

Homogeneous Catalysis. $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})_2]^{2+}$: An Air-Stable, Water-Tolerant Diels-Alder Catalyst

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The classical Diels-Alder reaction is promoted by a variety of Lewis acids, usually derived from the halides of trivalent boron and aluminum and from tetravalent titanium and tin. As catalysts, these traditional Lewis acids present a number of inherent problems which are difficult to circumvent. Among these problems are their extreme sensitivity to water, which leads to inactivation of the catalyst, and in many, but not all, cases their low turnover number. As a consequence, very high catalyst loadings ranging from 10 to 100% have been employed to compensate for adventitious water and to promote the reaction. When these traditional Lewis acids are modified for enantioselection by incorporation of chiral ligands, new problems arise. Depending on the chiral ligand, traditional Lewis acids have a strong tendency to oligomerize and are subject to disproportionation and to facile ligand exchange. Because of this, the identification of the catalytic species is made extremely difficult even if the catalyst is isolated. For enantioselective transformations, the chiral catalyst is almost always prepared in situ, which may lead to a variety of species having different selectivities. Moreover, since the parent halide is generally more catalytically active than the modified chiral catalyst, there is the possibility that much of the catalysis could proceed by an achiral path if some of the starting halide remains. Despite these difficulties, very high enantiomeric excesses have been reported by the use of in situ derived chiral catalysts.¹

In order to obviate some of these inherent problems associated with traditional Lewis acids, we investigated the possibility of developing new classes of Lewis acids derived from transition metal complexes. These species potentially could provide chiral catalysts which are stable, have defined geometries, and may be insensitive to water. We describe here such a Lewis acid catalyst and report on its effectiveness in catalyzing the classical Diels-Alder reaction.

We chose the catalyst $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})_2](\text{CF}_3\text{SO}_3)_2^{2+}$ which is readily prepared from $[\text{Ti}(\text{Cp}^*)_2\text{Cl}_2]^{2+}$ by reaction with AgCF_3SO_3 . The ligand Cp^* is the pentamethylcyclopentadienyl anion. The dark-violet crystals of $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})_2](\text{CF}_3\text{SO}_3)_2$ are stable and can be handled in air. It is soluble in moderately polar solvents such as CH_2Cl_2 and CH_3NO_2 , but it is not soluble in nonpolar solvents such as benzene. We found that CH_2Cl_2 and CH_3NO_2 were the most suitable solvents. For catalysis, neither the solvent nor the Diels-Alder substrates need to be dried.

The results of catalysis are collected in Table I. Catalysis was carried out using 1 mol % catalyst loading and 1 M concentration in each substrate in CD_2Cl_2 solution at 25 °C. Included in Table I are the times for 90% completion of catalysis and the corresponding isomer ratios. Also included are the estimated times for 90% completion of the thermal reaction and the corresponding thermally produced isomer ratios. The thermal times were estimated by extrapolating a second-order plot to 90% reaction. Where no thermal reaction was observed after 24 h at 25 °C at 1 M concentration in each substrate in CD_2Cl_2 solutions, we estimated that the time for 90% completion of the thermal reaction was $>10^5$ h.

An inspection of Table I reveals that at 1 mol % catalyst loading catalytic rate accelerations of between 10^2 and $>10^5$ are observed over the corresponding thermal reaction. Of course, these differences can be accentuated with increased catalyst loading. As is nearly always observed, the catalytic reaction increases the selectivity.

The catalysis is remarkably insensitive to the presence of water. Thus using the substrates shown in entry 1, we find that the catalytic rate is about the same in CD_3NO_2 as it is in CD_2Cl_2 . Using 1 mol % catalyst and 1 M in each substrate in CD_3NO_2 solution, addition of 100 equiv of H_2O (1 M), which gives essentially a saturated CD_3NO_2 solution, slows the rate of catalysis by about a factor of 3. Addition of 10 equiv of water has no effect on the rate. Further, the present catalyst does not appear to exhibit product inhibition which might occur by competitive binding of the product to the catalyst. Thus for the Diels-Alder pair shown in entry 1, we find that the rate of catalysis is not detectably decreased in the presence of 100 initial equiv (1 M) of product. It therefore appears that catalysis will continue indefinitely.

Although the catalyst has these desirable features, it is restricted to substrates which are readily catalyzed because it slowly polymerizes 1,3-dienes. Thus at 1 mol % catalyst, isoprene and cyclohexa-1,3-diene are slowly polymerized over a period of about 80 h at 25 °C in CD_2Cl_2 . As a consequence, the catalytic yield for Diels-Alder partners which have slow turnover frequencies tend to be low because of competitive polymerization. For example, the catalysis of isoprene with crotonaldehyde and cinnamaldehyde gave 40% and 11% Diels-Alder product, respectively, after 21 h with concurrent polymerization of isoprene. With isoprene and 2-cyclopentenone, 2-cyclohexenone, or methylacrylate, only polymerization was observed.

