chemical shift for the iminosilaacyl carbon at δ 299.07.[3a,b] Addition of 1 equiv of CN(Xyl) to a benzene solution of **4**, or reaction of **1** with 2 equiv of CN(Xyl), results in formation of a blue complex **5**. The combustion analysis of isolated **5** is consistent with a 1:2 adduct of **1** with isocyanide, $Cp_2Sc(CN(Xyl))_2Si(SiMe_3)_3$. However, ^1H NMR data for **5** indicate a complex structure and the presence of three inequivalent $SiMe_3$ groups in a 1:1:1 ratio.[5] Formation of X-ray-quality, blue crystals from diethyl ether allowed complete characterization of this compound.

The crystal structure[7] (Figure 1) shows that **5** is the product of an isocyanide-coupling reaction that results in further rearrangements. The structure drawn in Scheme I reflects the observed structural parameters. The chelate ring of **5** is derived from the two isocyanide groups and contains a Sc(1)-N(1) single bond (2.133 (7) Å), a longer (dative) Sc(1)-N(2) bond (2.324 (8) Å), and a C=C double bond (C(1)-C(2) = 1.375 (12) Å). Migration of an $SiMe_3$ group to C(1) results in reduction of the C(1)-N(1) bond order, which exhibits a C-N bond distance (1.413 (12) Å) that is intermediate between those observed for single and double bonds. The C(2)-N(2) distance is significantly longer, 1.469 (11) Å, and more typical for a C-N single bond, while the C(3)-N(2) distance (1.322 (11) Å) clearly reflects double-bond character. The $Si(SiMe_3)_2$ group is incorporated as part of a five-membered ring that is fused to both the chelate ring and a cyclohexadiene ring derived from the xylyl group of an isocyanide.

A possible mechanism for formation of **5** from **4** and CN(Xyl) is given in Scheme I. Precedents in η^2-silaacyl chemistry suggest that the iminosilaacyl group of **4** should be susceptible to nucleophilic attack by isocyanide to give a ketenimine intermediate (A).[2a,3a] A closely related ketenimine complex, $Cp_2(Cl)Zr[OC(SiMe_3)(CN(Xyl))]$, has been characterized in solution.[3a] Migration of a trimethylsilyl group to the α-carbon of the ketenimine ligand results in intermediate B, which possesses a reactive Si=C double bond. Ishikawa and co-workers have observed 1,3-silyl shifts from silicon to carbon to generate silene (Si=C) intermediates in the coordination sphere of nickel.[8] Cycloaddition of the Si=C double bond in B to the adjacent xylyl ring then gives the connectivity observed for the product. Although attempts to trap the proposed silene intermediate with $(MeO)_3SiH$, Me_3SiOMe, and 2,3-dimethylbutadiene were unsuccessful, this is not unexpected since intramolecular rearrangement of high-energy intermediate B to **5** should be quite rapid. It is hoped that further insight into mechanistic details of this unprecedented rearrangement will result from future investigations.

Acknowledgment is made to the Air Force Office of Scientific Research, Air Force Systems Command, USAF, for support of this work under Grant No. AFOSR-88-0273. T.D.T. thanks the Alfred P. Sloan Foundation for a research fellowship (1988-1990).

Supplementary Material Available: Characterization data for **1** and **3-5** and tables of crystal, data collection, and refinement parameters, atomic coordinates and isotropic displacement parameters, bond distances and angles, and hydrogen atom coordinates for **5** (10 pages); listings of observed and calculated structure factors for **5** (14 pages). Ordering information is given on any current masthead page.

(7) $C_{37}H_{46}N_2Si_4Sc$: monoclinic, $P2_1/c$, a = 17.97 (1) Å, b = 8.613 (5) Å, c = 25.88 (2) Å, β = 101.86 (7)°, V = 3921 (5) Å^3, Z = 4, μ = 3.32 cm^{-1}, Mo Kα radiation (λ = 0.71073 Å), 297 K (24 °C), Nicolet R3m/V diffractometer with graphite monochromator; 4166 reflections were collected ($3° \le 2\theta \le 40°$), using 2θ scans. Of these, 3674 reflections were unique (R_{int} = 3.26%) and 2171 were considered observed ($F > 6.0\sigma(F)$). Solution was by Patterson methods and refinement by full-matrix least-squares methods (SHELXTL PLUS computer programs, Nicolet Instrument Corp., Madison, WI). Due to limited data, only the scandium, silicon, nitrogen, and C(1)-C(8) atoms were refined anisotropically, and hydrogen atoms were refined in fixed and idealized positions. The Cp ligands were refined as rigid, idealized pentagons, and the C(11)-C(16) aromatic ring was refined as an idealized hexagon. R_F = 6.21%, R_{wF} = 6.72%, data/parameter = 9.8, GOF = 2.07, largest Δ/σ = 0.033, highest peak = 0.53 e/Å^3.

