Selective Hydrogenation of Substituted Dienes Catalyzed by an Organoyttrium Complex

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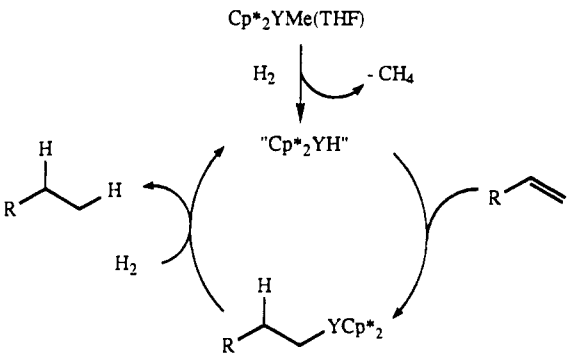
Summary: $Cp^*_2YMe(THF)$ has been developed as an efficient catalyst for the selective reduction of substituted dienes.

Catalytic hydrogenation of olefins stands as one of the most important and fundamental transformations in synthetic organic chemistry. The strive for selectivity in this process has led to the development of numerous heterogeneous[2] and homogeneous catalysts.[3] Although kinetic rate studies indicate that many of these should provide high selectivity in reduction of monosubstituted olefins in the presence of more highly hindered alkenes,[2-4] in fact relatively few studies demonstrate this capability in polyfunctional molecules.[2,3,5] Furthermore, the extremely challenging task of site-selective reduction of α,ω-dienes, in which the two olefins are differentiated only by allylic substitution of one of the alkenes, has apparently not been addressed. Our interest in utilizing lanthanide reagents for stereoselective organic transformations[6] prompted us to initiate a program exploring the use of organolanthanide and group 3 organometallic catalysts to address these issues.

Organolanthanides and group 3 organometallics have proven to be efficient catalysts for alkene and alkyne hydrogenation. Unfortunately, the process has yet to be developed into a useful, general synthetic technique.[7] One major concern at the outset of our studies was that of functional-group compatibility. The extreme Lewis acidity of highly electron-deficient organolanthanides and group 3 organometallics[8] makes them incompatible with many functional groups. Even ethers are not tolerated by some of these complexes, because ethers complex irreversibly with the metal or are readily cleaved by the catalyst, either of which destroy the catalytic activity of the organometallic.[8,9] Additionally, the scope of selectivity to be expected in the hydrogenation of polyenes by these organometallic catalysts has not been critically examined. In the single example wherein selective hydrogenation with lanthanide catalysts has been demonstrated, $[Me_2Si(C_5Me_4)_2NdH]_2$ reduces (+)-limonene at the terminal olefin to the near exclusion of the endocyclic trisubstituted alkene.[7c]

Scheme I



In catalytically viable organolanthanide and group 3 organometallic complexes (i.e., those possessing terminal, nonbridging ligands[10]) the reactivity and selectivity observed in rate-dependent olefin insertion reactions are determined largely by the "cone angle of reaction" formed by the two cyclopentadienyl rings in the bent metallocenes. The wider this angle, the more reactive (less selective) the complex is likely to be, and conversely a smaller angle will result in less reactive (more selective) catalysts. Selectivity in reactions of these complexes with polyfunctional organic substrates can therefore arise as a result of either "metal tuning" or "ligand tuning". Metal tuning can be achieved by taking advantage of the well-known lanthanide contraction. Because early lanthanides have a larger ionic radius, bent metallocenes incorporating these metals will have a larger "cone angle of reaction". All other factors being equal, catalysts containing early lanthanides should provide greater reactivity relative to complexes incorporating the late lanthanides or yttrium.[7] Reactivity can also be adjusted by varying the ligands on the metal. Chelating bis(cyclopentadienyl) ligands with a silicon atom hinge provide a wider angle than simple bis(pentamethyl)-cyclopentadienyl ligands, and catalysts incorporating the former are anticipated to be more reactive (less selective) than catalysts containing the latter.[7,8,10,11]

With these factors in mind, we set out to develop a highly selective organolanthanide or group 3 organometallic catalyst which would be capable of reducing only monosubstituted olefins. A further goal was to achieve site selectivity in the monoreduction of α,ω-dienes in which the two olefins were differentiated only by allylic substitution on one of the olefins. As a starting point we chose to investigate the use of $Cp^*_2YMe(THF)$[12] as a precatalyst

(1) Alfred P. Sloan Fellow, 1987-1991; American Cyanamid Academic Awardee, 1989.

