, H-2), 3.65 (dd, J = 6.4, 11.6, 1 H, H-5), 3.70 (dd, J = 5.0, 11.6, 1 H, H-5), 4.04 (dt, J = 4.4, 5.0, 1 H, H-4), 4.43 (dt, J = 4.2, 5.5, 1 H, H-3), 5.60 (t, J = 4.2, 1 H, H-1); α form δ 1.85–1.92 (m, 1 H, H-2), 2.44 (ddd, J = 5.9, 7.0, 14.0, 1 H, H-2), 3.65 (dd, J = 6.4, 11.6, 1 H, H-5), 3.70 (dd, J = 5.0, 11.6, 1 H, H-5), 4.29 (m, 2 H, H-3, H-4), 5.56 (dd, J = 2.0, 5.2, 1 H, H-1); ^{13}C NMR (D_2O) δ 41.4, 41.6 (C-2), 45.1, 45.6 (C-5), 72.6, 72.7 (C-3), 84.9, 85.5 (C-4), 98.9, 99.0 (C-1); HRMS ((M$^+$) – OH) calcd 135.0213, found 135.0200; ^{13}C NMR (CD_3OD) δ 41.0, 41.3, 42.8, 42.9, 45.5, 46.3, 47.9, 48.0, 70.1, 70.2, 73.5, 73.9, 85.3 (2C), 86.8 (2C), 97.9, 98.0, 99.5, 99.8.

2,5-Dideoxy-D-*erythro*-pentofuranose (5b): 32% yield; ^{1}H NMR (D_2O) of β form δ 1.26 (d, J = 6.5, 3 H, H-5), 2.14 (2 H, H-2), 3.94 (dq, J = 4.0, 6.4, 1 H, H-4), 4.15 (dt, J = 4.0, 5.8, 1 H, H-3), 5.54 (t, J = 4.9, 1 H, H-1); α form δ 1.19 (d, J = 6.4, 3 H, H-5), 1.80 (ddd, J = 2.8, 5.0, 14.1, 1 H, H-2), 2.49 (ddd, J = 5.7, 7.2, 14.1, 1 H, H-2), 3.96 (dt, J = 5.0, 7.2, 1 H, H-3), 4.11 (dq, J = 5.0, 6.5, 1 H, H-4), 5.48 (dd, J = 2.8, 5.7, 1 H, H-1); ^{13}C NMR (D_2O) δ 18.4, 20.0 (C-5), 38.8, 41.2 (C-2), 76.0, 76.0 (C-3), 81.0, 82.4 (C-4), 97.7, 98.3 (C-1); HRMS (M$^+$) calcd 118.0630, found 118.0634.

2-Deoxy-D-*erythro*-pentose (6b): 65% yield. The ^{1}H-NMR spectrum of this compound was consistent with the published data.[18]

2-Deoxy-D-allose (7b): 62% yield. The ^{1}H-NMR spectrum of this compound was consistent with the published data.[18]

2,5,6-Trideoxy-D-*erythro*-hexofuranose (8b): 18% yield; ^{1}H NMR ($CDCl_3$) of major anomer δ 0.96 (t, J = 7.4, 3 H, H-6), 1.45 (dq, J = 7.2, 7.2, 2 H, H-5), 2.05–2.1 (2 H, H-2), 3.40 (br s, OH), 4.06 (dt, J = 1.5, 5.1, 1 H, H-3), 4.15 (dt, J = 1.3, 6.9, 1 H, H-4), 4.32 (br s, OH), 5.55 (app d, J = 3.7, 1 H, H-1); ^{13}C NMR ($CDCl_3$) 9.9, 10.2 (C-6), 26.8, 27.7 (C-5), 40.9, 42.2 (C-2), 74.8, 74.9 (C-3), 87.7 (C-4), 98.1, 98.7 (C-1); HRMS (M – H)$^+$ calcd 133.0864, found 133.0866.

