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Mechanism and Stereochemistry of the Zirconocene-Catalyzed Cyclomagnesiation of Dienes

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Abstract: Kinetics, stoichiometric model reactions, and stereochemical studies have been employed to investigate the mechanism of the zirconocene-catalyzed cyclization of nonconjugated dienes with organomagnesium reagents. Transmetalation of a zirconacyclopentane intermediate with magnesium alkyls has been implicated as a key step in the catalytic reaction. A zirconacyclopentane derived from 9,9-diallylfluorene was prepared and structurally characterized. Zirconium metallacyclopentanes transmetalate with dialkylmagnesium reagents having β-hydrogens to form bis(magnesiomethyl)-substituted carbocycles and products resulting from the elimination of alkane from dialkylzirconocene. Metallacycles of this type also act as catalyst precursors for the catalytic cyclomagnesiation of 1,7-octadiene. The kinetics of the catalytic cyclomagnesiation of 9,9-diallylfluorene have been examined. The reaction obeys the following rate law: rate = $k_{obs}[Zr][Bu_2Mg]$ when $[Bu_2Mg] < 0.35$ M, and rate = $k_{obs}[Zr]$ when $[Bu_2Mg] > 0.35$ M. The stereochemistry of the products depends upon the substrate, the magnesium reagent, the magnesium reagent concentration, and the temperature of the cyclization. The diastereoselectivity of the reaction depends on the relative rate of metallacycle formation, isomerization, and transmetalation. An understanding of these relative rates allows for the rational control of the diastereoselectivity to reflect either the kinetic selectivity of metallacycle formation or the thermodynamic stabilites of the diastereomeric metallacycles.

Introduction

Transition metal mediated strategies are among the most efficient modern synthetic methods for the construction of carbo- and heterocyclic rings, particularly for ring systems not readily accessed by traditional methods.[2] The coupling of unsaturated fragments at a transition metal center represents one important strategy toward this goal. Cyclizations involving later transition metals, such as the Pauson–Khand reaction, have emerged as useful methods for the synthesis of cyclopentenones and other structurally important ring systems.[3,4]

A number of efficient methods have been developed for the coupling of two olefins at a transition metal center. For many of these reactions, the coupling of a bis-olefin adduct to a metallacyclopentane intermediate has been invoked as a key step (eq 1).[5]

(1)

Examples include the rhodium-catalyzed 2 + 2 dimerization of norbornadiene,[6] for which an analogous iridium metallacyclopentane has been isolated,[7] and the nickel-catalyzed cyclodimerization of methylenecyclopropane and strained olefins,[8] in which metallacyclopentane intermediates have been trapped out as their pyridine adducts. Ethylene has been catalytically dimerized to cyclobutane via a nickelacyclopentane catalyst,[9] and metallacyclopentanes have been invoked to explain the selective trimerization of ethylene by chromium catalysts.[10] Butadiene complexes of titanium and zirconium catalyze the dimerization of ethylene and propylene in a reaction where metallacyclic intermediates have been suggested to explain the absence of higher oligomers.[11] A catalytic dimerization of unstrained α-olefins employing metallacyclopentane intermediates has been developed by Schrock using tantalum complexes.[12] α-ω-Diolefins have been cyclized by such catalysts to form α-methyl methylenecycloalkanes. A rhodium-based catalytic system has also been reported to achieve a similar result.[13]

Some of the earliest reports of transition metal mediated carbocyclization reactions involved early transition metals.[14,15] On the basis of early work of Vol'pin[14] and Whitesides,[15,16] Negishi[17] and Nugent[18,19] developed a useful *stoichiometric*

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method for the intramolecular cyclization of diynes using reduced titanocene or zirconocene derivatives. Using a similar procedure, these authors have also demonstrated an efficient intramolecular cyclization of enynes[20,21] and dienes.[22] These carbocyclization reactions show impressive regio- and stereoselectivity and have been used as a key step in several natural product syntheses.[23,24] Generally, these titanium- and zirconium-mediated carbocyclization reactions have required stoichiometric amounts of the transition metal reagents;[25] nevertheless, these reactions have proven to be of considerable synthetic utility as they provide a rapid entry into carbocyclic and carbobicyclic ring systems.

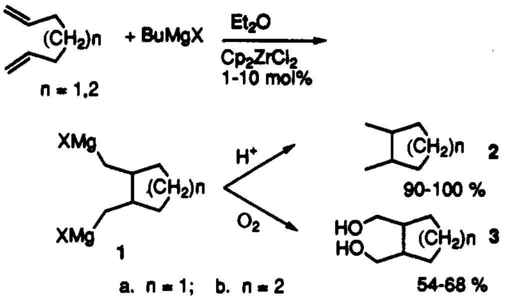
We have recently communicated the development of a zirconium-catalyzed system for the reductive cyclization of dienes to yield dimagnesium reagents, a formal cyclomagnesiation of the diolefin.[26,27] On the basis of known stoichiometric chemistry, we proposed a mechanism for the catalytic cycle as one involving metallacycles as key intermediates. The critical, but poorly precedented, step of this proposed mechanism is the transmetalation[28-30] of the zirconacyclopentane with butylmagnesium reagents to generate the products and dibutylzirconocene. We now wish to report our studies of the mechanism and stereochemistry, along with studies addressing details of the transmetalation step. These studies provide compelling evidence for the chemical and kinetic competence of metallacycle transmetalation as the key turnover process in this catalytic reaction.

Results

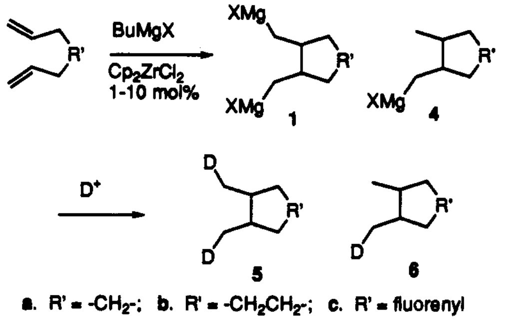
Cyclomagnesiation of Dienes. Zirconocene dichloride is an effective catalyst precursor for the cyclomagnesiation of nonconjugated 1,6- and 1,7-dienes in the presence of alkylmagnesium reagents such as butylmagnesium halides and dibutylmagnesium. Treatment of 1,7-octadiene (1 equiv) with dibutylmagnesium (1.5 equiv) or butylmagnesium chloride (3 equiv) in ether in the presence of 10 mol % Cp_2ZrCl_2 yields the 1,2-bis(magnesiomethyl)cyclohexane **1b**, as determined by hydrolysis or oxidation (eq 2). Minor products include cyclized dienes in which only one of the exocyclic methyl groups contains an organomagnesium functionality, as examined by deuteriolysis (eq 3). The rate, yields, selectivity for difunctionalized products, and stereochemistry of these reactions are quite sensitive to the nature of the diene, the magnesium reagent, the temperature of the reaction, and the solvent. A summary of representative cyclomagnesiation reactions is given in Table 1.