(8) (a) Ishikawa, M.; Ono, T.; Saheki, Y.; Minato, A.; Okinoshima, H. *J. Organomet. Chem.* **1989**, *363*, C1. (b) Ohshita, J.; Isomura, Y.; Ishikawa, M. *Organometallics* **1989**, *8*, 2050.

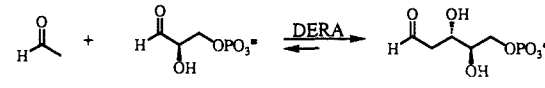
Deoxyribose-5-phosphate Aldolase as a Synthetic Catalyst[1]

Carlos F. Barbas, III, Yi-Fong Wang, and Chi-Huey Wong*

Department of Chemistry
The Research Institute of Scripps Clinic
La Jolla, California 92037

Received November 29, 1989

Enzyme-catalyzed stereocontrolled aldol condensations are valuable in organic synthesis, particularly in the synthesis of carbohydrates and related substances.[2,3] We report here an initial study on the synthetic utility of a bacterial 2-deoxyribose-5-phosphate aldolase (DERA, EC 4.1.2.4) overexpressed in *Escherichia coli*.[4] The enzyme DERA catalyzes the reversible aldol reaction of acetaldehyde and D-glyceraldehyde 3-phosphate to form 2-deoxyribose 5-phosphate[5] (eq 1). This enzyme is unique among the aldolases in that it is the only aldolase that condenses two aldehydes. Other aldolases use ketones as aldol dononors and aldehydes as acceptors.



(1)

The purified DERA[4] showed optimal activity at pH 7.5 with the following kinetic constants: V_{max} = 210 units/mg based on the cleavage of 2-deoxyribose 5-phosphate (k_{cat} = 521.1 s^{-1}) and K_m for 2-deoxyribose 5-phosphate = 1.93 mM. At 25 °C in 0.1 M triethanolamine buffer (TEA), pH 7.5, the enzyme is fairly stable, with 70% of the original activity retained after 10 days.

Examination of the substrate specificity[6] of DERA (Tables I and II) indicates that acetone, fluoroacetone, and propionaldehyde can replace acetaldehyde as the nucleophilic component in the aldol reaction. Substitution at C-2 of acetaldehyde with other than a single methyl group is not tolerated. It is of particular interest that the bond formation for fluoroacetone occurs regioselectively at the nonfluorinated carbon. With regard to the specificity of acceptors, many aldehydes as well as aldose sugars and their phosphates are accepted as weak substrates.

Although the enzyme possesses such a broad substrate specificity, the rates of condensation with unnatural substrate are relatively low and a relatively large amount of enzyme is required to achieve useful synthesis. The high stability and specific activity and the ready availability of the enzyme, however, appear to outweigh this shortcoming.

The following are representative syntheses with DERA.

(*S*)-4-Hydroxy-5-methylhexan-2-one. To a 100-mL solution containing 0.2 M acetone, 0.1 M isobutyraldehyde, 0.1 M TEA, and 1 mM EDTA was added 1000 units of DERA in a dialysis bag.[2] The reaction vessel was stoppered, and the solution was stirred for 3 days at room temperature and then continuously extracted with ether for 16 h. The solvent was removed by slow fractional distillation to yield the crude product, which was chromatographed on silica gel (ether/hexane, 1:1), to yield 0.56 g, 44% yield of the title compound: $[\alpha]_D$ -55.0° (c 1.4, $CHCl_3$);

(1) Taken from the Ph.D. Thesis of C.F.B. at Texas A&M University, 1989. This work was supported by the NIH (GM 44154-01).