Synthesis of DL-2-hydroxybutanal diethyl acetal (8c):[9] CH_3Li from a 1.4 M ethereal solution (52 mL, 73 mmol) was added to a solution of CuCN (40 mmol) in 80 mL of anhydrous ether at –78 °C under N_2 over a period of 15 min. Glycidaldehyde diethyl acetal (27.4 mmol) was added dropwise to this solution over 30 min, and the reaction mixture was stirred at –78 °C for 1 h, –22 °C for 2 h, and finally allowed to warm to room temperature and stirred overnight. The reaction was quenched with 4 M NH_4Cl in 2.5% NH_4OH at –78 °C and stirred for 30 min. Saturated NaCl (100 mL) was added, and the solid was filtered off. The filtrate was extracted with 3 × 150 mL of ether. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to reveal pure product in 93% yield (25.5 mmol): ^{1}H NMR ($CDCl_3$) δ 1.01 (t, J = 7.4, 3 H, CH_3), 1.22 (t, J = 7.1, 3 H, CH_3CH_2O), 1.24 (7.1, 3 H, CH_3CH_2O), 1.43 (ddq, J = 7.4, 8.8, 14.4, 1 H, $CHCH_2CH_3$), 1.67 (ddq, J = 3.4, 7.4, 14.4, 1 H, $CHCH_2CH_3$), 2.16 (br s, OH), 3.49 (ddd, J = 3.4, 6.0, 8.8, 1 H, H-CHOH), 3.57 (dq, J = 7.1, 9.3, 1 H, OCH_2CH_3), 3.59 (dq, J = 7.1, 9.3, 1 H, OCH_2CH_3), 3.73 (dq, J = 7.1, 9.3, 1 H, OCH_2CH_3), 3.79 (dq, J = 7.1, 9.3, 1 H, OCH_2CH_3), 4.27 (d, J = 6.0, 1 H, $CH(OEt)_2$); ^{13}C NMR ($CDCl_3$) δ 9.9 (CH_3), 15.4 (2 × CH_3CH_2O), 24.7 (CH_2CHOH), 63.4, 63.5 (2 × OCH_2CH_3), 73.0 (CHOH), 104.9 ($CH(OEt)_2$); HRMS (M – Na)$^+$ calcd 185.1154 found 185.1154.

DL-2-Acetoxybutanal diethyl acetal (8d): To a solution of 2-hydroxybutanal diethyl acetal (24.0 mmol) in 5 mL of anhydrous ether at 0 °C under N_2, a mixture of acetic anhydride (48.0 mmol) and pyridine (72.0 mmol) was added over 5 min. The solution was then stirred for 1 day at room temperature and poured into 40 mL of brine. The solution was extracted with ether (3 × 70 mL), and the combined ether layers were washed consecutively with 40 mL each of 1 N NCl (twice), saturated $NaHCO_3$, and brine. After drying with $MgSO_4$, the ether was removed to give 96% yield of **8d** as a liquid: ^{1}H NMR ($CDCl_3$) δ 0.96 (t, J = 7.4, 3 H, CH_3CH_2CH), 1.17 (t, J = 7.0, 3 H, CH_3CH_2O), 1.20 (t, J = 7.0, 3 H, CH_3CH_2O), 1.58 (ddq, J = 7.4, 9.0, 14.6, 1 H, CH_3CH_2CH), 1.74 (ddq, J = 3.7, 7.4, 14.6, 1 H, CH_3CH_2CH), 2.08 (s, 3 H, CH_3CO), 3.52 (dq, J = 7.0, 9.4, 1 H, OCH_2CH_3), 3.53 (dq, J = 7.0, 9.4, 1 H, OCH_2CH_3), 3.68 (dq, J = 7.0, 9.4, 1 H, OCH_2CH_3), 3.69 (dq, J = 7.0, 9.4, 1 H, OCH_2CH_3), 4.40 (d, J = 5.4, 1 H, $CH(OEt)_2$), 4.88 (ddd, J = 3.7, 5.4, 9.1, 1 H, CHOAc); ^{13}C NMR ($CDCl_3$) δ 9.6 (CH_3CH_2CH), 15.2, 15.3 (2 × CH_3CH_2O), 21.0 (CH_3CO), 22.2 (CH_3CH_2CH), 62.6, 63.4 (2 × OCH_2CH_3), 74.2 (CHOAC), 102.3 ($CH(OEt)_2$), 170.6 (CO); HRMS (M – Cs)$^+$ calcd 337.0416, found 337.0411.