Table 1. Cyclomagnesiation of Dienes Catalyzed by Zirconocene Reagents

entry	diene	solvent	Mg reagent	yield (%)	mono- vs difunct products
1	1,7-octadiene	Et_2O	Bu_2Mg	96	7:93
2	1,7-octadiene	Et_2O	BuMgCl	89	11:89
3	1,6-heptadiene	Et_2O	Bu_2Mg	85	6:94
4	9.9-diallylfluorene	Et_2O	Bu_2Mg	95	9:91
5	9,9-diallylfluorene	THF	Bu_2Mg	60	55:45
6	9.9-diallylfluorene	Et_2O	BuMgCl	90	19:81
7	9.9-diallylfluorne	THF	BuMgCl	58	68:32
8	9.9-diallylfluorene	Et_2O	BuMgBr	86	54:46
9	9,9-diallylfluorene	THF	BuMgBr	56	60:40



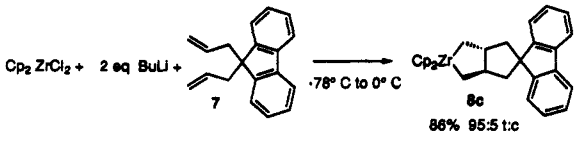
(2)



(3)

The selectivity for difunctionalized products is highest in the presence of dibutylmagnesium reagents in diethyl ether. Grignard reagents and more strongly coordinating solvents such as THF result in slower rates, lower yields, and a higher percentage of monofunctionalized products (Table 1).

Stoichiometric Model Studies. We have previously proposed metallacycles as key intermediates in the catalytic cyclomagnesiation of dienes.[26] To probe for the intermediacy of metallacycles, metallacycle **8c** was synthesized from zirconocene dichloride by the method of Nugent[22] using a diene derived from bis-allylation of fluorene (eq 4). Crystallization of this material



(4)

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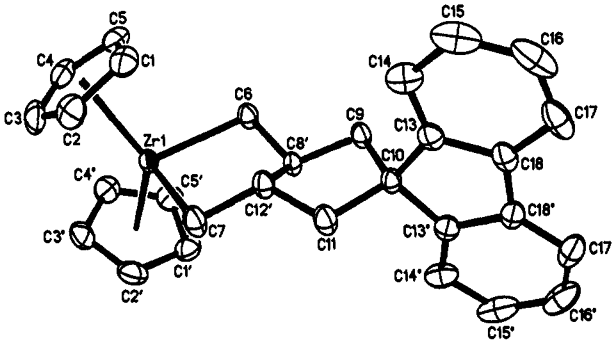
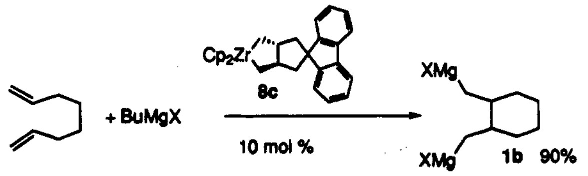


Figure 1. Zirconacyclopentane **8c** derived from diallylfluorene.

from toluene afforded crystals suitable for an X-ray structural determination, shown in Figure 1.

The metallabicycle crystallizes on a crystallographic mirror plane in space group *Pnma*, resulting in a 50:50 disorder for C8 and C12, corresponding to the two enantiomers. Representative bond lengths and angles are given in Table 2. The bond lengths and angles for the metallacyclopentane moiety are similar to those reported for a related titanacyclopentane,[31] except that the Zr–C bond lengths (2.296 and 2.301 Å) are longer than the analogous Ti–C bond lengths (2.189 and 2.214 Å).

Zirconacyclopentanes are catalytically competent intermediates for the cyclization of dienes. Cyclomagnesiation of 1,7-octadiene occurs smoothly in the presence of 10 mol % **8c**; of the hydrolyzed products, 10% was the dimethylcyclopentane derived from **8c** (eq 5).



(5)

Transmetalation. A series of NMR studies were carried out using metallacycle **8c** to observe and explore the transmetalation step postulated in the catalytic cycle. Solutions of the metallacycle were combined with organomagnesium reagents, and the reactivity was monitored by observing the disappearance of metallacycle and the appearance of products. No transmetalation was detected when **8c** was treated with a stoichiometric amount of $PhCH_2MgBr$ in benzene or 4:1 benzene:THF. Transmetalation is barely detectable by NMR in the presence of Me_2Mg. Similar transmetalation behavior is observed with MeMgBr in diethyl ether or THF. However, transmetalation was observed in the presence of magnesium reagents containing β-hydrogens; for ethylmagnesium reagents in 4:1 benzene:THF, disappearance of the metallacycle cyclopentadienyl (Cp) peak at δ 5.90 and the concurrent appearance of a peak at δ 5.47 could be monitored by ^1H NMR (Scheme 1). The latter peak is assigned to the zirconocene ethylene adduct **9d**, by comparison to the products resulting from the decomposition of an independently prepared sample of diethylzirconocene.[17a] Diethylzirconocene was not detected as an intermediate. Deuterolysis of the products of the reaction between Et_2Mg and metallacycle **8c** afforded predominantly the monodeuterated product **6c**. The ratio of monodeuterated to dideuterated products was 84:16 (**6c**:**5c**) for reactions carried out in Et_2O and higher for reactions carried out in THF (**6c**:**5c** 91:9).

Transmetalation of the metallacycle with butylmagnesium reagents occurs readily at 19.5 °C in 4:1 benzene: THF, THF, or diethyl ether. In this case dibutylzirconocene was observed, as evidenced by the transient appearance of a Cp resonance at

Table 2. Interatomic Distances (Å) and Interatomic Angles (deg) with ESD's

Zr(1)–C(1)	2.550(3)	C(13)–C(14)	1.387(4)
Zr(1)–C(2)	2.539(3)	C(14)–C(15)	1.390(4)
Zr(1)–C(3)	2.505(3)	C(16)–C(17)	1.378(5)
Zr(1)–C(4)	2.507(3)	C(18)–C(18′)	1.471(5)
Zr(1)–C(5)	2.539(3)	C(1)–C(5)	1.413(4)
Zr(1)–C(6)	2.296(3)	C(3)–C(4)	1.414(4)
Zr(1)–C(7)	2.301(3)	C(6)–C(8)	1.545(5)
Zr(1)–Cnt[a]	2.227	C(8)–C(9)	1.546(5)
C(1)–C(2)	1.408(4)	C(8)–C(8′)	0.824(9)
C(2)–C(3)	1.402(4)	C(9)–C(10)	1.575(4)
C(4)–C(5)	1.395(4)	C(10)–C(13)	1.517(3)
C(7)–C(12)	1.514(5)	C(12)–C(12′)	0.538(12)
C(8)–C(12)	1.541(6)	C(13)–C(18)	1.400(3)
C(8)–C(12′)	1.386(6)	C(15)–C(16)	1.385(4)
C(10)–C(11)	1.559(5)	C(17)–C(18)	1.393(4)
C(10)–C(11)	1.520(5)		
C(6)–Zr(1)–C(7)	87.4(1)	Cnt–Zr(1)–C(6)	106.5
Cnt–Zr(1)–C(6)	107.2	Cnt–Zr(1)–Cnt′	132.8
Zr(1)–C(6)–C(8)	98.9(2)	Zr(1)–C(7)–C(12)	98.8(2)
C(2)–C(1)–C(5)	107.2(2)	C(1)–C(2)–C(3)	107.9(2)
C(2)–C(3)–C(4)	108.2(2)	C(3)–C(4)–C(5)	107.8(2)
C(1)–C(5)–C(4)	108.4(2)	C(6)–C(8)–C(9)	114.6(3)
C(6)–C(8)–C(12)	113.4(3)	C(9)–C(8)–C(12)	100.6(3)
C(8)–C(9)–C(10)	106.6(3)	C(9)–C(10)–C(11)	103.4(2)
C(9)–C(10)–C(13)	112.4(2)	C(11)–C(10)–C(13)	113.8(2)
C(13)–C(10)–C(13′)	101.4(3)	C(10)–C(11)–C(12)	106.6(3)
C(7)–C(12)–C(8)	116.9(4)	C(7)–C(12)–C(11)	118.0(3)
C(8)–C(12)–C(11)	104.2(3)	C(10)–C(13)–C(14)	128.5(2)
C(10)–C(13)–C(18)	111.0(2)	C(14)–C(13)–C(18)	120.5(2)
C(13)–C(14)–C(15)	118.1(3)	C(14)–C(15)–C(16)	121.4(3)
C(15)–C(16)–C(17)	120.8(3)	C(16)–C(17)–C(18)	118.5(3)
C(13)–C(18)–C(17)	120.7(3)	C(13)–C(18)–C(18′)	108.2(1)
C(17)–C(18)–C(18′)	131.0(2)		