(2) Toone, E. J.; Simon, E. S.; Bednarski, M. D.; Whitesides, G. M. *Tetrahedron* **1989**, *45*, 5365 and references cited.

(3) Wong, C.-H. *Science* **1989**, *244*, 1145 and references cited.

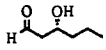
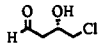
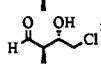
(4) To construct an overproducing *E. coli* species, plasmid p VH 17 which contains the deo C gene (Valentin-Hansen, P.; Aiba, H.; Schumperli, D. *EMBO J.* **1982**, *1*, 317) was introduced into *E. coli* EM2929. A 6-L growth of *E. coli* EM2929/pVH17 produced approximately 124000 units of the aldolase. One unit = 1 μmol of 2-deoxyribose 5-phosphate cleaved per minute. About 3.1 × 10^4 units can be prepared for synthesis.

(5) The equilibrium constant for the condensation is 4.2 × 10^3 M^{-1} (Pricer, W. E.; Horecker, B. L. *J. Biol. Chem.* **1960**, *235*, 1292).

(6) The substrate specificity of *E. coli* DERA was not reported previously. The enzyme from *Lactobacillus plantarum* was reported to accept glycoaldehyde phoshate, D-ribose 5-phosphate, and D-erythrose 4-phosphate as acceptor substrate, and propionaldehyde as donor according to the activity assay (Rosen, O. M.; Hoffee, P.; Horecker, B. L. *J. Biol. Chem.* **1965**, *240*, 1517.

0002-7863/90/1512-2013$02.50/0

Table I. Substrate Specificity of DERA[a]

Donor	Acceptor	Presumed Product	R_f
		—	
			0.38(1)
			0.41(1)
			0.6(2)
			0.26(1)
			0.34-0.55(1)
		—	
			0.6(1)
			0.78(1)
			0.26(1)
			0.56(2)
			0.39(2)
			0.65(2)
		—	
			0.6(2)

[a] Reactions were conducted in a 1-mL solution containing 0.1 M triethanolamine, 0.1 mM EDTA, 0.1 M donor, 0.1 M acceptor, and 30 units of DERA. A control reaction was performed containing all components except the enzyme. After incubation overnight, TLC (silica gel) was used to identify the appearance of product by staining with *p*-anisaldehyde reagent. Solvent systems: 1, ether:hexane = 9:2; 2, ether:$CHCl_3$ = 1:1. The rate of each reaction is about 1% of the rate of the natural reaction. [b] Stereochemistry at the α position was not determined.

Table II. Relative Activities of Carbohydrates as Acceptor Substrates (100 mM) in DERA-Catalyzed Reactions at pH 7.5 with Acetaldehyde (25 mM)

acceptor substrates	V_{rel}
D-glyceraldehyde 3-phosphate	100
D-glyceraldehyde	0.40
L-glyceraldehyde	0.40
D-ribose	0.44
D-ribose 5-phosphate	0.36
D-arabinose	0.30
D-glucose	0.40
D-glucose 6-phosphate	0.05
2-deoxy-D-glucose	0.23
N-acetylglucosamine	0.25

^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (m, 6 H), 1.63 (m, 1 H), 2.15 (s, 3 H), 2.64 (m, 2 H), 3.0 (br, 1 H), 3.78 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$, APT) δ 17.71, 18.29 (CH_3), 30.79 (CH_3), 32.99 (CH), 46.96 (CH_2), 72.17 (CH), 210.32 (CO). Anal. Calcd for $C_7H_{14}O$ (114.5): C, 73.68; H, 12.28. Found: C, 73.70; H, 12.22.

(*S*)-1-Fluoro-3-hydroxy-4-methylhexan-2-one. To a 66-mL solution containing 0.2 M fluoroacetone, 0.1 M isobutyraldehyde, 0.1 TEA, and 1 mM EDTA was added 2000 units of DERA in a dialysis bag. After reaction for 1 day, 0.6 mL of isobutyraldehyde was added and the solution was stirred for an additional 2 days. The product was isolated as described above to yield 750 mg (40% yield): $[\alpha]_D$ -46.3° (*c* 0.8, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (d, 3 H, J = 3.6 Hz), 0.93 (d, 3 H, J = 3.7 Hz), 1.7 (m, 1 H), 2.5 (br s, 1 H), 2.65 (m, 2 H), 3.88 (q, 1 H), 4.82 (d, 2 H, J_{HF} = 47.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$, APT) δ 17.59, 18.27 (CH_3), 33.32 (CH), 42.22 (CH_2), 71.8 (CH), 85.14 (d, CFH_2, $^1H_{CF}$ = 183.9 Hz), 207.79 (C, $^2J_{CF}$ = 18.9 Hz). Anal. Calcd for $C_7H_{13}OF$ (122.4): C, 68.85; H, 10.66. Found: C, 68.84; H, 10.61.

