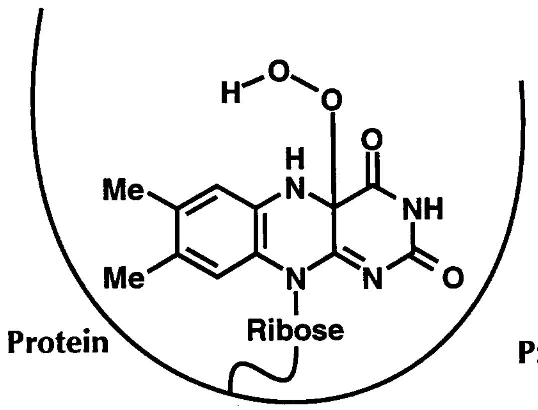
Bioinspired Oxidations Catalyzed by Transition Metal Complexes

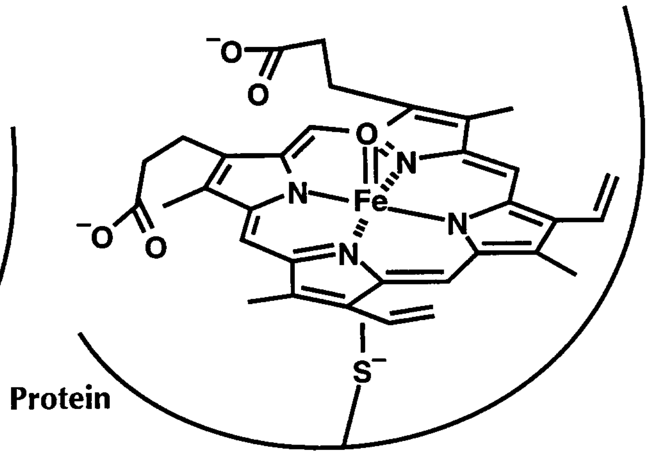
Professor Dr. Shun-Ichi Murahashi

Department of Chemistry, Graduate School of Engineering Science
Osaka University

Biomimetic Oxidation Reactions Using Transition Metal Catalysts

Metabolism of Amines with Oxygenase





Flavoenzyme

Fl—OOH

M—OOH

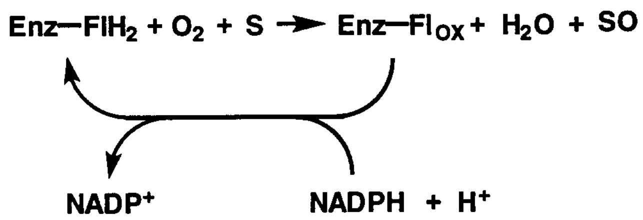
Cytochrome P-450

M=O

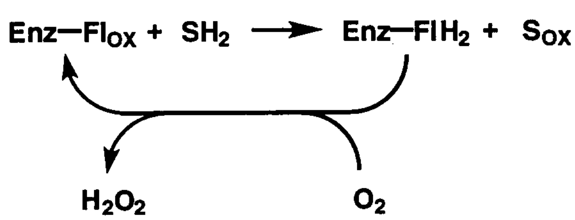
Exploitation of Flavoenzyme-Type Catalytic Oxidation Reactions