[a] Cnt is the centroid of the C(1)–C(5) ring.

δ 5.79 (4:1 benzene:THF). Treatment of **8c** with Bu_2Mg in the presence of diphenylacetylene yielded the dimagnesium reagent **1c** and tetraphenylzirconacyclopentadiene **10**, consistent with intermediacy of a labile zirconocene butene adduct resulting from decomposition of dibutylzirconocene.[17a,32,33] The bis(magnesiomethyl)-substituted cyclopentanes derived from transmetalation of the metallacycle **8c** with butylmagnesium reagents have been characterized as the deuterolysis products. Transmetalation in diethyl ether with dibutylmagnesium shows a high level of dideuteration consistent with the bis(magnesiomethyl) products (11:89 **6c**:**5c** by high-resolution mass spectroscopy). Slightly lower yields of dideuterated product are observed when the reaction is performed using BuMgCl in diethyl ether (19:81 **6c**:**5c**) or using dibutylmagnesium in THF (30:70 **6c**:**5c**).

The rates of transmetalation between **8c** and organomagnesium reagents (Table 3) with excess dibutylmagnesium in 4:1 benzene: THF could be followed under pseudo-first-order conditions and were found to obey the following rate law:

$$\text{rate} = k_{\text{obs}}[\text{metallacycle}][R_2Mg] \qquad (6)$$

Similar kinetic behavior but faster rates are observed in the transmetalation with diethylmagnesium.

Dibutylzirconocene Decomposition. Dibutylzirconocene generated from the reaction of zirconocene dichloride and 2 equiv of butyllithium in THF at 20 °C has been reported to decay to form a zirconocene butene adduct with first-order kinetics and a rate constant of (7.6(0.7) × 10^{-4} s^{-1}).[17a,32,34] We find a similar

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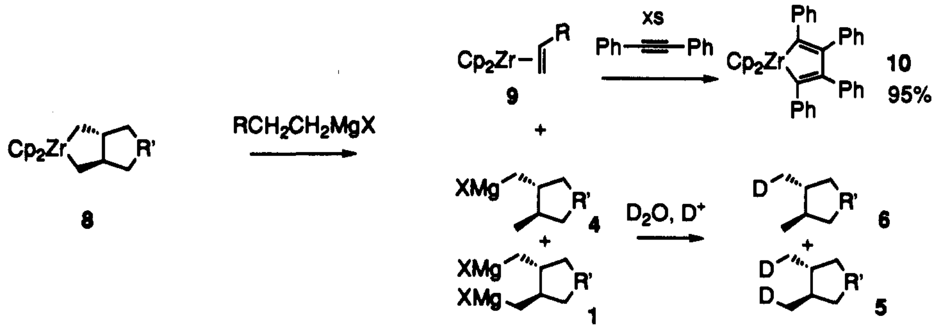
Scheme 1. Transmetalation of Metallacycles



a. R = Et, R' = -CH_2-; **b.** R = Et, R' = -CH_2CH_2-; **c.** R = Et, R' = fluorenyl;
d. R = H, R' = fluorenyl.

Table 3. Kinetic Data for the Transmetalation of Metallacycle **8c** with Magnesium Reagents[a]

	Mg reagent	solvent	[Mg reagent]	temp (°C)	k_{obs} (s^{-1})	k_{obs}/[Mg] (s^{-1} M^{-1})
1	Bu_2Mg	4/1PhH/THF	0.144	19.5	4.7×10^{-4}	3.3×10^{-3}
2	Bu_2Mg	4/1PhH/THF	0.072	19.5	2.2×10^{-4}	3.0×10^{-3}
3	Bu_2Mg	4/1PhH/THF	0.036	19.5	1.1×10^{-4}	3.1×10^{-3}
4	Bu_2Mg	4/1PhH/THF	0.018	19.5	5.3×10^{-5}	2.9×10^{-3}
5	Et_2Mg	4/1PhH/THF	0.089	19.5	1.4×10^{-3}	1.6×10^{-2}
6	Bu_2Mg	THF	0.036	19.5	3.2×10^{-5}	8.8×10^{-4}
7	Bu_2Mg	4/1PhH/Et_2O	0.300	19.5	4.8×10^{-4}	1.6×10^{-3}
8	Bu_2Mg	Et_2O	0.036	19.5	6.8×10^{-5}	1.9×10^{-3}
9	Bu_2Mg	Et_2O	0.036	16.0	4.3×10^{-5}	1.2×10^{-3}

[a] All solvents used were perdeuterated. $[\text{Metallacycle}]_0 = 0.0043$ M.

Table 4. Decomposition of Dibutylzirconocene at Differing [Bu_2Mg]

[Bu_2Mg]	Bu_2Mg excess (equiv)	k_{obs} (s^{-1})
0.12	7	$7.0(3) \times 10^{-4}$
0.15	8	$6.9(3) \times 10^{-4}$
0.172	10	$6.6(3) \times 10^{-4}$
0.26	16	$6.6(3) \times 10^{-4}$

rate for the decomposition of dibutylzirconocene generated from the reaction of dibutylmagnesium in ether at 19.5 °C (6.8(0.5) × 10^{-4} s^{-1}). At 16 °C, the temperature of our kinetic studies of catalytic cyclomagnesiation, this reaction occurs with a rate constant of 5.0(0.5) × 10^{-4} s^{-1}. The order of this reaction and its rate constant do not change with increasing dibutylmagnesium concentration (Table 4). The rate is also independent of the presence or concentration of the trapping agent diphenylacetylene.

