

**Investigations in Enantioselective Catalysis.  
Development of Novel Asymmetric Organocatalytic  
Reactions.**

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For Liz, with more love and gratitude than words can express

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## Abstract

A new strategy for the catalysis of organic transformations using iminium ion activation has been developed. Using this strategy, the first asymmetric organocatalytic Diels-Alder reaction has been developed. This methodology has demonstrated the possibility of an imidazolidinone salt to function as an effective asymmetric catalyst for a wide variety of chemical transformations.

The iminium ion activation strategy has also proved successful for conjugate additions, and an asymmetric organocatalytic Mukaiyama-Michael reaction has been developed using the principles of LUMO-lowering catalysis. A more reactive and selective chiral imidazolidinone catalyst was developed, and this secondary amine has extended the range of transformations possible with iminium ion catalysis.

Progress has been made towards the development of an enantioselective organocatalytic alpha-oxidation of ketones. Proline catalysis has been demonstrated to effectively catalyze the asymmetric alpha-oxidation of cyclohexanone, but extension of this methodology to other ketones has not been successful. These studies have further demonstrated the utility of proline as a catalyst, and provide a platform for the extension of HOMO-raising catalysis to other organic transformations.

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## Abbreviations

**Cbz:** Benzyloxycarbonyl

**CI:** Chemical Ionization

**DBA:** DiBromoAcetic acid

**DCA:** DiChloroAcetic acid

**DFA:** DiFluoroAcetic acid

**DME:** 1,2-DiMethoxyEthane

**DMSO:** DiMethylSulfonyl Oxide

**DNBA:** 2,4-DiNitroBenzoic Acid

**d.r.:** Diastereomer Ratio

$E_T^N$ : Normalized empirical solvent polarity parameter; derived from the solvatochromism of a standard pyridinium-*N*-phenoxide betaine dye<sup>a</sup>

**EDG:** Electron-Donating Group

**ee:** Enantiomeric Excess

**EI:** Electrospray Ionization

**EtOAc:** Ethyl acetate

**EWG:** Electron-Withdrawing Group

**FAB:** Fast Atom Bombardment ionization

**FMO:** Frontier Molecular Orbital

**GLC:** Gas Liquid Chromatography

**h:** hour

**Hex:** hexanes

**HOAc:** Acetic acid

**HOAcCN:** Cyanoacetic acid

**HOMO:** Highest Occupied Molecular Orbital

**HPLC:** High Performance Liquid Chromatography

**HRMS:** High Resolution Mass Spectroscopy

**Hz:** Hertz

**IR:** Infrared

**LUMO:** Lowest Unoccupied Molecular Orbital

**M:** Molar

***m:*** *meta*

**mg:** milligram

**min:** minute

**mL:** milliliter

**mmol:** millimole

**MsOH:** Methanesulfonic acid

**mT:** millitorr

**NMR:** Nuclear Magnetic Resonance spectroscopy

***o:*** *ortho*

**organocatalysis:** Catalysis of a transformation by a wholly organic catalyst (not by an organometallic catalyst)

**organocatalyst:** A catalyst of wholly organic composition (not organometallic)

***p:*** *para*

**ppm:** Parts Per Million

**PTSA:** *para*-Tolune Sulfonic Acid

**TBS:** *tert*-ButyldimethylSilyl

**TIPS:** TriIsopropylSilyl

**TMS:** TriMethylSilyl

**TCA:** TriChloroAcetic acid

**TFA:** TriFluoricAcetic acid

**TfOH:** Trifluoromethanesulfonic acid

**THF:** TetraHydroFuran

**TLC:** Thin Layer Chromatography

**XRD:** X-Ray Diffraction

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<sup>a</sup> Reichardt, C.; Harbusch-Görnert, E. *Liebigs. Ann. Chem.* **1983**, 721. Laurence, C.; Nicolet, P.; Lucon, M.; Reichardt, C. *Bull. Soc. Chim. Fr.* **1987**, 125. Laurence, C.; Nicolet, P.; Lucon, M.; Reichardt, C. *Bull. Soc. Chim. Fr.* **1987**, 1001.