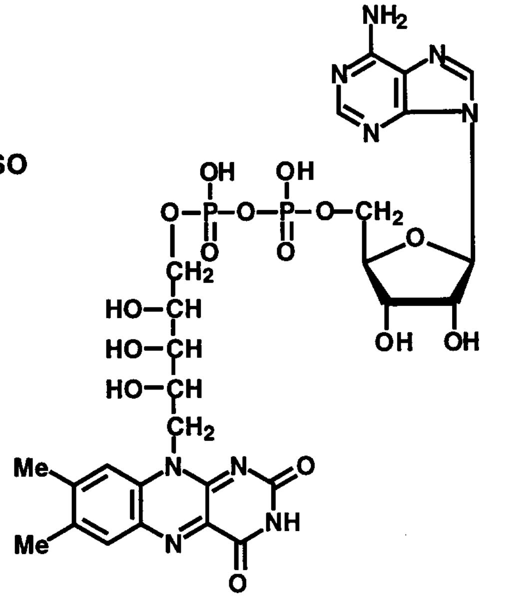
Flavoenzyme

Oxygenase



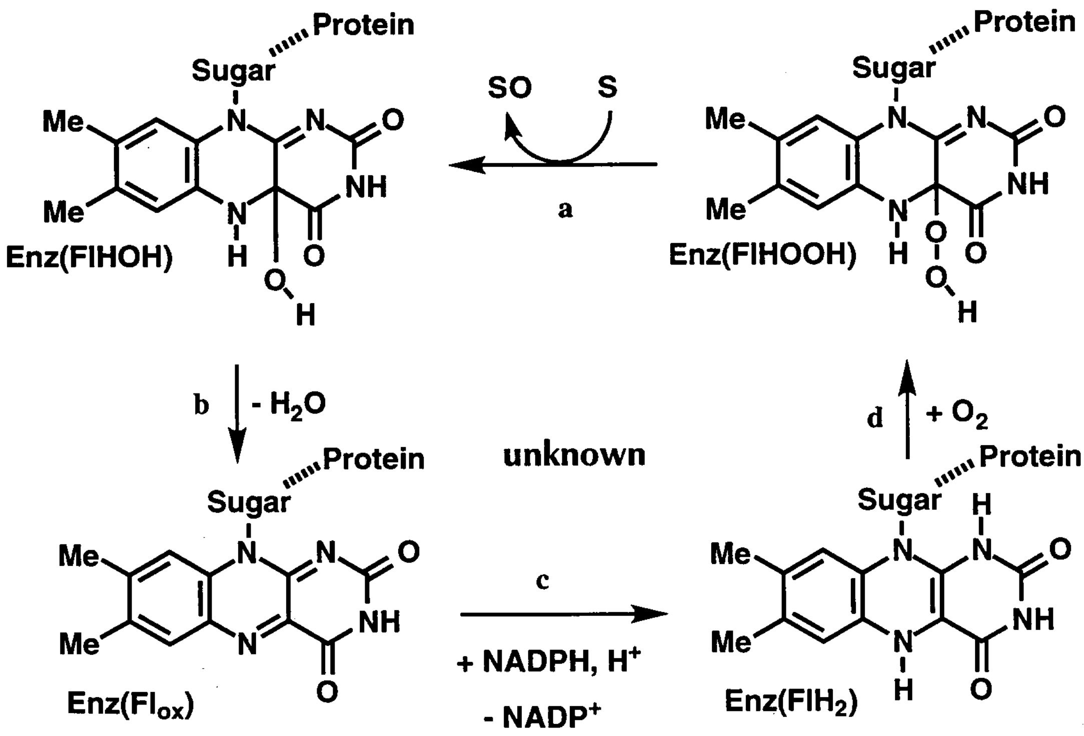
Oxidase



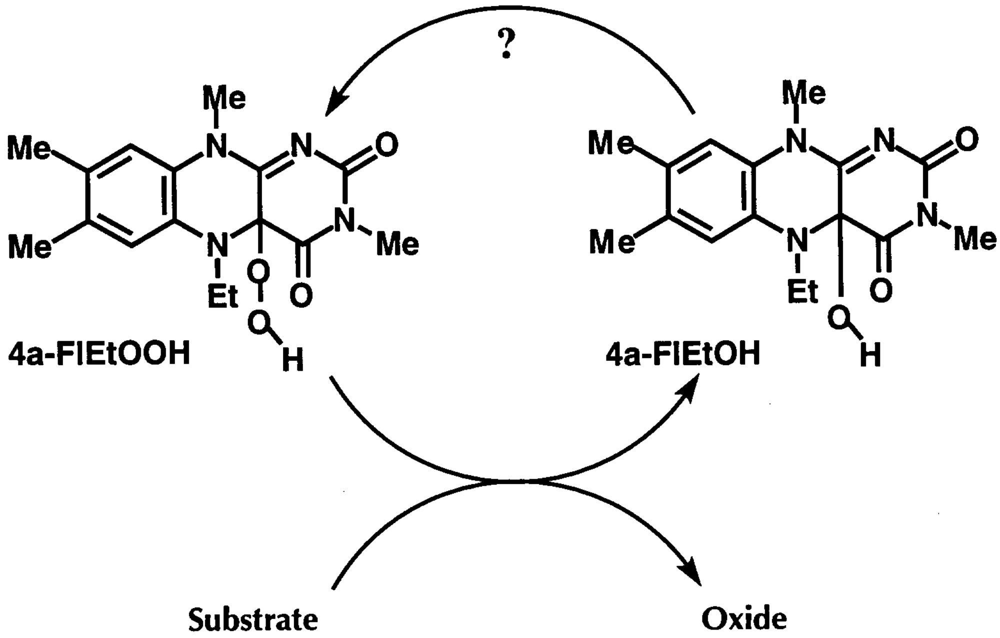


Flavin Adenine Dinucleotide (FAD)

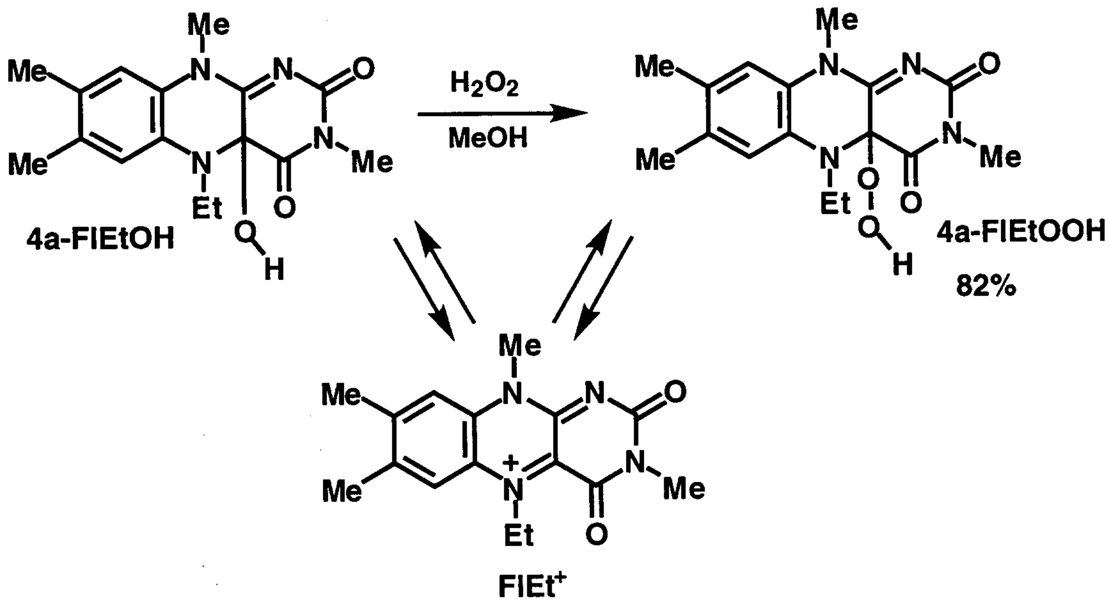
Mechanism of Flavin-Containing Monooxygenase



Mechanism of 4a-FlEtOH (Model Compound)