Cyclomagnesiation Kinetics. The rate of the cyclomagnesiation of 9,9-diallylfluorene with dibutylmagnesium using zirconocene dichloride as a catalyst precursor was monitored by observing the appearance of cyclized alkane in the GC traces of hydrolyzed aliquots. Rate constants were taken from the initial slope of the reaction after the first catalytic turnover and were measured over a time period sufficient to allow for multiple turnovers (Figure 2). Kinetic investigations were carried out in diethyl ether at 16 °C. Under these conditions, the reaction is zero-order in diene, but first-order in [Zr] and [Mg] for low concentrations of magnesium reagent. For [Bu_2Mg] < 0.35 M, the reaction is second-order according to the following rate law: rate = k_{obs} [Zr][Bu_2Mg] for k_{obs} = 8.3(0.4) × 10^{-4} M^{-1} s^{-1} (Figure 3). At higher Bu_2Mg concentrations ([Bu_2Mg] > 0.35 M), the reaction becomes zero-order in Mg according to the following rate law: rate = k_{obs}[Zr] for k_{obs} = 3.1(0.5) × 10^{-4} s^{-1} (Table 5). At low conversion, prior to the first catalytic turnover, the rate of the reaction appears to be independent of the concentration of magnesium and occurs with a rate constant of k_{obs} = 4.6(0.9) × 10^{-4} s^{-1}, similar to that observed for the stoichiometric decomposition of dibutylzirconocene.

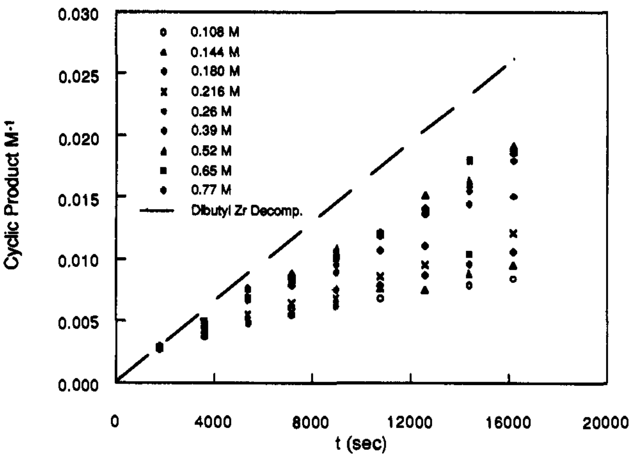


Figure 2. Catalytic cyclomagnesiation of 9,9-diallylfluorene in diethyl ether at 16 °C with dibutylmagnesium at concentrations from 0.108 to 0.77 M. [Catalyst] = 3.4 × 10^{-3} M; [diene] = 5.6 × 10^{-2} M.

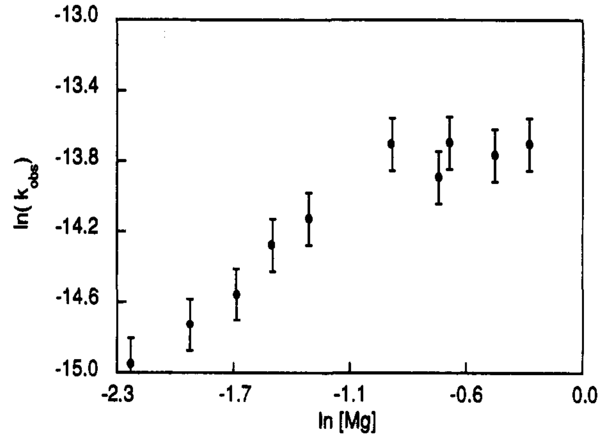


Figure 3. Plot of ln(k_{obs}) as a function of ln[Bu_2Mg].

Catalytic Species. The catalytic cyclomagnesiation of 9,9-diallylfluorene with dibutylmagnesium in the presence of zirconocene dichloride was monitored by ^{1}H NMR in diethyl ether-d_{10}. Two zirconocene species can be observed in solution: the zirconocyclopentane derived from 9,9-diallylfluorene and dibutylzirconocene. The ratio of these two species is dependent upon [Bu_2Mg] (Figure 4). At lower magnesium concentrations, the diallylfluorene metallacycle is present almost exclusively. At higher magnesium concentrations the ratio of dibutylzirconocene to metallacycle shifts toward greater proportion of dibutylzirconocene. The relative concentration of dibutylzirconocene appears to approach a limiting value as the concentration of dibutylmagnesium increases above 0.4 M. Under conditions of

Table 5. Kinetic Data for the Catalytic Cyclomagnesiation of 9,9-Diallylfluorene with Bu_2Mg in the Presence of Zirconocene Dichloride[a]

entry	[Zr]	[olefin]	[Mg]	rate (M s^{-1})	k_{obs} (s^{-1})	k_{obs} (s^{-1} M^{-1})
1	0.0011	0.054	0.43	3.2×10^{-7}	2.9×10^{-4}	
2	0.0022	0.054	0.43	6.8×10^{-7}	3.1×10^{-4}	
3	0.0046	0.054	0.43	1.8×10^{-6}	3.9×10^{-4}	
4	0.0090	0.054	0.43	3.3×10^{-6}	3.7×10^{-4}	
5	0.0034	0.058	0.49	9.3×10^{-7}	2.7×10^{-4}	
6	0.0034	0.015	0.49	8.6×10^{-7}	2.5×10^{-4}	
7	0.0034	0.116	0.49	8.4×10^{-7}	2.5×10^{-4}	
8	0.0034	0.056	0.39	1.12×10^{-6}	3.3×10^{-4}	
9	0.0034	0.056	0.52	1.13×10^{-6}	3.3×10^{-4}	
10	0.0034	0.056	0.65	1.05×10^{-6}	3.1×10^{-4}	
11	0.0034	0.056	0.77	1.12×10^{-6}	3.3×10^{-4}	
12	0.0034	0.056	0.108	3.2×10^{-7}		8.7×10^{-4}
13	0.0034	0.056	0.144	4.0×10^{-7}		8.2×10^{-4}
14	0.0034	0.056	0.18	4.8×10^{-7}		7.8×10^{-4}
15	0.0034	0.056	0.22	6.3×10^{-7}		8.6×10^{-4}
16	0.0034	0.056	0.26	7.3×10^{-7}		8.3×10^{-4}

[a] Reactions performed at 16 ± 1.5 °C in diethyl ether under a nitrogen atmosphere.

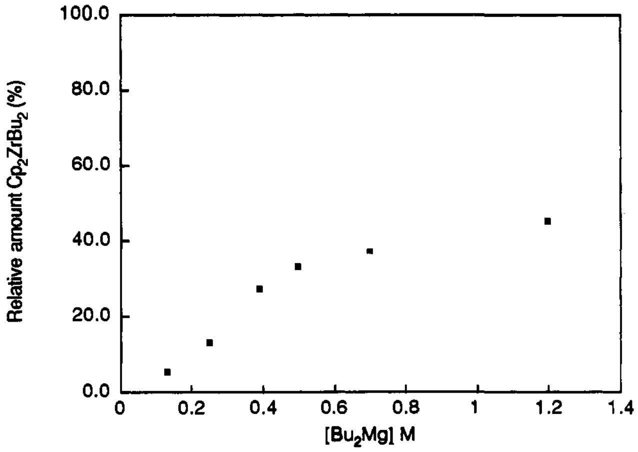
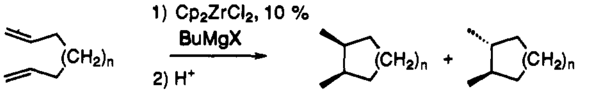


Figure 4. Ratio of observed catalytic intermediates vs initial magnesium concentration.

excess and therefore effectively constant dibutylmagnesium, these ratios do not change with time over the first half-life of the reaction. At lower dibutylmagnesium concentration, the level of dibutylzirconocene falls with conversion of dibutylmagnesium.