The diaquo complexes of bent metallocenes tend to be moderately strong acids,^{2,4} and it is conceivable that the observed catalysis is wholly or partly due to proton catalysis.⁵ This does not appear to be the case because we observe no acid catalysis of methyl vinyl ketone with isoprene after 24 h at 25 °C in the presence of 1 mol % trifluoroacetic acid ($\text{p}K_a = 0.52$)⁶ in CD_2Cl_2 solution. It is probable that the proton activity of trifluoroacetic acid is greater than that of the bound aquo groups.⁴ In concurrence, we find that the non-acidic species $[\text{Ti}(\text{Cp}^*)_2(\text{dimethylformamide})_2](\text{CF}_3\text{SO}_3)_2^{2+}$ also catalyzes the Diels-Alder reaction, albeit at a much slower rate than the diaquo analog.

That labile ligands are required for catalysis is supported by our observation that neither $[\text{Ti}(\text{Cp}^*)_2\text{Cl}_2]$ nor $[\text{Ti}(\text{Cp}^*)_2(\text{O}_2\text{CCF}_3)_2]$ acts as a catalyst. It is probable that catalysis proceeds via an intermediate of the type $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})(\text{dienophile})]^{2+}$, where the oxygen atom of the dienophile binds to the titanium atom.

A variety of transition metal based Lewis acids have been reported,⁸ and some have been employed for catalysis.⁹ The most notable of these in the present context are certain tungsten,¹⁰ molybdenum,¹¹ and zirconium¹² complexes which, although water sensitive and although some are polymerization catalysts, act in catalyzing a number of Diels-Alder reactions. It is clear that the

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

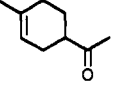

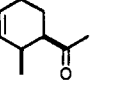

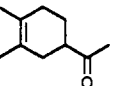

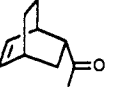


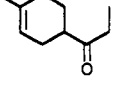

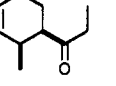

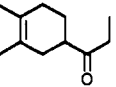

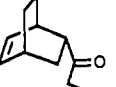


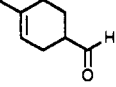

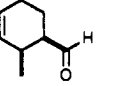

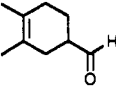

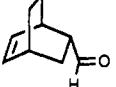


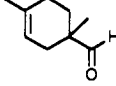

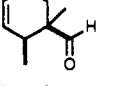

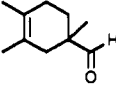

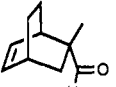
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Table I. Diels-Alder Catalysis by $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})_2](\text{CF}_3\text{SO}_3)_2$ in CD_2Cl_2 Solutions at 25 °C

	dienophile ^a	diene ^a	catalytic reaction		major product	thermal reaction	
			time for 90% reaction (h)	isomer ratio		time for 90% reaction (h)	isomer ratio
1			13	94:6		6×10^3	70:30
2			3.6	94:4:2:0 ^f		7×10^3	72:16:9:3
3			3.2			4×10^3	
4			2.1	95:5		$>10^5$	93:7
5			6.7 ^b	89:11		4×10^3	66:34
6			13	ND ^{c,d}		$>10^5$	ND
7			11			3×10^3	
8			10	100:0		$>10^5$	ND
9			6.7	95:5		5×10^3	70:30
10			5.0	93:4:3:0 ^f		4×10^3	86:9:5:0
11			1.3			3×10^3	
12			3.2	94:6		$>10^5$	89:11
13			32	91:9		$>10^5$	70:30
14			7.8	95:4:1:0 ^f		$>10^5$	ND
15			4.4			$>10^5$	
16			76 ^e	75:25		$>10^5$	ND

^aCatalysis was carried out at 1 M concentration in each substrate and 1 mol % catalyst except as noted. ^b2 mol % catalyst. ^cND = not determined. ^dOverlapping signals prevented determination of isomeric ratios. ^ePolymerization observed during the catalysis. ^fThe isomer ratio sequence is *cis*-1,2:*trans*-1,2:*cis*-1,3:*trans*-1,3.

present catalyst can be transformed readily into chiral catalysts of defined structure.

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Supplementary Material Available: Details of improved preparations of $[\text{Ti}(\text{Cp}^*)_2\text{Cl}_2]$, $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})_2](\text{CF}_3\text{SO}_3)_2$, and $[\text{Ti}(\text{Cp}^*)_2(\text{O}_2\text{CCF}_3)_2]$, details on performance of the catalyses, and a second-order plot for Diels-Alder catalysis (3 pages). Ordering information is given on any current masthead page.

