

epoxy silanes were deoxygenated to afford vinylsilanes. The results are shown in Table 1. As shown in the table, this method is quite general for the synthesis of vinylsilanes except epoxy silanes containing phenyl group (entries h and i).³

It is interesting to note that the mixture of E and Z isomers of α, β -epoxysilanes which were prepared by the Magnus method,¹ afforded vinylsilanes having an (E)-configuration in >90% (entries e-h). From these results we can assume that E-vinylsilanes are obtained predominantly (over Z-isomers) regardless of the stereochemistry of epoxy silanes. The stereoselectivity observed in our study is quite similar to the results reported by Ito² and Barluenga.⁵

The greater electron transfer ability of lithium over alkyl-copper species may be responsible for the deoxygenation reaction of α, β -epoxy silanes which do not have any alkoxy groups on silicon atom.⁶

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- 1e** was prepared from phenylacetone by the Magnus method¹. **1e**: 73% yield; ¹H-NMR (CDCl₃, 270 MHz) δ 0.11 and 0.17 (two s, 9H total, 1/1 ratio), 1.20 (s, 3H), 2.14 and 2.17 (two s, 1H total) 2.70-2.93 (m, 2H) and 7.2-7.4 (m, 5H). **2e** (E isomer): ¹H-NMR (CDCl₃, 270 MHz) δ 0.10 (9H, s), 1.72 (3H, s), 3.27 (2H, s), 5.28 (1H, s), 7.1-7.3 (5H, m). **2e** (Z isomer): ¹H-NMR (CDCl₃, 270 MHz) δ 0.15 (9H, s), 1.69 (3H, s), 3.47 (2H, s), 5.41 (1H, s), 7.1-7.3 (5H, m).

Enzyme Resolution of 1-formyl-trimethylene-methane-iron-Tricarbonyl with Horse Liver Alcohol Dehydrogenase in Microemulsion

Kang Min Lee*, Daniel Martina[†], Chung Ung Park, and Jean-Francois Biellmann[‡]

Department of Molecular Biology, Chonbuk National University, Chonju 560-756

[†]Laboratoire de Chimie Organique Synthétique, ERA-687 Institut de Chimie, Université Louis Pasteur, 1 Rue Blaise Pascal, 67008 Strasbourg, France

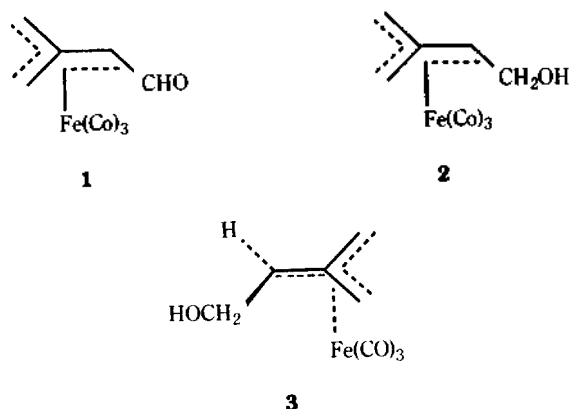
[‡]Laboratoire de Chimie Organique Biologique, UA-31, Institut de Chimie, Université Louis Pasteur, 1 Rue Blaise Pascal, 67008 Strasbourg, France

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The use of enzymes in organic synthesis is limited by the low water solubility of many substrates and by the high sensitivity of enzymes toward organic solvent¹⁻³. To overcome these problems, much attention has been paid to the solubilisation of hydrophilic enzymes in organic solvents in presence of a small amount of water with help of surfactant. For instance we studied cholesterol oxidase in microemulsion where cholesterol is highly soluble and extended this study to the preparative conversion of cholesterol to Δ^4 -cholestenone⁴⁻⁶. The stability and the kinetics of horse liver alcohol dehydrogenase (HLADH, EC.1.1.1.1)⁷, have been studied in microemulsion⁸⁻¹⁰. The cosurfactant of in the microemulsion, 1-butanol, is also a substrate of the enzyme and can be used to regenerate coenzyme NAD⁺ to NADH⁸. We have studied the kinetics of the reduction of cinnamaldehyde in buffer and in microemulsion. Cinnamaldehyde shows substrate inhibition. In microemulsion, through the partitioning of the substrate between the organic phase and the buffer, the concentration at which substrate inhibition occurred was so increased that a concentration of preparative significance was attained⁸.