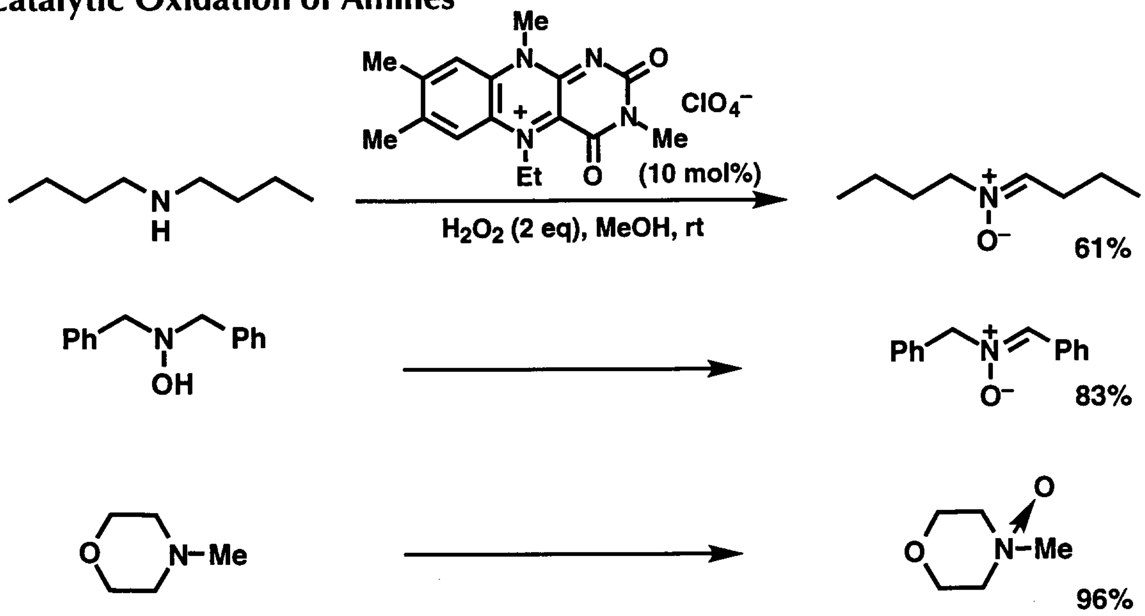


The Reactivity of 4a-FlEtOH and Formation of 4a-FlEtOOH

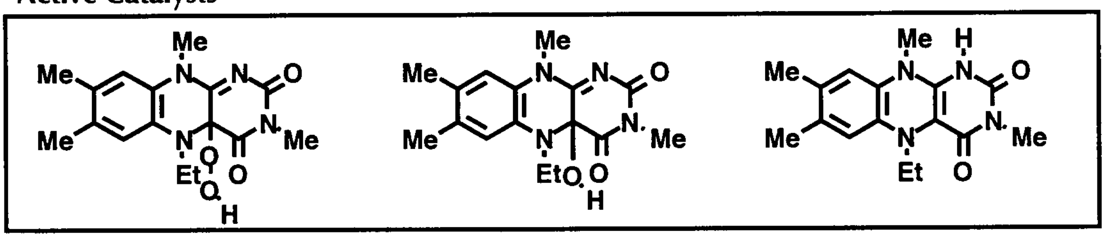


J. Am. Chem. Soc. 1989, *111*, 5002.

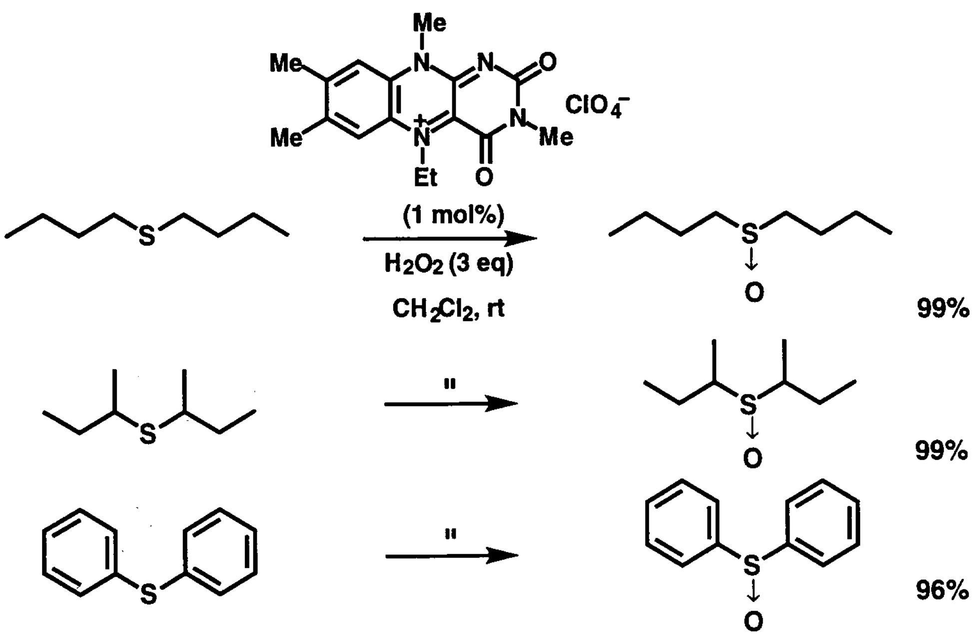
Catalytic Oxidation of Amines



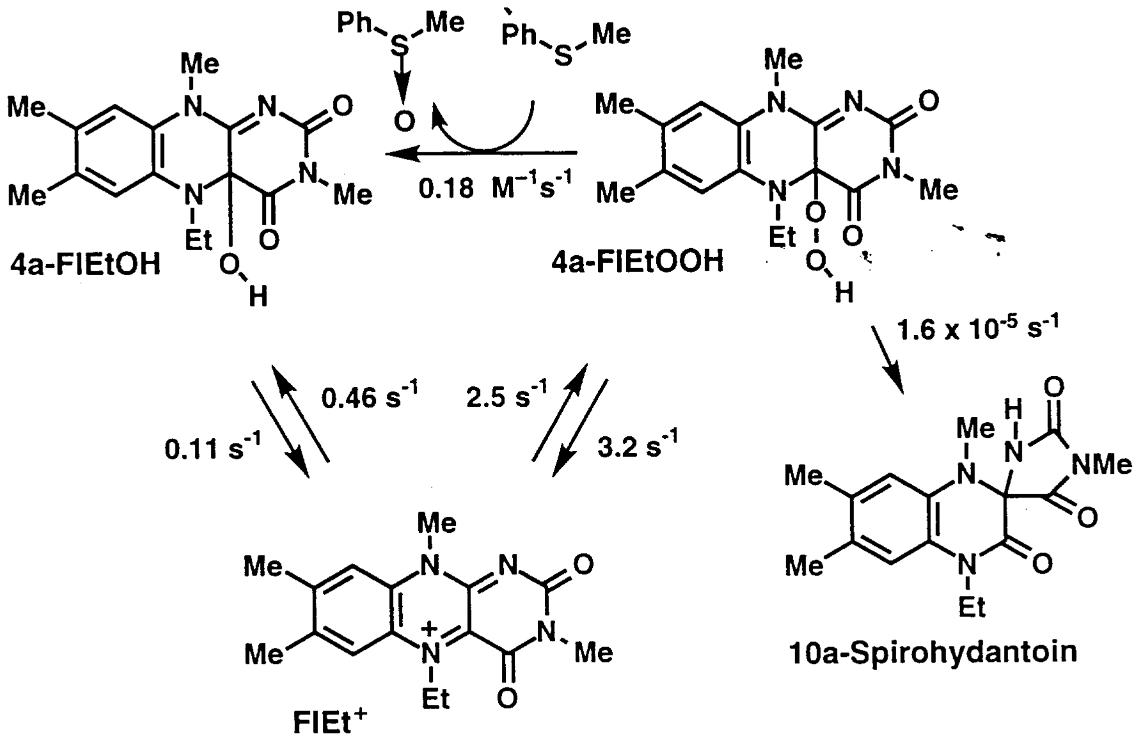
Active Catalysts



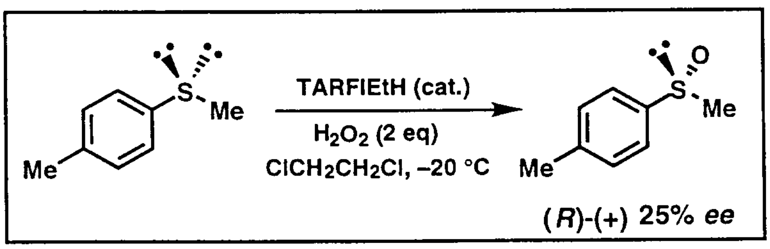
Catalytic Oxidation of Sulfides

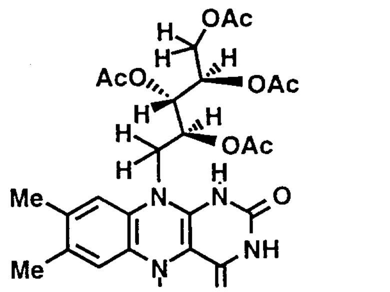


Flavin-Catalyzed Oxidation of Sulfide

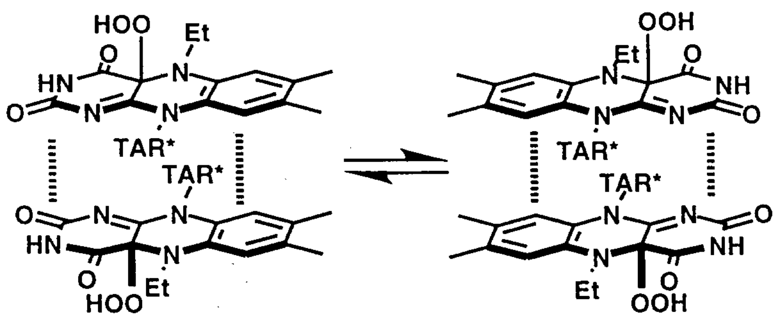


Riboflavin-Catalyzed Asymmetric Oxidation of Sulfide





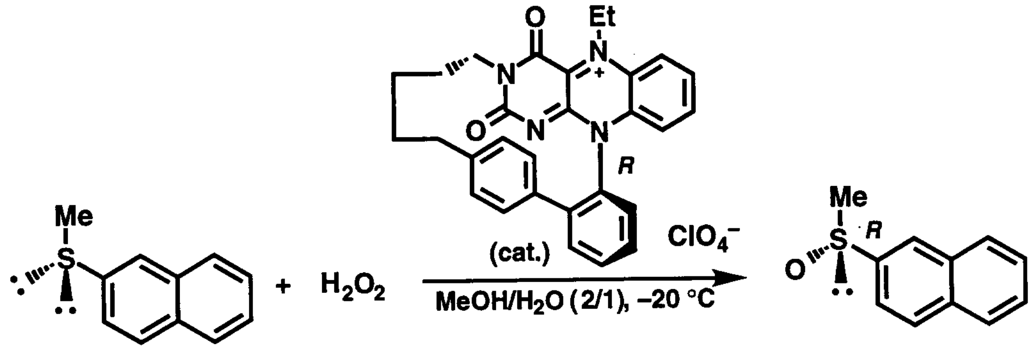
Tetraacetyl-5-ethyl-1,5-dihydroriboflavin
(TARFlEtH)