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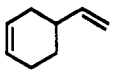
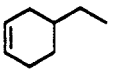
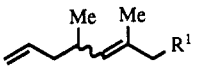
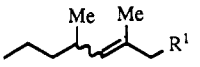
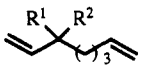
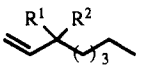
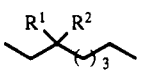
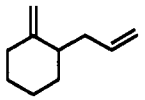
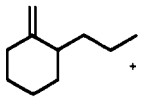
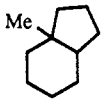
Table I. Selective Hydrogenation of Substituted Dienes Utilizing Catalytic $Cp^*_2YMe(THF)$

substrate	reaction time (h)	mol % catalyst	product(s) (% isoltd yield)[a]	R^1	R^2
	2	1			
1			**2** (70)		
	2	1			
3			**4** (72)		
					
5a	1	2	**6a** (98)	OTBS	
5b	2	2	**6b** (74)	OMe	
5c	2	2	**6c** (99)	OBn	
5d			**6d** (0)	OAc	
5e			**6e** (0)	Cl	
			 		
7a	1	3	**8a** (85)	**9a** (10)	OTBS	H
	1.5	4	(0)	(99)		
7b	1	3	**8b** (64)	**9b** (23)	Ph	H
	1.5	4	(0)	(92)		
7c	1.1	3	**8c** (70)	**9c** (16)	*i*-Pr	H
7d	1	3	**8d** (96)	**9d** (1)	$OCPh_3$	H
7e	1	3	**8e** (42)	**9e** (20)	Me	Me
	1	4	 		
10			**11** (67) **12** (20)		

[a] Isolated by distillation as a mixture of the indicated products. Percentage of each product was determined on the crude reaction mixture by fused silica capillary gas chromatography. All of these compounds have been fully characterized spectroscopically (^1H NMR, ^{13}C NMR, IR), and elemental composition has been established by high-resolution mass spectrometry and/or combustion analysis.

for the reductions. Compared to the organoneodymium catalyst mentioned above, this complex was expected to possess a much smaller cone angle of reactivity because both the ligand and the metal have been appropriately tuned for increased selectivity. The anticipated catalytic cycle is outlined in Scheme I. All of the individual steps as well as the overall transformation are well documented.[7,8,9b,13]

In practice, the protocol works exceptionally well. Reactions were typically carried out utilizing 1–4% precatalyst in benzene or toluene solvent under 1 atm H_2 pressure and were generally complete within 1–2 h (Table I).[14] In all cases good to excellent yields were achieved in spite of the fact that many of the products were volatile liquids difficult to isolate.

Several features of the reaction are noteworthy. For substrates **1**, **3**, **5**, and **10**, no effort was made to "titrate", or control, the amount of available hydrogen. In spite of this, no disubstituted alkenes, not even highly reactive alkenes such as limonene, 5-methylenebicyclo[2.2.1]hept-2-ene, 1,5,5-trimethyl-3-methylenecyclohexene, nor bicyclo[2.2.1]heptenes such as **4**, are reduced under the reaction conditions. Consequently, this protocol provides an extremely selective method to hydrogenate terminal olefins in the presence of virtually any other olefin substitution pattern. In spite of the extreme Lewis acidity of the electron-deficient organoyttrium catalyst,[8,9] ether groups survive the reaction intact. Furthermore, allylic ethers, which are rather easily hydrogenolyzed with palladium and other metal catalysts,[15] are untouched by the organoyttrium catalyst. Another important point is that complementary site-selectivity patterns are observed in yttrium-promoted hydrogenation of allylically substituted dienyl ethers as compared to those catalyzed by Wilkinson's catalyst and related homogeneous, alkoxy-directing hydrogenation catalysts.[16]

The extreme sensitivity of this particular catalyst to steric and electronic effects led us to examine the selective hydrogenation of the α,ω-dienes **7**, in which the two olefins were differentiated only by allylic substitution of one of the alkenes. Indeed, very good selectivity was exhibited in some of these systems, although hydrogen pressure and reaction times did have to be monitored carefully to prevent overreduction of the substrates.

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(14) All reactions were carried out with strict exclusion of oxygen. In a typical procedure $Cp^*_2YMe(THF)$ (0.02 mmol), 2 mL of benzene, and the diene (1.0 mmol) were loaded into a 50-mL flask equipped with an Ace needle valve. The heterogeneous mixture was cooled to −78 °C and purged-filled three times with hydrogen. After being stirred for 1 h at room temperature the mixture was opened and filtered through 2 g of Florisil and purified by bulb to bulb distillation.