The resolution of (\pm) formyl-trimethylenemethane iron tricarbonyl **1**¹¹⁻¹³ through derivatives, has been hampered by partial racemisation during regeneration of the aldehyde **1**¹³. (\pm) Aldehyde **1** is a substrate of HLADH (Michaelis constant 0.23 mM and maximum velocity 2.9 mmol min⁻¹ mg⁻¹ in 50 mM TES buffer, pH 7.5) showing substrate inhibition at a concentration above 0.45 mM. Hydroxymethylferrocene has been shown to be a substrate for this enzyme¹¹. For some unknown reasons, the kinetics of the reduction of aldehyde **1** by NADH with HLADH could not be determined in microemulsion made with t-butanol as cosurfactant⁸ since the reduction rate was not constant at what should have been the steady state.

We undertook the preparative reduction of the (\pm) aldehyde **1** (1.1 g; 4.9 mmol) in a microemulsion (5 ml: cyclohexane 60 g; 1-butanol 11 g; cetyltrimethyl ammonium bromide 11 g; 50 mM TES buffer pH 7.5, 18 g) containing the enzyme (HLADH 50 mg) and NAD⁺ (800 mg)¹⁵. After three days at 4°, the volatile solvents were removed under partial vacuum. The oily residue was treated with methylene chloride and filtrated on a porous glass filter. The solvent was evaporated and the crude material chromatographed on silica gel (30 g; hexane-ether). Aldehyde **1** (0.53 g) was eluted first and alcohol **2** second (0.50 g). The ee of the aldehyde was determined by ¹H-NMR analysis with a chiral agent: Tris (d,d-dicampholylmethanato) europium III¹⁶. The ee of the unreacted aldehyde was 68%. In order to determine the ee of the alcohol (0.5 g), its oxidation to the aldehyde **1** with manganese dioxide (2 g) in benzene (30 ml) for 3 hrs with a yield of 80% was performed. Using the NMR chiral



agent mentioned above, the ee of the obtained aldehyde ($[\alpha]_D + 248^\circ$; $c = 0.45$, CH_2Cl_2) was found to be 89%. The alcohol obtained by the enzymic reduction was recrystallised several times in pentane and after two recrystallisations, the melting point and specific rotation remained constant on further recrystallisations: mp. $64\text{--}65^\circ$ and $[\alpha]_D + 47^\circ$ ($c = 0.4$, CH_2Cl_2). Thus HLADH catalyses the reduction of both enantiomers of aldehyde **1** with a kinetic sufficiently different so that partial resolution can be achieved during the enzymic reduction (17).

Since its substrate specificity has been related to its tridimensional structure in the diamond lattice^{18,19} and the cubic space model²⁰, we attempted to explain with these models the enantioselective reduction of aldehyde **1**. The HLADH molecular model of the substrate was built with the bond lengths and angles published for phenyl trimethylenemethane iron tricarbonyl^{21,22}. The two enantiomers of aldehyde **1** were built in the cubic-space model and the Kendrew model of the active site was used. We assumed that hydride is delivered to the Re face of the carbonyl group for both enantiomers. We analyzed the (1-S) 1-formyl trimethylene methane iron tricarbonyl forms a complex with fewer violations of forbidden regions than the (1-R) enantiomer does. On the basis of this analysis, the (+) 1-hydroxymethyl trimethylene methane iron tricarbonyl ($[\alpha]_D + 47^\circ$), produced more rapidly in the enzyme reduction of (\pm) aldehyde **1**, is tentatively proposed to be of (1-S) chirality as presented in formula **3**. Enantioselective hydrolysis by pig liver esterase and enantioselective reduction by baker's yeast of organometallic compounds has been described²³⁻²⁶.

The work illustrates the preparative use of horse liver alcohol dehydrogenase in microemulsion for the stereoselective reduction of carbonyl compounds of low water solubility with cofactor recycling.

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Tandem Addition of α -Lithiomethane Phosphonate to Nitriles-N-Acylation: A Convenient Route to Enamine Phosphonates

Kilsung Lee and Dong Young Oh*

Department of Chemistry, Korea Advanced Institute of Science & Technology, Seoul 130-650

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