Stereochemistry. The stereochemistry of the catalytic cyclometalation of 1,6-heptadiene reaction is different than analogous stoichiometric reactions.[22] Our initial results for the catalytic cyclization of 1,6-heptadiene with Bu_2Mg at 25 °C in diethyl ether yielded lower stereoselectivity (64:36 trans:cis) than that observed in stoichiometric reactions with BuLi (97:3 trans:cis).

We have found that the stereochemistry of the catalytic cyclomagnesiation of 1,6-heptadiene is quite sensitive to the reaction conditions. The diastereoselectivity depends on both temperature and on the concentration of the magnesium reagent. The selectivity for the trans product improves as the temperature increases and also increases as the MgR_2 concentration decreases (eq 7, Table 6). At sufficiently low magnesium reagent



(7)

concentration, the diastereoselectivity approaches that seen in the stoichiometric reaction. Generally higher trans selectivity is seen using organomagnesium halides relative to the dialkylmagnesium reagents for similar concentrations and temperatures. No dependence of the stereochemistry on the olefin concentration was detected. In contrast to these variable results with 1,6-heptadiene, cyclization of 9,9-diallylfluorene occurred with 95:5 (trans:cis) diastereoselectivity regardless of the concentration of olefin catalyst or magnesium reagent.[26b] Isomer ratios were uniform throughout the course of our kinetic studies.

Table 6. Stereoselectivity in the Catalytic Cyclization of 1,5-Heptadiene

	solvent	Mg reagent	[Mg] (/M)	temp (°C)	[diene] (/M)	[catalyst] (/M)	trans:cis	yield[a] (%)
1	Et_2O	Bu_2Mg	0.7	25	0.17	0.017	62:38	94
2	Et_2O	Bu_2Mg	0.35	25	0.17	0.017	78:22	92
3	Et_2O	Bu_2Mg	0.18	25	0.17	0.017	94:6	91
4	Bu_2O	Bu_2Mg	0.7	0	0.17	0.017	60:40	85
5	Bu_2O	Bu_2Mg	0.7	25	0.17	0.017	68:32	90
6	Bu_2O	Bu_2Mg	0.7	60	0.17	0.017	85:15	83
7	Et_2O	BuMgCl	1.0	25	0.17	0.017	85:15	84
8	Et_2O	BuMgBr	0.5	25	0.17	0.017	85:15	86

[a] Yield and isomer ratios determined by GC.

Catalytic cyclization of 1,7-octadiene at 25 °C in ether, followed by hydrolysis, affords an 18:82 trans:cis ratio of dimethylcyclohexanes, a ratio similar to that seen in stoichiometric reactions. This ratio is observed over a wide range of magnesium reagent concentrations (0.1–1.5 M BuMgCl and 0.2–0.7 M Bu_2Mg) and also appears to be independent of diolefin or catalyst concentration. However, there is a significant influence of temperature on the stereochemistry of the cyclization of octadiene (eq 7, Table 7). Cyclization of 1,7-octadiene at 120 °C in dibutyl ether at low organomagnesium reagent concentration results in a reversal of stereochemistry to yield predominantly the trans product. At this temperature the diastereoselectivity is also dependent on $[Bu_2Mg]$. The trans selectivity increases with decreasing $[Bu_2Mg]$. At low $[Bu_2Mg]$, a 91:9 trans:cis ratio of products was obtained.

The stoichiometric reaction of dibutylzirconocene with 1,6-heptadiene was reported by Nugent and Taber[22] to afford a 97:3 trans:cis ratio of products. The reported conditions for this reaction involve generation of dibutylzirconocene from Cp_2ZrCl_2 and 2 equiv of butyllithium at -78 °C followed by gradual warming to room temperature in the presence of the diene.

A series of reactions were carried out to establish if the diastereoselectivity of the stoichiometric cyclization was constant under these conditions. In an effort to determine the kinetic diastereoselectivity for the stoichiometric cyclization with zirconocene dichloride and BuLi, reactions were monitored at low conversion. Under conditions of warming from -78 °C to room temperature, the ratio of hydrolysis products observed after 20 min and at 17% conversion was 57:43 (trans:cis). After warming to room temperature over the course of 2 h, the reaction was 95% complete and the product was greater than 90% trans.[35]

A similar, although slower, isomerization is observed if the reaction sequence is performed at a constant temperature of 0 °C. Under these conditions, the cis:trans ratio also depends on conversion. The initial ratio of 60:40 trans:cis increases with conversion toward a greater preference for the trans isomer (80:20 trans:cis at 89% conversion). The reaction at this temperature is complicated by the formation of unidentified side products at high conversion.

Discussion

The cyclomagnesiation of dienes catalyzed by zirconocenes provides a powerful method for carbocyclic ring construction (Scheme 2). This reaction provides a facile synthesis of 1,4-dimagnesium reagents from olefins. At this point, we have not determined the precise nature of the bis(organomagnesium) products. They may be present as an equilibrium mixtures of magnesacycles, (bis)magnesium reagents, and oligomeric and polymeric species.[36]

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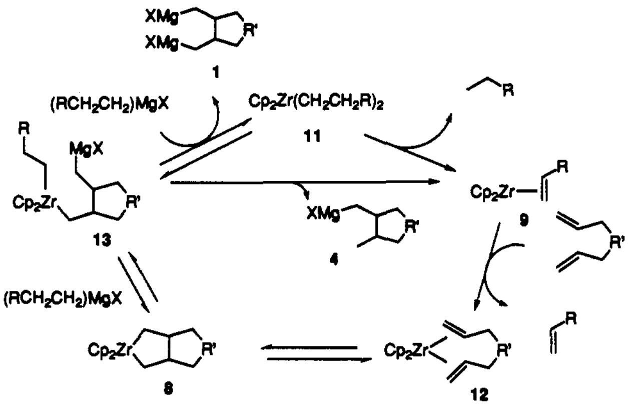
(35) Akita, M.; Yasuda, H.; Yamamoto, H.; Nakamura, A. *Polyhedron* **1991**, *10*, 1-9.

Table 7. Stereoselectivity in the Catalytic Cyclization of 1,7-Octadiene

	solvent	Mg reagent	[Mg] (/M)	temp (°C)	[diene] (/M)	[catalyst] (/M)	trans:cis	yield[a] (%)
1	Et_2O	Bu_2Mg	0.1–0.7	25	0.22	0.009	18:82	90–96
2	Et_2O	BuMgCl	0.25–1.0	25	0.167	0.009	18:82	85–94
3	Et_2O	BuMgCl	0.5	25	0.08–0.33	0.009	18:82	84–93
4	Et_2O	BuMgCl	0.5	25	0.167	0.0045–0.017	18:82	80–94
5	Bu_2O	Bu_2Mg	0.053	120	0.045	0.0045	91:9	84
6	$(i\text{-}Pr)_2O$	Bu_2Mg	0.085	70	0.045	0.0045	44:56	81
7	Bu_2O	Bu_2Mg	0.35	120	0.017	0.017	70:30	80

[a] Yield and isomer ratios determined by GC.