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In suitably functionalized 1,5-dienes, cyclooligomerization occurs to some extent (substrate **10**). In previous studies we have established that this process dominates when terminal 1,5- and 1,6-dienes are employed.[17] Finally, selected functional groups (substrates **5d**, **5e**) totally inhibit the reaction. Irreversible reaction of the catalyst with these functional groups is probably responsible for these results, although studies are still underway to determine precisely the reason for failure in these cases.

In summary, excellent results have been obtained for the organoyttrium-catalyzed reductive hydrogenation of substituted dienes. The facile process that has been developed provides excellent selectivities and yields. Although nominal total reduction and competing cyclization occurs in selected diene substrates using the current protocol, further studies designed to optimize the organometallic catalyst by both "ligand tuning" and "metal tuning" are expected to resolve these problems.

Acknowledgment. We thank the National Institutes of Health for their generous support of this research.

Supplementary Material Available: Complete experimental details and spectral data for all the hydrogenation reactions described herein (33 pages). Ordering information is given on any current masthead page.

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Photosensitized Pyrimidine Dimer Splitting by a Methoxyindole Bound to a Dimer-Recognizing Macrocycle

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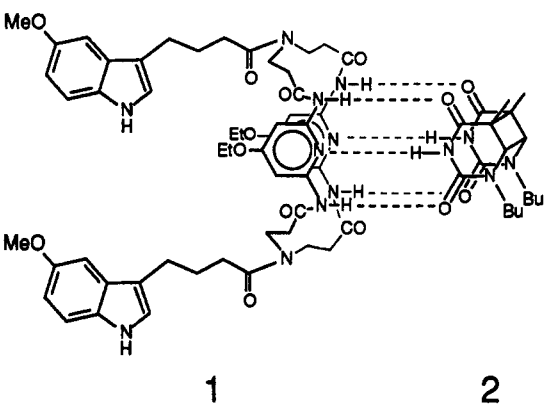
Summary: A macrocycle has been prepared that binds to a pyrimidine dimer by hydrogen bonding and photosplits the bound dimer with quantum efficiency greater than 0.1 in both protic and aprotic solvents.

Mimicry of enzyme-mediated photorepair of pyrimidine dimers in DNA by simple organic systems offers to both demystify and enhance the appreciation for the natural repair enzymes, the photolyases.[1] These enzymes photosplit dimers that arise in DNA from exposure to ultraviolet light. We recently devised and synthesized a macrocycle[2] that binds to pyrimidine dimers by use of the characteristic hydrogen-bonding pattern of the dimer as a recognition[3a,b] motif. The macrocycle employed two diaminopyridines[3c] for complexation to the dimer and an indole as photosensitizer. Although the macrocycle sensitized dimer splitting, the quantum yield was low ($\Phi \simeq 0.01$ in CH_3CN), and the mode of sensitization could not be identified due to overlap of diaminopyridine and indole absorption bands. We now report that a new macrocycle **1**, with well-separated absorption bands of sensitizer and recognition components, induces cycloreversion of the complexed dimer **2** (Chart I) upon excitation of the sensitizer.[4] Quantum efficiency was significantly higher ($\Phi = 0.11$ in acetonitrile) than the previous macrocycle. Also, complexation and splitting were found to occur in a protic solvent, in spite of the tendency of such solvents to disrupt hydrogen-bonded complexes.

Chart I



1 **2**

The absorption band of the diaminopyridine, which is required for recognition, was separated from the sensitizer's band by use of substituents. The γ-ethoxy group on the diaminopyridine resulted in a blue shift in the absorption band (red edge < 300 nm), as well as tighter binding;[2,5] a 5-methoxy group on the indole resulted in a red shift in the sensitizer's absorption band (red edge > 320 nm). Irradiation[6] at 313 nm resulted in virtually sole excitation of the methoxyindole, with little or no direct excitation of

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(4) The synthesis of **1** will be presented elsewhere (see supplementary material). High-resolution FAB MS and ^{1}H-NMR spectra were consistent with the assigned structure (e.g., high-resolution FAB MS of **1**: theoretical exact mass for $C_{52}H_{62}N_{10}O_{10} + H^+$ 987.4729, found 987.4742).

(5) Hamilton, A. D.; Little, D. *J. Chem. Soc., Chem. Commun.* **1990**, 297-300.

(6) A 500-W Hg-Xe arc lamp and a 0.25-m monochromator were used as previously described: Kim, S. T.; Hartman, R. F.; Rose, S. D. *Photochem. Photobiol.* **1990**, *52*, 789-794.

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