2-Deoxyribose 5-phosphate was prepared similarly from a 100-mL solution containing 0.3 M acetaldehyde, 0.1 M D-glyceraldehyde 3-phosphate, and 100 units of DERA. After 6 h, $BaCl_2$ (14 mmol) was added, followed by addition of ethanol (200 mL) to obtain a precipitate, which contained 86% 2-deoxyribose 5-phosphate and 10% inorganic phosphate.[7]

In summary, we have made available the enzyme DERA for use in stereocontrolled aldol condensations and have established that the enzyme accepts a number of aldehydes as acceptors and propionaldehyde, acetone, and fluoroacetone, in addition to acetaldehyde, as donors. The enzyme appears to be a useful catalyst for synthesis of a number of β-hydroxy aldehydes and ketones. Work is in progress to optimize the conditions to increase the yield and to explore new substrates for the enzyme.

Supplementary Material Available: Details of the production, purification, stability, pH profile, and kinetic analyis of the enzyme DERA (3 pages). Ordering information is given on any current masthead page.

(7) For enzymatic determination of deoxyribose 5-phosphate, see: Bergmeyer, H. U. *Methods of Enzymatic Analysis*; Verlag Chemie: Weinheim, 1974. For inorganic phosphate analysis, see: Ames, B. N. *Methods Enzymol.* **1966**, *8*, 115. D-Glyceraldehyde 3-phosphate was prepared from (*R*)-glycidaldehyde diethyl acetal and inorganic phosphate as outlined below.

Infrared Multiple Photon Dissociation of Butyrophenone Cation. A Stepwise McLafferty Rearrangement

Thomas H. Osterheld and John I. Brauman*

Department of Chemistry, Stanford University
Stanford, California 94305-5080
Received September 22, 1989

Although the McLafferty rearrangement[1] (eq 1) is one of the most extensively studied unimolecular reactions in mass spectrometry,[2] its mechanism is still controversial. Theoretical studies

(1)

have supported both stepwise[3] and concerted[4] pathways. Experimental studies on the benzyl ethyl ether cation rearrangement have also supported conflicting mechanisms.[5] For a few systems,

(1) (a) McLafferty, F. W. *Anal. Chem.* **1956**, *28*, 306. (b) McLafferty, F. W. *Anal. Chem.* **1959**, *31*, 82.
(2) Kingston, D. G. I.; Bursey, J. T.; Bursey, M. M. *Chem. Rev.* **1974**, *74*, 215.
(3) (a) Boer, F. P.; Shannon, T. W.; McLafferty, F. W. *J. Am. Chem. Soc.* **1968**, *90*, 7239. (b) Hudson, C. E.; Griffin, L. L.; McAdoo, D. J. *Org. Mass Spectrom.* **1989**, *24*, 866. (c) Dorigo, A. E.; Loncharich, R. J.; Houk, K. N., submitted.
(4) (a) Dougherty, R. C. *J. Am. Chem.* **1968**, *90*, 5788. (b) Ha, T.-K.; Radloff, C.; Nguyen, M. T. *J. Phys. Chem.* **1986**, *90*, 2991.
(5) (a) Stone, D. J. M.; Bowie, J. H.; Underwood, D. J.; Donchi, K. F.; Allison, C. E.; Derrick, P. J. *J. Am. Chem. Soc.* **1983**, *105*, 1688. (b) Wesdemiotis, C.; Feng, R.; McLafferty, F. W. *J. Am. Chem. Soc.* **1985**, *107*, 715. (c) Allison, C. E.; Stringer, M. B.; Bowie, J. H.; Derrick, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 6291. (d) Tureček, F.; Drinkwater, D. E.; McLafferty, F. W., submitted.

0002-7863/90/1512-2014$02.50/0