Kinetic Resolution of 8d: Immobilized PS-800 lipase was used to resolve **8d** (20.5 mmol) at pH 7.0 (Scheme IV) as described previously[8] to yield D-(+)-**8c** (8.1 mmol, 39.4%) in >99% ee, $[\alpha]^{25}_D$ = +15.4° (*c* 2.9, $CHCl_3$), and L-(–)-**8d** (8.7 mmol, 42.4%) in 94.6% ee, $[\alpha]^{25}_D$ = –39.02° (*c* 2.9, $CHCl_3$), after column chromatography on silica gel using a gradient of 1:10 to 1:4 EtOAc/hexane). L-(–)-**8d** was deacetylated in 1 M NaOMe in methanol to give L-(–)-**8c** which was purified after removal of the solvent by passing the mixture through a short silica gel column using chloroform as the eluant. The (+)-MTPA esters were prepared,[24] and the chemical shifts at d 4.54 and 4.45 for D- and L-enantiomer, respectively, were used for determination of the optical purities.

L-Glyceraldehyde-3-phosphate (9a): This compound was synthesized as described previously[8] with L- rather than D-glycidaldehyde diethyl acetal: 50% yield.

2-Deoxy-L-*threo*-pentofuranose 5-phosphate (9b): 70% yield; ^{1}H NMR (D_2O) of β form δ 1.7 (m, 1 H, H-2), 2.40 (dd, J = 6.1, 15.7, 1 H, H-2), 3.8–4.2 (m, 3 H, H-4, H-5), 4.54 (m, 1 H, H-3), 5.20 (dd, J = 2.8, 10.4, 1 H, H-1); α form δ 2.0–2.1 (m, 1 H, H-2), 2.20 (dt, J = 5.8, 14.9, 1 H, H-2), 3.8–4.2 (m, 2 H, H-5), 4.34 (dt, J = 3.0, 6.1, 1 H, H-4), 4.61 (m, 1 H, H-3), 5.78 (t, J = 5.3, 1 H, H-1).

6-Azido-1,3,5-trideoxy-D-*erythro*-hexulose (10): 66% yield; ^{1}H NMR (D_2O) of major anomer δ 2.24 (s, 3 H, CH_3), 2.68 (dd, J = 9.2, 16.6, 1 H, H-3), 2.89 (dd, J = 3.4, 16.6, 1 H, H-3), 3.40 (dd, J = 7.0, 13.1, 1 H, H-6), 3.52 (dd, J = 3.1, 13.1, 1 H, H-6), 3.69 (dt, J = 3.1, 6.9, 1 H, H-5), 4.07 (ddd, J = 3.1, 6.8, 7.0, 1 H, H-4); ^{13}C NMR (D_2O) δ 28.4 (C-1), 45.0 (C-3), 51.3 (C-6), 66.6, 71.4 (C-4, C-5), 88.3 (C-2); HRMS (M – Cs)$^+$ calcd 305.9855, found 305.9871.

6-Azido-1-fluoro-1,3,5-trideoxy-D-*erythro*-hexulose (11): 70% yield; ^{1}H NMR ($CDCl_3$) of major anomer δ 2.07 (d, J = 13.9, 1 H, H-3), 2.26 (ddd, J = 1.2, 6.0, 13.9, 1 H, H-3), 2.68 (br s, 2 H, 2 × OH), 3.30 (dd, J = 5.1, 13.0, 1 H, H-6), 3.34 (dd, J = 4.7, 13.0, 1 H, H-6), 4.26 (br d, J = 5.9, 1 H, H-4), 4.37 (d, J = 47.0, 2 H, H-1), 4.38 (br t, J = 4.6, 1 H, H-5); minor anomer δ 2.14 (ddd, J = 1.7, 6.8, 13.8, 1 H, H-3), 2.36 (dd, J = 1.9, 60, 13.7, 1 H, H-3), 2.68 (br s, 2 H, 2 × OH), 3.47 (dd, J = 5.3, 12.8, 1 H, H-6), 3.50 (dd, J = 4.5, 12.8, 1 H, H-6), 4.0 (q, J = 4.8, 1 H, H-5), 4.34 (dd, J = 2.7, 47.0, 2 H, H-1), 4.46 (app q, J = 5.8, 1 H, H-4); ^{13}C NMR ($CDCl_3$) δ 41.2, 42.1 (C-3), 52.3, 52.6 (C-6), 72.4, 73.6 (C-4), 85.0, 86.2 (C-5), 83.65, 84.86 (C-1, $^1J_{CF}$ = 182.34), 104.1, 105.1 (C-2, $^2J_{CF}$ = 20.2); HRMS (M – Cs)$^+$ calcd 323.9761, found 323.9785.