Scheme 2. Catalytic Cycle for Diene Cyclomagnesiation



a. R = Et, R' = -CH_2-; b. R = Et, R' = -CH_2CH_2-; c. R = Et, R' = fluorenyl; d. R = H, R' = fluorenyl.

To evaluate the influence of the reaction parameters on this reaction, an understanding of the mechanism is critical. We have previously proposed a mechanism for the cyclomagnesiation reaction on the basis of well-precedented stoichiometric chemistry[22] where dibutylzirconocene is formed from Cp_2ZrCl_2 and Bu_2Mg. Elimination of butane forms a zirconocene butene adduct;[17a,32] displacement of butene by the diene followed by cyclization forms a metallacycle. Transmetalation[28–30] of the metallacycle to BuMgX completes the catalytic cycle by regenerating the dibutylzirconocene species.

The rate, yields, diastereoselectivity, and selectivity of this reaction for dimagnesium products are quite sensitive to the reaction conditions. Both monomagnesium products and dimagnesium products are observed; the selectivity for dimagnesium products is highest in the presence of Bu_2Mg in Et_2O at room temperature. The chemoselectivity of this reaction can be interpreted in terms of the competitive reactions of the bimetallic Zr–Mg intermediate **13** (Scheme 3). Transmetalation of **13** with another equivalent (or direct cyclization to the magnesiacycle) would afford the difunctionalized product **1** and dibutylzirconocene. However, direct formation of the butene adduct would afford the monomagnesium product **4**.[37] This scheme is consistent with the observed solvent effects on the chemoselectivity for mono- and difunctionalized products. Our stoichiometric studies indicate that transmetalation with Bu_2Mg in diethyl ether at 19.5 °C is faster than that in THF by roughly a factor of 2. Thus, in Et_2O the second transmetalation step is faster than elimination of **4**, resulting in a high selectivity for the difunctionalized **1**. In THF, transmetalation of **13** is slower and elimination of **4** can compete, leading to a diminished selectivity for **1**.

Evidence for this mechanism was provided by stoichiometric transmetalations of the metallacycle **8c**. Stoichiometric transmetalation of the metallabicycle **8c** in THF afforded more of the monofunctionalized product upon deuteriolysis (30% d_1) when compared with the same reaction in Et_2O (11% d_1).

In addition, stoichiometric transmetalation of **8c** with EtMgBr or Et_2Mg afforded predominantly the monomagnesium product **4c**. In this case, extrusion of ethane from **13a** is apparently faster than transmetalation with a further equivalent of Et_2Mg. This is also consistent with our monitoring of the transmetalation reactions by NMR. In the case of Bu_2Mg, the buildup of dibutylzirconocene could be observed; however, we did not observe the transient appearance of diethylzirconocene when the transmetalation was carried out with ethylmagnesium reagents under the same conditions. This is likely a result of rapid decomposition of the diethylzirconocene species.

Model Studies. An X-ray crystal structure was carried out on a metallacycle derived from diallylfluorene. Other structurally characterized metallacyclopentanes include those of Ti,[31] Ta,[38] Re,[39] Pt,[40] Ni,[41] Fe,[42] and Mo.[43] A notable feature of the structure is the trans stereochemistry for the metallabicycle, which can also be deduced from the ^1H NMR spectra. In contrast, a related tantalacyclopentane derived from 1,6-heptadiene was obtained only as the cis isomer.[38] The cis structure for the tantala[3.3.0]-bicyclooctane was proposed to be the most stable, in analogy with the related carbobicycles. However, such analogies are imperfect, as we have shown the *trans*-zircona[3.3.0]bicyclooctane **8c** is the thermodynamically preferred isomer (vida infra). The origin of the different stabilities is undoubtedly due to the difference in the Zr–C bond lengths of the metallabicycle (2.3 Å) relative to the analogous carbobicycle (approximately 1.5 Å).

Stoichiometric investigations on the transmetalation of metallacycles with magnesium reagents have revealed interesting details on this step. Transmetalation was not observed in the presence of methyl- or benzylmagnesium reagents, but was observed for ethyl- and butylmagnesium reagents. These results imply that the extrusion of the alkane from the dialkylzirconocene provides an important thermodynamic driving force for the transmetalation step. These stoichiometric investigations suggest that under these conditions (THF/benzene, 19.5 °C) the equilibrium constant for transmetalation of the metallacycle is quite low, and transmetalation is only observed if followed by an irreversible step (i.e. decomposition of diethyl- or dibutylzirconocene). Thus, the extrusion of the alkane derived from the dialkylmetallocene is a key step in the catalytic cycle which helps overcome the unfavorable equilibrium of the transmetalation step.

The rate of transmetalation of the metallacycles with butylmagnesium reagents is slower in THF than in Et_2O. The transmetalation obeys second-order kinetics, first-order in [Bu_2Mg] and first-order in metallacycle. These results suggest that

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(36) Magnesium 1,3-butadiene is postulated to exist as a polymer. (a) Fujita, K.; Ohnuma, Y.; Yasuda, H.; Tani, H. *J. Organomet. Chem.* **1976**, *113*, 20. (b) Kai, Y.; Kanehisa, N.; Miki, K.; Kasai, N.; Nashima, K.; Yasuda, H.; Nakamura, A. *Chem. Lett.* **1982**, 1277. (c) Rieke, R. D.; Xiong, H. *J. Org. Chem.* **1991**, *56*, 3109.

(37) This "shunt" pathway is quite common in the related ethylmagnesiation of alkenes with ethylmagnesium reagents.[27,34]

(38) Churchhill, M. R.; Young, W. J. *J. Am. Chem. Soc.* **1979**, *101*, 6462.

(39) Yang, G. K.; Bergman, R. G. *Organometallics* **1985**, *4*, 129.

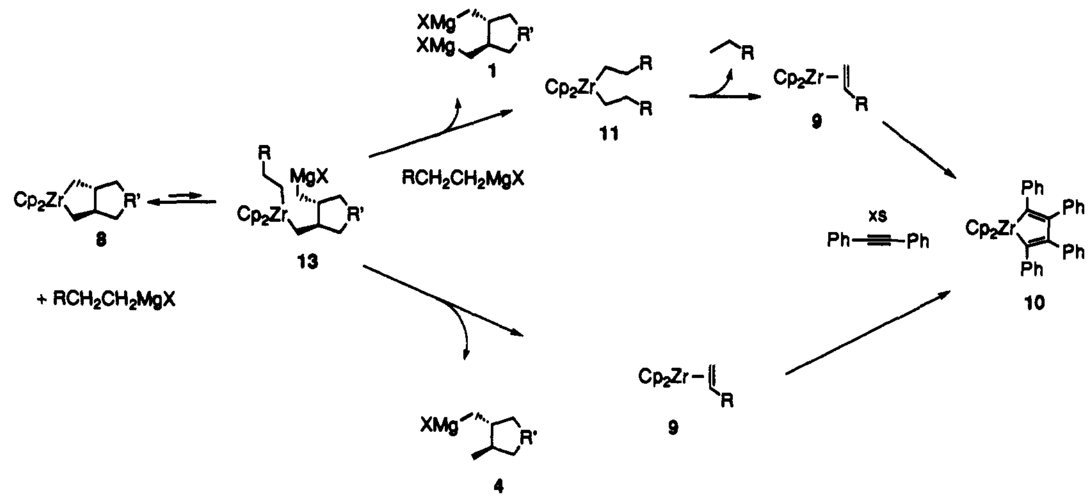
(40) Cheetham, A. K.; Puddephatt, R. J.; Zalkin, A.; Templeton, D. H.; Templeton, L.K. *Inorg. Chem.* **1976**, *15*, 2997. Green, M.; Howard, J. K.; Mitrprachachon, P; Pfeffer, M.; Spencer, J. L.; Stone, F. G. A.; Woodward, P. *J. Chem. Soc., Dalton Trans.* **1979**, 306. Beifeld, C. G.; Eick H. A.; Grubbs, R. H. *Inorg. Chem.* **1973**, *12*, 2166. Frölich, H. O.; Wyrwa, R.; Görls, H. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 387.