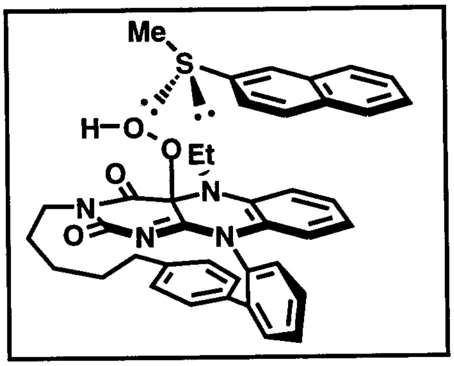
(*re*)–(*re*) stacking
4a-(*S*)-TARFlEtOOH

(*si*)–(*si*) stacking
4a-(*R*)-TARFlEtOOH

Biomimetic, Asymmetric, Catalytic Oxidation Reactions



94% yield
72%*ee*



Asymmetric Oxidation
Catalyzed by
Organic Molecules

Simulation of Hydroperoxyflavins with Hydroperoxymetals

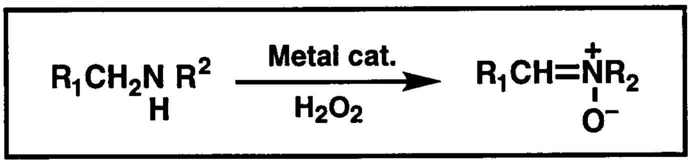
$$\mathrm{S + Fl{-}OOH \longrightarrow SO + Fl{-}OH}$$

$$\mathrm{S + M{-}OOH \longrightarrow SO + M{-}OH}$$

$$\mathrm{M \xrightarrow{H_2O_2} M{-}OOH \quad (M = W, Mo)}$$

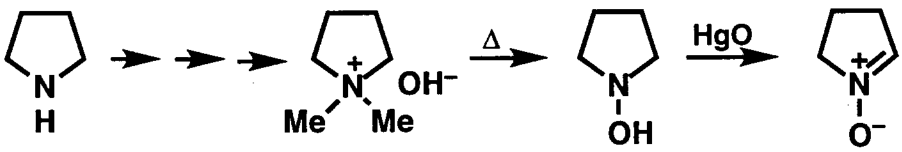
$$\mathrm{M{-}H \xrightarrow{O_2} M{-}OOH \quad (M = Pd)}$$

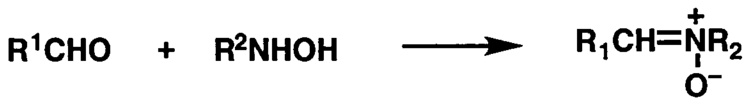
Metal-Catalyzed Oxidation of Secondary Amines



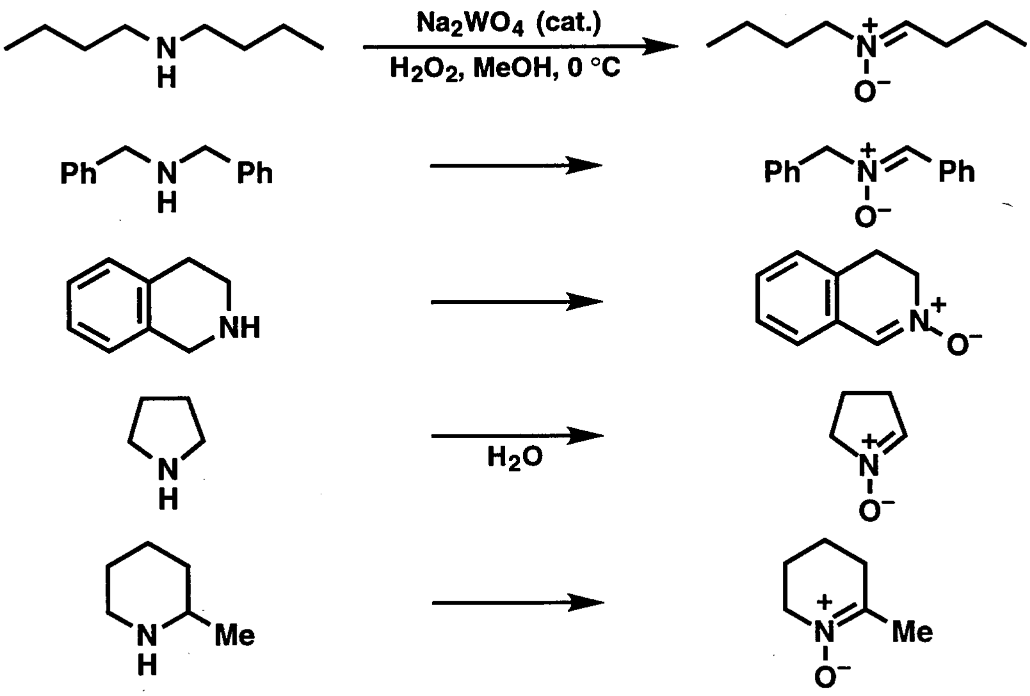
important synthetic
key intermediates

(*cf*) Conventional Methods for Synthesis of Nitrones





Tungstate-Catalyzed Synthesis of Nitrones



89%

85%

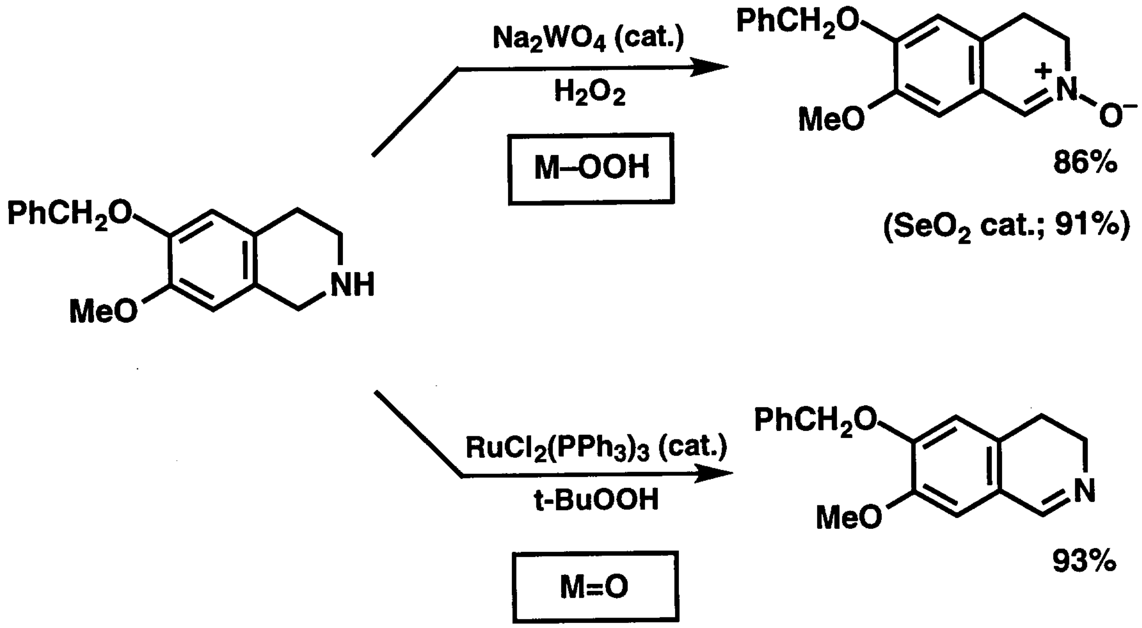
89%

44%

71%

Org. Syntheses 1992, *70*, 265.