5-Azido-(2*R*)-methyl-2,5-dideoxy-D-*ribo*-furanose (12): 20% yield; ^{1}H NMR (D_2O) of β form δ 1.02 (d, J = 7.2, 3 H, CH_3), 2.17 (1 H, m, 1 H, H-2), 3.39 (dd, J = 7.1, 13.2, 1 H, H-5), 3.49 (dd, J = 3.2, 13.2, 1 H, H-5), 3.65 (ddd, J = 3.2, 5.7, 7.1, 1 H, H-4), 4.22 (dd, J = 3.6, 6.1, 1 H, H-3), 5.14 (d, J = 5.1, 1 H, H-1); α form δ 1.02 (d, 3 H, CH_3), 2.28 (m, 1 H, H-2), 3.39 (dd, J = 6.6, 13.2, 1 H, H-5), 3.5 (dd, J = 4.5, 13.2, 1 H, H-5), 4.01 (dt, J = 3.9, 6.7, 1 H, H-4), 4.08 (dd, J = 2.1, 6.2, 1 H, H-3), 5.39 (d, J = 5.0, 1 H, H-1); ^{13}C NMR (D_2O) δ 7.4 (CH_3), 42.4 (C-2), 51.1 (C-5), 72.4 (C-3), 81.6 (C-4), 102.4 (C-1); HRMS (M – Cs)$^+$ calcd 305.9855, found 305.9871.

7-Azido-(2*R*,4*S*)-dimethyl-2,4,7-trideoxy-D-glycero-D-*allo*-heptopyranose (13): 2.1% yield; ^{1}H NMR (D_2O) of major anomer δ 0.87 (d, J = 6.7, 3 H, CH_3 of C-2), 0.93 (d, J = 7.4, 3 H, CH_3 of C-4), 1.38–1.47 (m, 1 H, H-2), 1.73 (ddq, J = 2.7, 7.4, 14.8, 1 H, H-4), 3.40 (m, 1 H, H-3), 3.42 (dd, J = 6.6, 13.3, 1 H, H-7), 3.47 (dd, J = 3.6, 13.3, 1 H, H-7), 3.81 (ddd, J = 3.6, 5.0, 6.6, 1 H, H-6), 4.66 (d, J = 8.7, 1 H, H-1), 4.76 (m, 1 H, H-5); ^{13}C NMR δ 9.1, 9.3 (CH_3 of C-4), 11.2, 12.0 (CH_3 of C-2), 25.2, 25.3), 38.0, 41.3 (C-2, C-4), 51.7, 51.9 (C-7), 72.0, 71.7 (C-6), 77.4, 81.8 (C-3), 94.2, 97.1 (C-5), 91.9, 99.6 (C-1); HRMS (M – Cs)$^+$ calcd 364.0273, found 364.0273.

General procedure for the hydrogenolysis of azidosugars: A solution of azidosugar (0.3 mmol) and Pd/C (10%) in methanol (7 mL) was purged four times with hydrogen and agitated under 50 psi for 1 day. The catalyst was removed by filtration through a pad of Celite, and the solution was concentrated in vacuo to give the corresponding azasugar.

1,4,5,6-Tetradeoxy-1,5-imino-D-lyxitol (14): 93% yield; ^{1}H NMR ($CDCl_3$) δ 1.05 (d, J = 6.3, 3 H, H-1), 1.27 (q, J = 12.4, 1 H, H-3a), 1.67 (ddd, J = 2.5, 4.7, 12.5, 1 H, H-3e), 2.55 (ddq, J = 2.5, 6.3, 12.6, 1 H, H-2), 2.62 (dd, J = 1.3, 13.4, 1 H, H-6a), 3.06 (dd, J = 2.9, 13.4, 1 H, H-6e), 3.25 (br s, 3 H, 2 × OH, NH), 3.53 (ddd, J = 3.0, 4.7, 11.9, 1 H, H-4), 3.69 (br s, 1 H, H-5); ^{13}C NMR ($CDCl_3$) δ 22.1 (C-1), 37.7 (C-3), 50.1, 50.5 (C-2, C-6), 67.2, 69.9 (C-4, C-5); HRMS (M – Cs)$^+$ calcd 264.0001, found 264.0000.