(41) Jolly, P. W.; Krüger, C.; Salz, R.; Sekutowski, J. C. *J. Organomet. Chem.* **1979**, *165*, C39.

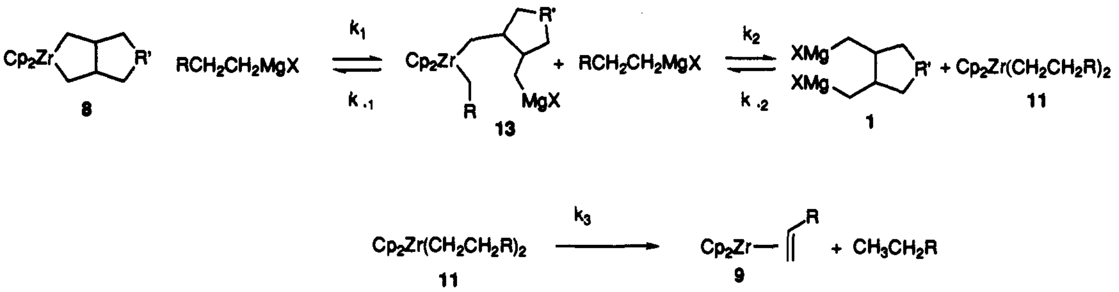
(42) Krüger, C.; Tsay, Y.-H. *Cryst. Struct. Commun.* **1976**, *5*, 215.

(43) Diversi, P.; Ingrosso, G.; Lucherini, A.; Porzio, W.; Zocchi, M. *J. Chem. Soc., Dalton Trans.* **1983**, 967.

Scheme 3. Transmetalation Pathways for Diene-Derived Metallabicycles



Scheme 4. Kinetic Scheme for Transmetalation of Metallacycles



the first transmetalation to give **13** is the slow step (Scheme 4). A rate law for this stoichiometric reaction can be derived where

$$-\frac{d[8]}{dt} = k_1[8][\mathrm{BuMgX}] - k_{-1}[13] \qquad (8)$$

Assuming steady state in **13**, this becomes

$$-\frac{d[8]}{dt} = k_1[8][\mathrm{BuMgX}] - k_{-1}\left[\frac{k_1[8][\mathrm{BuMgX}] + k_{-2}[1][11]}{k_{-1} + k_{-2}[\mathrm{BuMgX}]}\right] \qquad (9)$$

At high [BuMgX] this approaches

$$-\frac{d[8]}{dt} = k_1[8]\left[[\mathrm{BuMgX}] - \frac{k_{-1}}{k_2}\right] \qquad (10)$$

which is consistent with the observed rate law.

The decomposition of dibutylzirconocene to form a zirconocene alkene complex has been studied by Buchwald[32a,c] and Negishi[17a,32b,34] and is a first-order process. Our results suggest that excess BuMgX does not appear to affect this process, as the reaction order and rate remain constant with increasing [Bu_2Mg]. These results suggest that if tributyl zirconates[27,44] are formed by the additional alkylation of dibutylzirconocene, they do not play a significant role in this step in the catalytic cycle under these conditions.

Two regimes are observed in the kinetic analysis of the catalytic cyclomagnesiation reaction. At lower [Bu_2Mg], the reaction is second-order overall, first-order in zirconium and first-order in [Bu_2Mg]. For example, the catalytic cyclomagnesiation of 9,9-diallylfluorene occurs with a rate constant of 8.3(0.4) × 10^{-4} M^{-1} s^{-1} at 16 °C in diethyl ether for [Bu_2Mg] ≤ 0.35 M. This rate constant can be compared to that of the stoichiometric transmetalation of the 9,9-diallylfluorene metallacycle at 16 °C in diethyl ether (12(3) × 10^{-4} M^{-1} s^{-1}). These results suggest that under these conditions the turnover-limiting step in the catalytic cycle is transmetalation between the metallacycle and the magnesium reagent.

At higher concentrations of magnesium reagents [Bu_2Mg] ≥ 0.35 M, the catalytic rate is dependent only upon the concentration of the zirconium species. Cyclomagnesiation of 9,9-diallylfluorene at 16 °C in diethyl ether at dibutylmagnesium concentration above 0.35 M occurs with a rate constant of 4.6(0.5) × 10^{-4} s^{-1} over the first catalytic turnover, then drops to 3.1(0.5) × 10^{-4} s^{-1} thereafter, and remains at this level as long as the concentration of magnesium remains higher than 0.35 M. This rate constant can be compared to that for the decomposition of dibutylzirconocene at 16 °C in diethyl ether (5.0(0.5) × 10^{-4} s^{-1}). The fact that the saturation rate approaches that for the decomposition of dibutylzirconocene suggests that, under conditions of high dialkylmagnesium concentration, the turnover-limiting step is the decomposition of dibutylzirconocene.

The fact that the stoichiometric reactions are faster than the catalytic steps attests to the kinetic competence of these reaction steps in the catalytic cycle. The rate of the catalytic reactions decreases following the first turnover, even at high [Bu_2Mg]. Initially, the predominant species is dibutylzirconocene formed from alkylation of zirconocene dichloride. Following the first turnover, at least two zirconocene species are observed when the catalytic reaction is monitored by ^1H NMR: dibutylzirconocene and the metallacycle. The ratio of dibutylzirconocene to metallacycle increases as the dibutylmagnesium concentration is increased but reaches a limiting value at [Bu_2Mg] ≥ 0.35 M. Thus, the concentration of dibutylzirconocene available to undergo decomposition is less than the total zirconium concentration, and the rate of the catalytic reaction decreases after the first turnover. The origin of the lower apparent rate constants for the catalytic