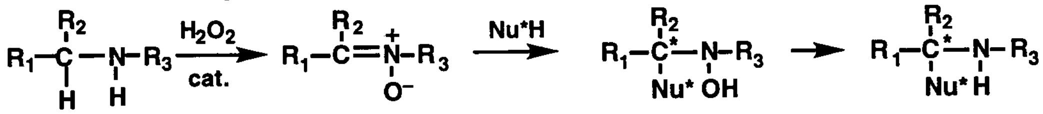
Difference between Active Species



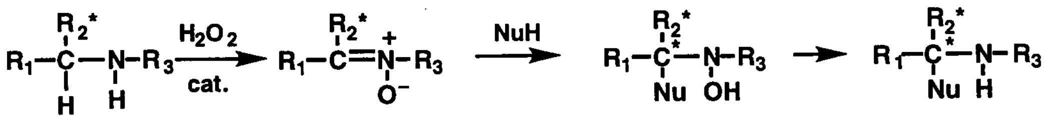
New Strategy for Synthesis of Optically Active Amines

Diastereoselective Reactions

A. Chiral Nucleophiles

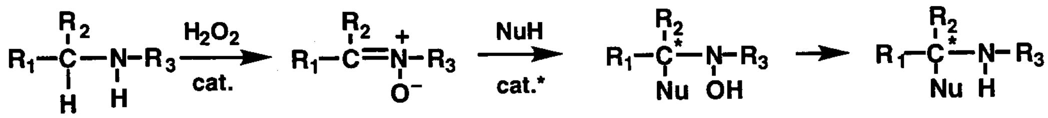


B. Chiral Nitrones

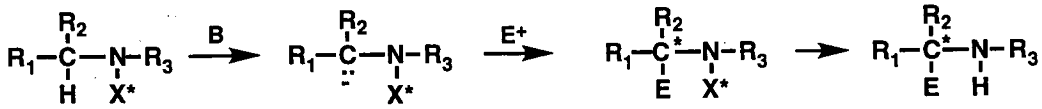


Enantioselective Reactions

C. Chiral Catalysts



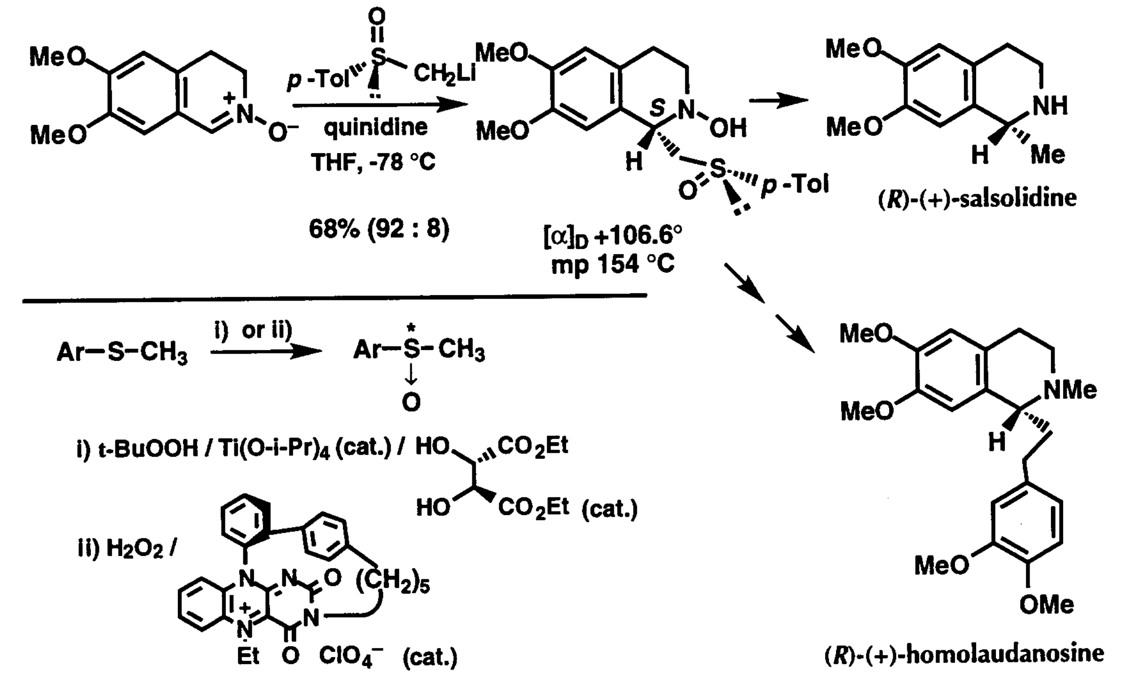
Conventional Method



B: *sec*-BuLi