6-Fluoro-1,4,5,6-tetradeoxy-1,5-imino-D-lyxitol (15): Hydrogenolysis of **11** resulted in a mixture of **14** (52% yield) and **15** (11% yield) after column chromatography on silica gel (^{i}PrOH/H_2O/NH_4OH, 14:1:1); ^{1}H NMR (D_2O) δ 1.50 (app q, J = 12.0, 1 H, H-3a), 1.66 (app dt, J = 3.8, 12.4, 1 H, H-3e), 2.69 (dd, J = 1.3, 14.3, 1 H, H-6a), 2.91-2.83 (dddd, J = 3.0, 5.7, 12.2, 25.3, 1 H, H-2), 3.03 (dd, J = 2.8, 14.3, 1 H, H-6e), 3.80 (ddd, J = 3.0, 7.7, 11.6, 1 H, H-4), 3.84-3.81 (m, 1 H, H-5), 4.37 (ddd, J = 5.7, 9.7, 47.2, 1 H, H-1), 4.46 (ddd, J = 3.0, 9.7, 47.2, 1 H, H-1); ^{13}C NMR (D_2O) δ 29.4 (C-3), $^3J_{C-F}$ = 5.9), 49.2 (C-6), 54.6 (C-2, $^2J_{C-F}$ = 18.1), 67.6, 69.8 (C-4, C-5), 87.00 (C-1, $^1J_{C-F}$ = 165.3); HRMS $(M - H)^+$ calcd 150.0930, found 150.0923.

(2S)-Methyl-1,2,5-trideoxy-1,5-imino-D-ribitol (16): 90% yield; ^{1}H NMR (D_2O) δ 0.91 (d, J = 7.0, 3 H, CH_3), 1.77-1.82 (m, 1 H, H-2), 2.45 (t, J = 12.4, 1 H, H-1a), 2.67 (t, J = 11.7, 1 H, H-5a), 2.70 (dd, J = 4.8, 12.4, 1 H, H-1e), 2.90 (dd, J = 4.6, 11.9, 1 H, H-5e), 3.72 (ddd, J = 3.0, 5.1, 11.7, 1 H, H-4), 3.85 (br s, 1 H, H-3); ^{13}C NMR (D_2O) δ 15.4 (CH_3), 35.5 (C-2), 44.8, 45.7 (C-1, C-5), 67.0, 72.6 (C-3, C-4); HRMS $(M - Cs)^+$ calcd 264.0001, found 264.0003.

1,2,5-Trideoxy-1,5-imino-D-erythritol (17): 97% yield; ^{1}H NMR (D_2O) δ 1.51 (m, 2 H, H-2), 2.55 (ddd, J = 4.8, 7.6, 13.1, 1 H, H-1), 2.67 (dd, J = 3.0, 13.4, 1 H, H-5), 2.90 (dd, J = 5.7, 13.4, 1 H, H-5), 2.86-2.96 (m, 1 H, H-1), 3.67 (dt, J = 2.5, 5.9, 1 H, H-4), 3.74 (ddd, J = 3.0, 4.6, 7.6, 1 H, H-3); ^{13}C NMR (D_2O) δ 29.9 (C-2), 41.9 (C-1), 48.1 (C-5), 68.8, 69.3 (C-3, C-4); HRMS (M^+) calcd 117.0790, found 117.0785.