New Copper(I)-Catalyzed Reactions of Oxaziridines: Stereochemical Control of Product Distribution

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The reactions of oxaziridines with various metals, notably iron, have been investigated since those heterocycles were first reported by Emmons in 1957.¹ In general, single-electron transfer effects N-O bond cleavage to afford nitrogen-centered radical/alkoxide pairs, which typically undergo protonation and β -scission or radical rearrangement reactions. Given the similarity of these reactions to radical-mediated reactions of *N*-chloroalkylamines² and contemporary interest in nitrogen-centered radicals in synthesis,³ an

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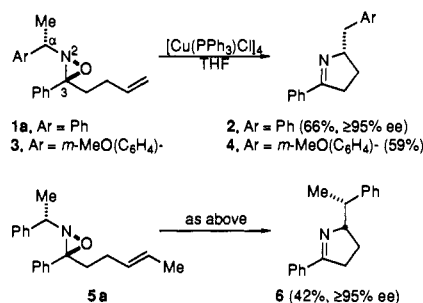
[†]X-ray crystallographic facility, Department of Chemistry.

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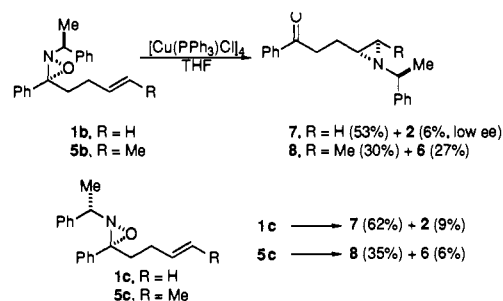
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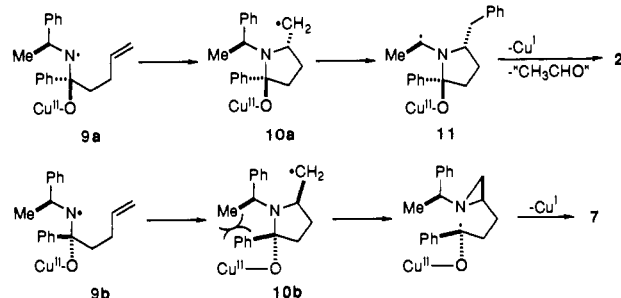
Scheme I



Scheme II



Scheme III



investigation of the intramolecular addition reactions of radicals generated from chiral oxaziridines⁴ was undertaken. Here, we report (1) conditions to effect N-O cleavage under nonaqueous, neutral conditions; (2) two remarkable, highly stereoselective reaction pathways for oxaziridine-derived radicals yielding enantiomerically enriched pyrrolines or aziridines, respectively; and (3) that the stereochemistry of the starting oxaziridine profoundly affects the course of its reaction.

A survey of several organometallic reagents showed that $[\text{Cu}(\text{PPh}_3)\text{Cl}]_4$ in THF could conveniently effect the formation of nitrogen-centered radicals from oxaziridines.⁶ Therefore, a 3-butenyloxaziridine **1**⁷ was dissolved in degassed THF with 5 mol

(4) Reviews: (a) Davis, F. A.; Jenkins, R. H., Jr. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds.; Academic: Orlando, FL, 1984; Vol. 4, pp 313-353. (b) Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703-5742.

(5) Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, J. *Inorg. Chem.* **1972**, *11*, 1818-1825.

(6) Depending on the structure of the starting oxaziridines, this reagent can effect N-O homolytic processes leading to C → N alkyl migration, α -cleavage, or allylic H-atom abstraction. All of these processes are consistent with the intervention of nitrogen radicals or related species. Wang, Y.; Peng, X.; Gülgeze, B.; Aubé, J. Unpublished work from these laboratories.

(7) The oxaziridines used in this study were prepared from the corresponding ketone via formation of the imine using (*S*)- α -methylbenzylamine and subsequent oxidation with *m*-CPBA. The structures were determined by NMR spectroscopy and the known⁸ stereochemical course of imine oxidation reactions (see supplementary material). All new compounds were fully characterized and gave satisfactory ¹H and ¹³C NMR, IR, MS, and HRMS or elemental analytical data.

(8) (a) Belzecki, C.; Mostowicz, C. *J. Org. Chem.* **1975**, *40*, 3878-3880. (b) Bucciarelli, M.; Forni, A.; Moretti, I.; Torre, G. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1339-1346. (c) Mostowicz, D.; Belzecki, C. *J. Org. Chem.* **1977**, *42*, 3917-3921. (d) Forni, A.; Garuti, G.; Moretti, I.; Torre, G.; Andreetti, G. D.; Bocelli, G.; Sgarabotto, P. *J. Chem. Soc., Perkin Trans. 2* **1978**, 401-405.