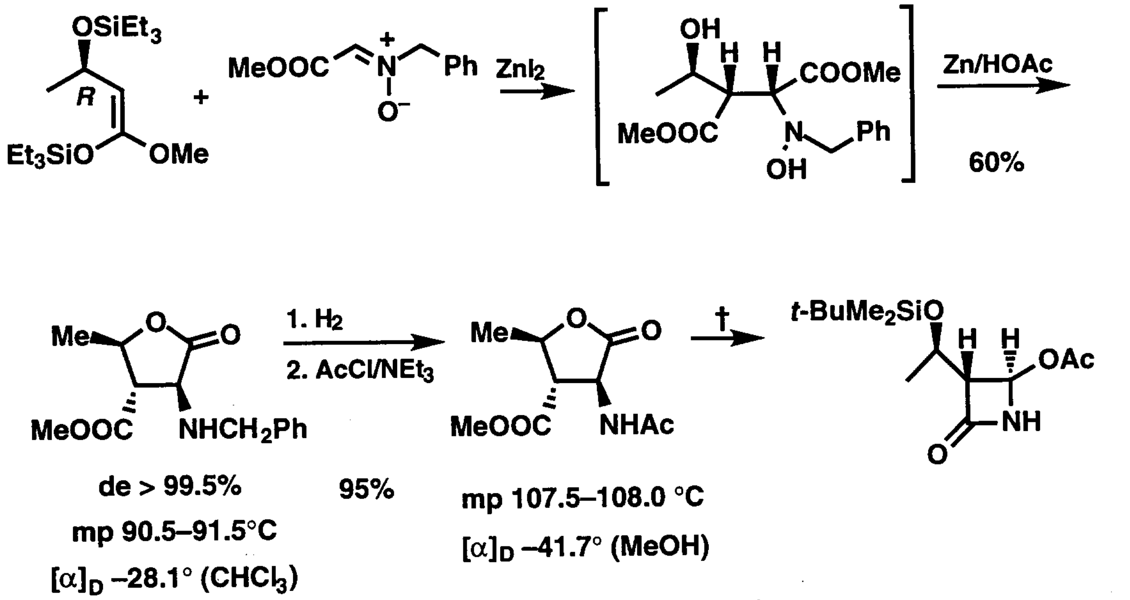
Beak, Meyers, Seebach

Synthesis of Isoquinoline Alkaloids —Introduction of Sulfinyl Anion—



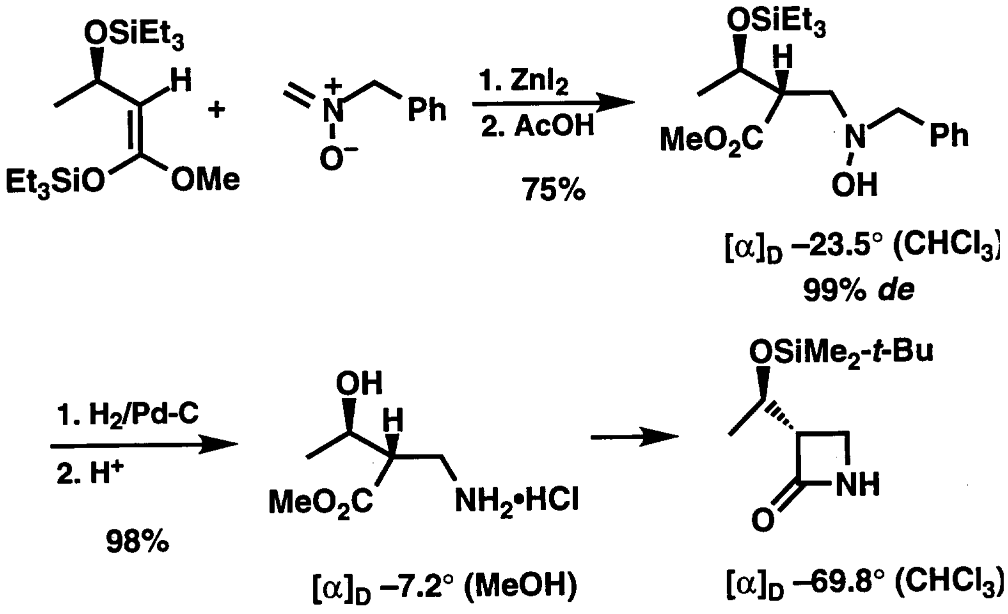
Tetrahedron Lett. 1993, *34*, 2645.

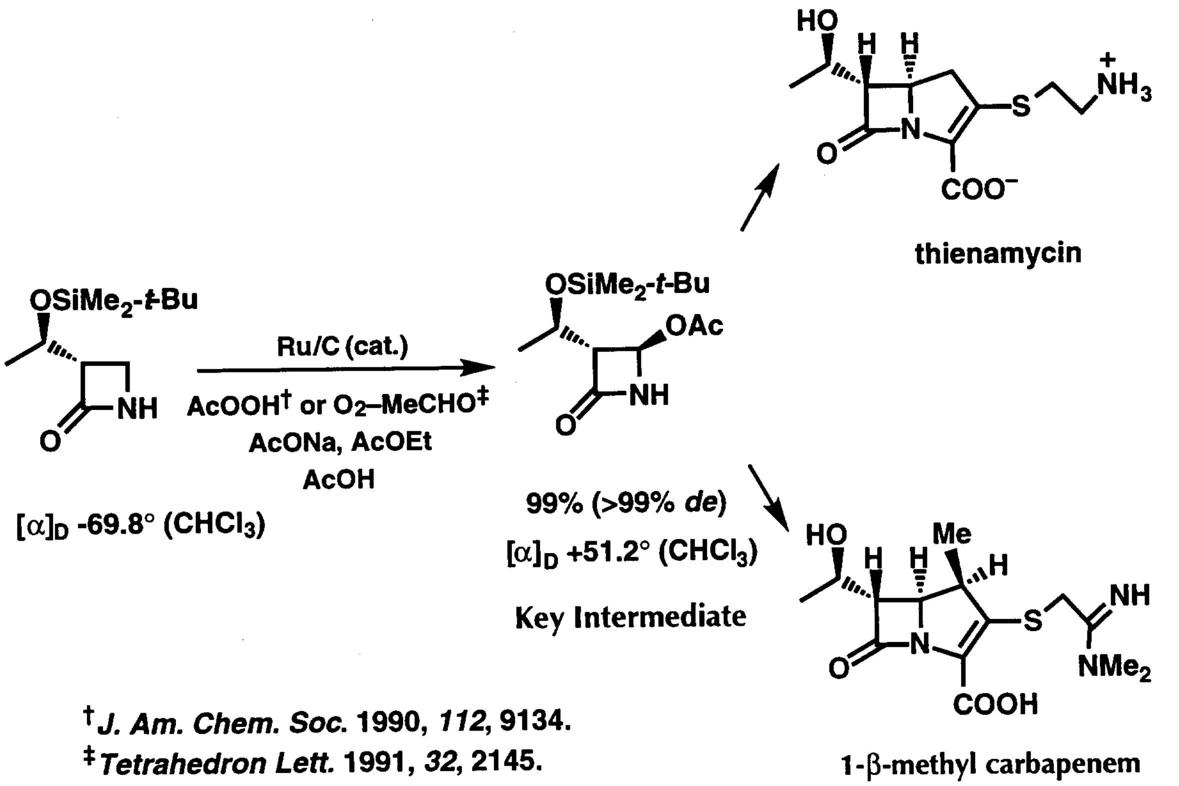
Stereoselective Synthesis of Acetoxy-β-lactams —Introduction of Chiral Enolates—



†Ciba-Geigy, J. P. 63-203661

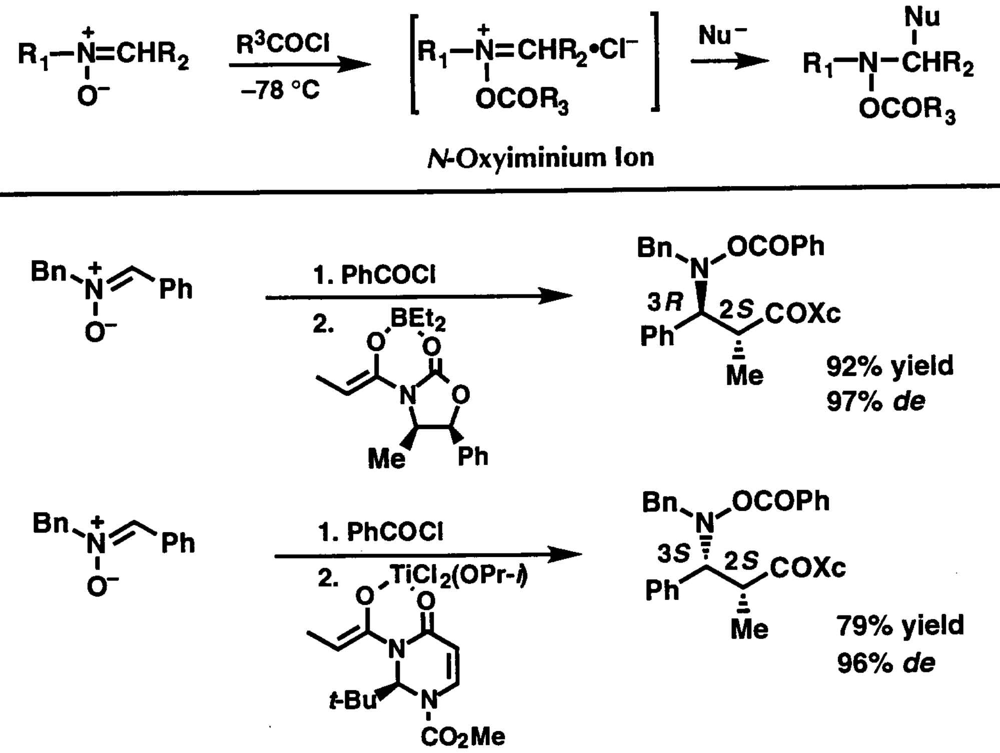
Synthesis of β-Amino Acids and β-Lactams