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[Tris(pyrazolyl)hydroborato]magnesium Alkyl Derivatives: Reactivity Studies

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Abstract: The reactivity of a series of 4-coordinate [tris(pyrazolyl)hydroborato]magnesium alkyl derivatives, $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR and $\{\eta^3$-HB(3,5-Me$_2$pz)$_3\}$MgR (3-Bu^{t}pz = 3-$C_3N_2Bu^tH_2$, 3,5-Me$_2$pz = 3,5-$C_3N_2Me_2H$; R = CH_3, CH_2CH_3, $(CH_2)_3CH_3$, $CH(CH_3)_2$, $C(CH_3)_3$, $CH{=}CH_2$, C_6H_5, CH_2SiMe_3), has been investigated. The complexes $\{\eta^3$-HB(3,5-Me$_2$pz)$_3\}$MgR undergo ligand redistribution reactions, analogous to the Schlenk equilibrium, to give the 6-coordinate sandwich complex $\{\eta^3$-HB(3,5-Me$_2$pz)$_3\}_2$Mg. In contrast, the 4-coordinate magnesium alkyl derivatives supported by the more sterically demanding tris(3-*tert*-butylpyrazolyl)hydroborato ligand, $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR, are stable with respect to the formation of $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}_2$Mg. The alkyl complexes $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR are useful precursors for a variety of other 4-coordinate complexes, including $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgX (X = $C{\equiv}CC_6H_5$, $C{\equiv}CSiMe_3$, OEt, OPr^i, OBu^t, OPh, OCH_2SiMe_3, $OSiMe_3$, OOBu^t, NHPh, SH, SCH_3, Cl, Br, I, NCO, NCS). CO_2 inserts into the Mg-C bond of $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCH$_3$ to give the η^1-acetato complex $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$Mg$\{\eta^1$-OC(O)CH$_3\}$. In contrast, the reactions with the ketones $CH_3C(O)CH_3$ and $CH_3C(O)Bu^t$ do not result in insertion to give the alkoxide derivatives, but preferentially give the enolate complexes $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$Mg$\{\eta^1$-OC(=CH$_2$)CH$_3\}$ and $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$Mg$\{\eta^1$-OC(=CH$_2$)Bu$^t\}$, accompanied by the elimination of methane. Insertion of O_2 into the Mg-R bond of the complexes $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$) results in formation of the alkylperoxo derivatives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOOR, which have been characterized by the use of ^{17}O NMR spectroscopy. In contrast, the reaction of the magnesium (trimethylsilyl)methyl complex $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCH$_2$SiMe$_3$ with O_2 gives the trimethylsiloxide derivative $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOSiMe$_3$ as a result of facile cleavage of the Si-C bond upon autoxidation. The molecular structures of $\{\eta^3$-HB(3,5-Me$_2$pz)$_3\}_2$Mg and $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCl have been determined by X-ray diffraction. $\{\eta^3$-HB(3,5-Me$_2$pz)$_3\}_2$Mg is triclinic, $P\bar{1}$ (No. 2), a = 8.837 (3) Å, b = 10.223 (3) Å, c = 10.773 (2) Å, α = 63.92 (3)°, β = 85.24 (2)°, γ = 79.87 (2)°, V = 860.4 (4) Å^3, Z = 1. $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCl is orthorhombic, *Pnma* (No. 62), a = 16.048 (7) Å, b = 16.006 (3) Å, c = 9.840 (1) Å, V = 2527 (1) Å^3, Z = 4.

Introduction

We have recently reported the syntheses and structures of a series of 4-coordinate organomagnesium complexes $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (A) and $\{\eta^3$-HB(3,5-Me$_2$pz)$_3\}$MgR (B) (3-Bu^{t}pz = 3-$C_3N_2Bu^tH_2$; 3,5-Me$_2$pz = 3,5-$C_3N_2Me_2H$)[1] that are stabilized by coordination of tris(pyrazolyl)hydroborato ligands,[2] as illustrated in Figure 1.

In contrast to Grignard reagents, which are well-known to (i) exist in solution as a complex mixture of species (e.g., the Schlenk equilibrium) and (ii) exhibit a variety of structures in the solid state,[3] the organomagnesium complexes illustrated in Figure 1 exist as well-defined 4-coordinate monomeric complexes both in the solid state and in solution. Furthermore, the solvent-free [tris(pyrazolyl)hydroborato]magnesium alkyl derivatives are soluble in noncoordinating hydrocarbon solvents (e.g., benzene) and possess valuable spectroscopic handles, in the form of the resonances due to the tris(pyrazolyl)hydroborato ligands, that are ideal for monitoring reactions. Here we report our studies of

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