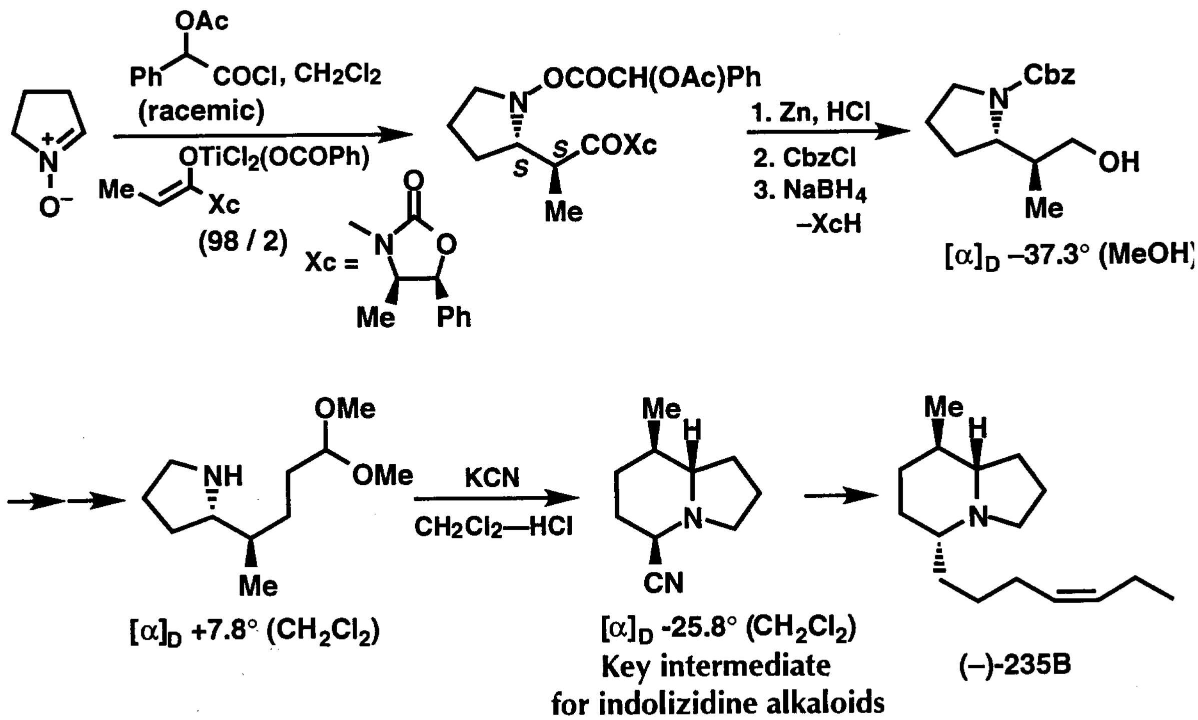


† *J. Am. Chem. Soc.* 1990, *112*, 9134.
‡ *Tetrahedron Lett.* 1991, *32*, 2145.

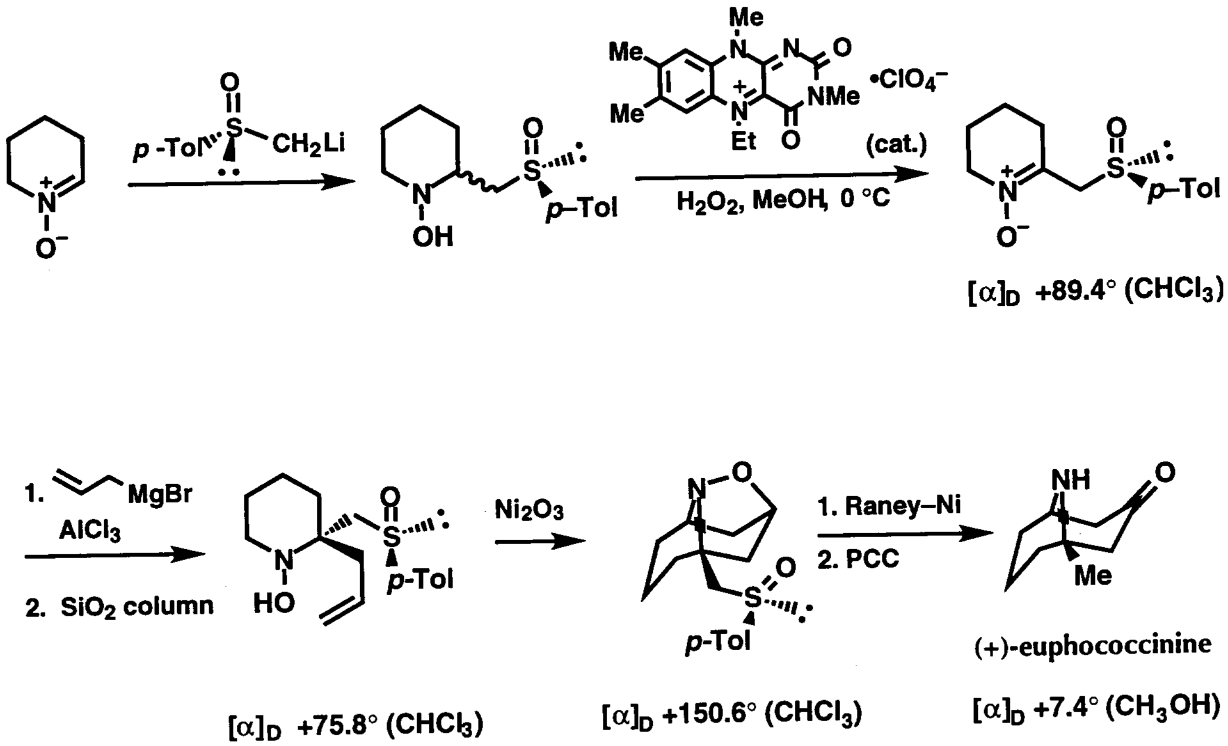
Generation of Highly Reactive *N*-Oxyiminium Ions



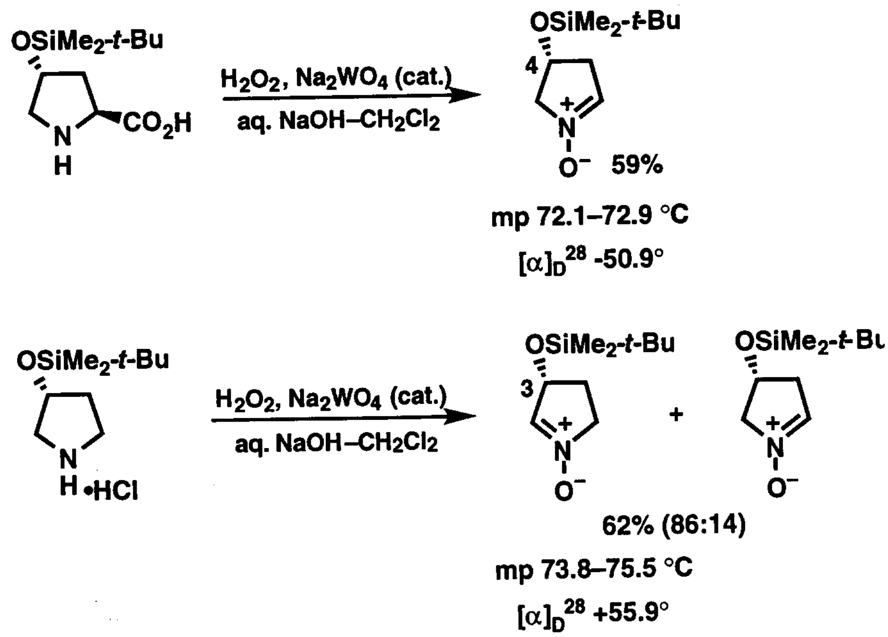
Asymmetric Synthesis of Indolizidine Alkaloids



Chiral β-Sulfinyl Nitrone —Synthesis of Pelletierine Alkaloid—

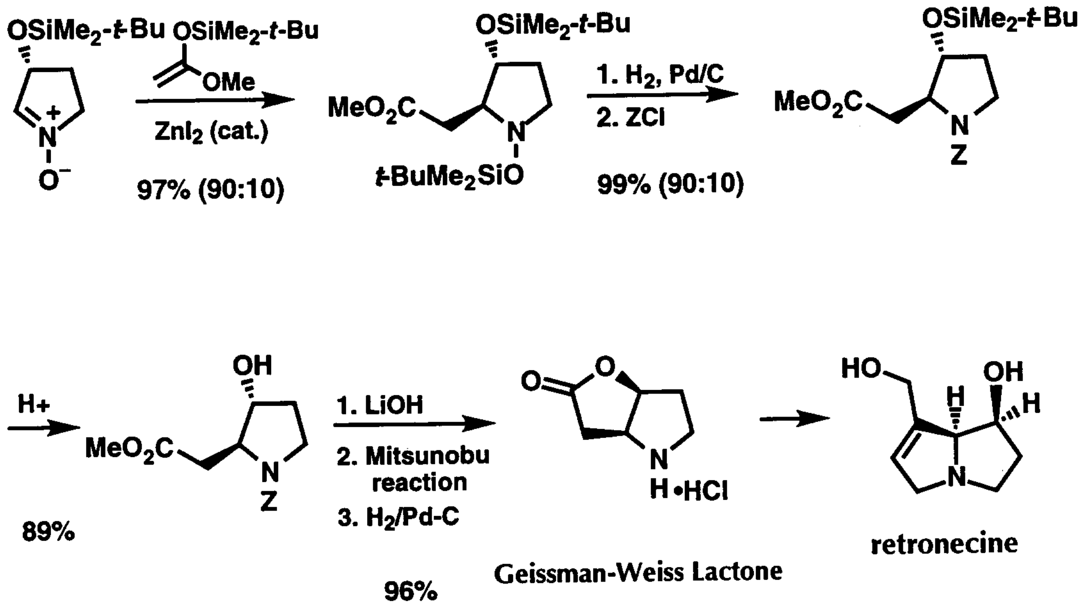


Regiocontrolled Synthesis of Chiral Nitrone



J. Org. Chem. 1994, *59*, 6170.

Synthesis of Geissman-Weiss Lactone (Key intermediate for pyrrolizidine alkaloids)

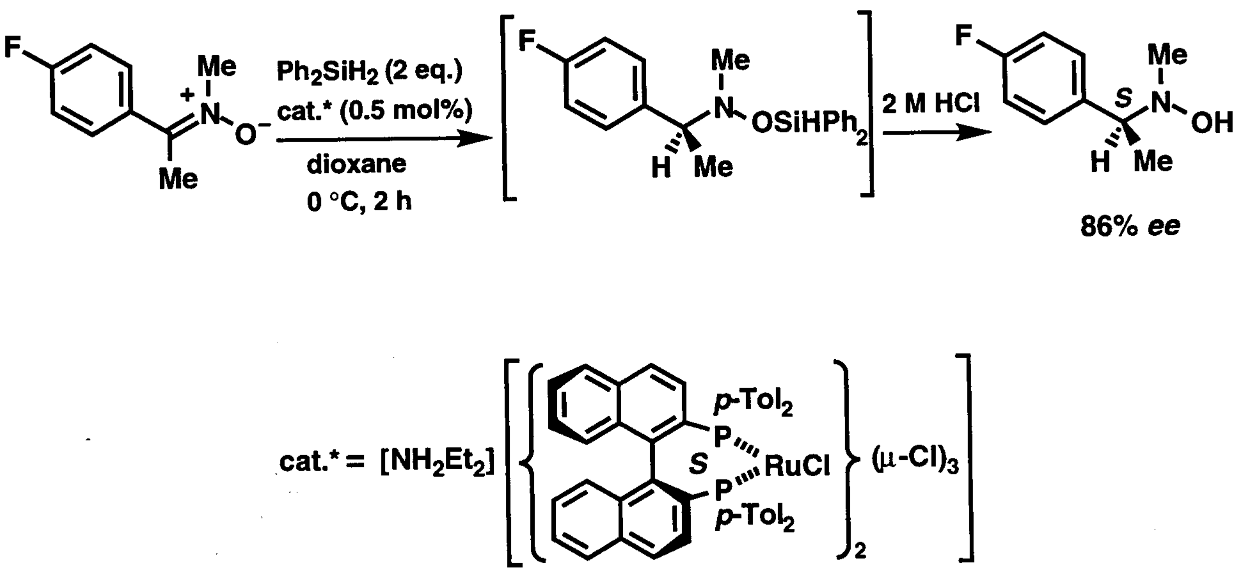


Geissman-Weiss Lactone

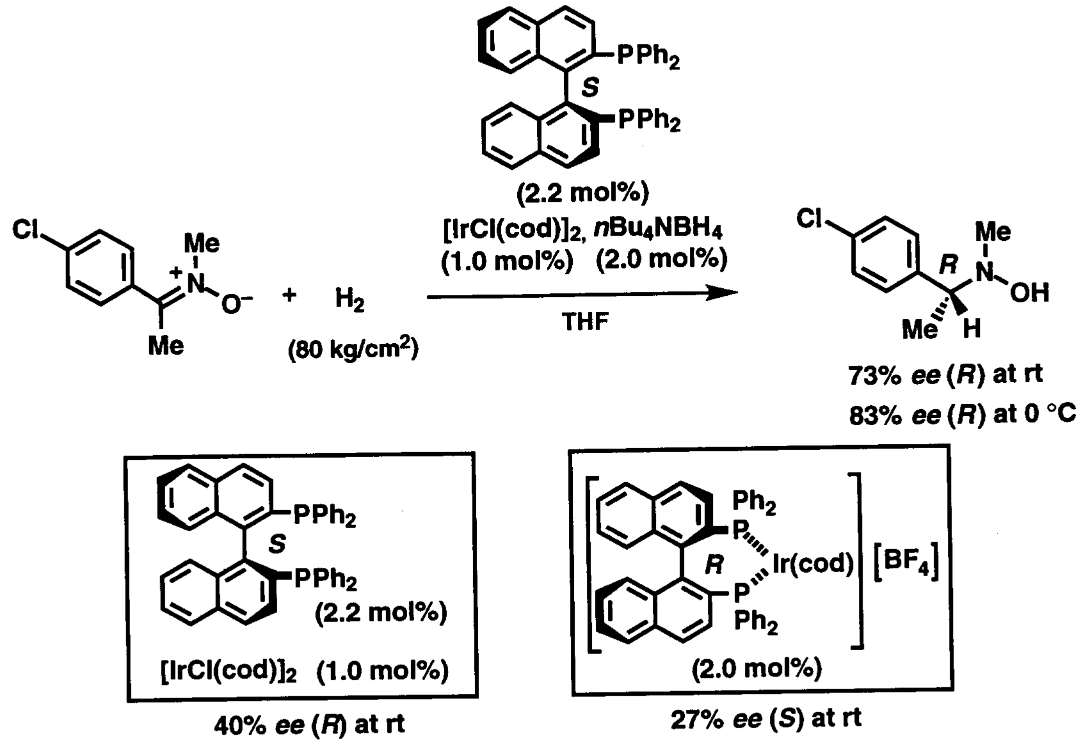
retronecine

Tetrahedron Lett. 1998, *39*, 2765.

Ruthenium-Catalyzed Hydrosilylation of Nitrones
—Asymmetric Synthesis of *N*-Hydroxylamines—



Iridium-Catalyzed Hydrogenation of Nitrones
—Asymmetric Synthesis of *N*-Hydroxylamine—



Reverse Enantioselectivity by Changing Achiral Ligands