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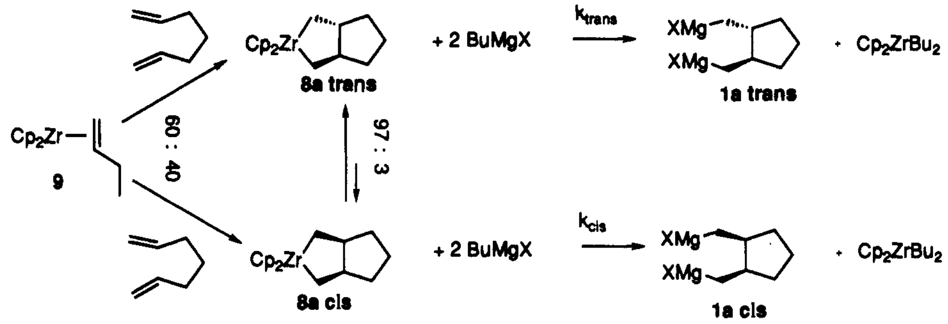
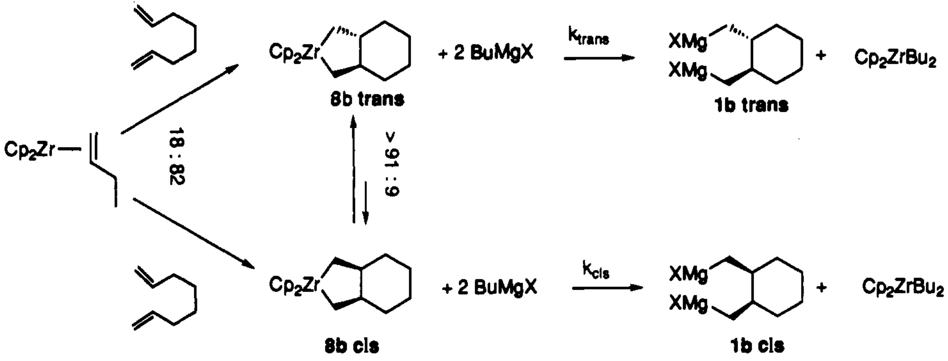
(44) Rousset, C. J.; Negishi, E.; Suzuki, N.; Takahashi, T. *Tetrahedron Lett.* **1992**, *33*, 1965–1968.

Scheme 5. Kinetic vs Thermodynamic Control in Cyclomagnesiation of 1,6-Heptadiene



Scheme 6. Kinetic vs Thermodynamic Control in Cyclomagnesiation of 1,7-Octadiene



reactions under limiting conditions is unclear, but may be the result of a rate-limiting equilibration of the steady-state intermediates or the oligomerization of the magnesium reagents.[45] Further studies are underway to address this point.

Stereochemistry

The diastereoselectivity of the catalytic cyclometalation of 1,6-heptadiene is different than that of the analogous stoichiometric reaction. The diastereoselectivity of the cyclization depends on both temperature and the concentration of the magnesium reagent. The trans *selectivity improves as the temperature increases* and also increases as the MgR_2 concentration decreases. These results can be rationalized in terms of a kinetic scheme where the rate and kinetic diastereoselectivity of metallacycle formation are in competition with metallacycle isomerization and transmetalation.

Our reinvestigation of the stoichiometric cyclization of 1,6-heptadiene revealed interesting details on the kinetic and thermodynamic diastereoselectivity for the zircona[3.3.0]-bicyclooctanes. Analysis of the stereochemistry of the stoichiometric cyclization at low conversion indicates that the kinetic selectivity for metallacycle formation is approximately 60:40 (trans:cis). At higher conversion, the trans selectivity improves, suggesting that the *trans*-metalla[3.3.0]bicyclooctane is thermodynamically more stable than the *cis*. These results imply that the previously observed high diastereoselectivity (97:3 t:c) of the stoichiometric cyclization of 1,6-heptadiene with Cp_2ZrCl_2/2BuLi is a result of equilibration of the metallacycles to the thermodynamically preferred *trans*-metalla[3.3.0]bicyclooctane.

Under the conditions of the catalytic reaction, the rate of transmetalation can compete with the rate of metallacycle isomerization, resulting in intermediate diastereoselectivity. Thus, at high [Bu_2Mg] the metallacycles transmetalate faster than they isomerize, and the kinetic diastereoselectivity (60:40 trans:cis) is observed. As the temperature is increased or the MgR_2 concentration is decreased, metallacycle isomerization begins to compete with transmetalation and the trans selectivity improves, reflecting the thermodynamic preference of the trans metallacycle. (Scheme 5, Table 6). Thus, through an appreciation of the relative rates of isomerization and transmetalation, the catalytic reaction can be carried out such that the high trans selectivity observed in the stoichiometric reaction can be approached (entry 3, Table 6).

The results with 1,7-octadiene can be interpreted in terms of a similar kinetic model, where the cis metallacycle is kinetically preferred but the trans metallacycle is the thermodynamic product.[35] In this case, the activation energy for metallacycle isomerization appears to be higher than that for the heptadiene metallacycles; thus, at room temperature, the kinetic ratio of 82:18 is observed, and as the temperature increases, the product ratio begins to reflect the kinetic competition between metallacycle isomerization and transmetalation.

For the cyclomagnesiation of octadiene, the kinetic and thermodynamic diastereoselectivity is quite different. This difference, when coupled with our ability to access either product ratio by controlling the reaction conditions, allows for stereoselectivity to be rationally controlled to select for the highly cis kinetic product or the predominantly trans thermodynamic product (Scheme 6).[46]

Conclusions

We have demonstrated that nonconjugated dienes react with alkylmagnesium reagents to form bis(magnesiomethyl)-substituted carbocycles in the presence of catalysts derived from zirconocene dichloride. The formation of a zirconacyclopentane derived from the diene and its transmetalation with alkylmagnesium reagents are key steps in the catalytic cycle. Such zirconacyclopentanes are effective catalyst precursors for the

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[45] Organomagnesium reagents in diethyl ether solutions are known to show significant fluctuations in level of association with changing concentration. The concentration of the species active in transmetalation may not increase linearly with increasing concentration: Ashby, E. C. *Bull. Soc. Chim. Fr.* **1972**, 2133. Ashby, E. C. *Pure Appl. Chem.* **1980**, *52*, 545.

[46] It should be appreciated that the diastereoselectivity of the catalytic reaction is a function both of the equilibrium constant for metallacycle isomerization *as well as* the relative rate of transmetalation of the cis and trans metallacycles. As yet, we have not independently measured the relative rate of transmetalation of the isomeric metallacycles. Nevertheless, the fact that the diastereoselectivity of the catalytic reactions at high [Bu_2Mg] closely matches the stoichiometric diastereoselectivities at low conversion implies that these rates are approximately the same ($k_{cis} = k_{trans}$).

cyclomagnesiation. The experimental rate expression is dependent upon the concentration of alkylmagnesium reagent and reflects a change in the turnover-limiting step with increasing [RMgX]. At lower concentrations of the magnesium reagent, transmetalation of the metallacycle limits the reaction rate; at higher concentrations of [RMgX], the rate approaches that of the decomposition of zirconocene dialkyl. Stoichiometric model studies suggest that β-hydrogen abstraction from the dialkylzirconocene intermediate provides an important driving force in transmetalation, allowing the system to overcome an unfavorable, two-step transmetalation equilibrium. The rate of transmetalation also plays a key role in determining the stereochemistry of the cyclomagesiation reaction. The stereoselectivity is determined by interplay between the kinetic and thermodynamic diastereoselectivity, the rate of metallacycle isomerization, and the rate of transmetalation of the metallacycle intermediates. An understanding of these relative rates allows for the rational control of the diastereoselectivity to reflect either the kinetic selectivity of metallacycle formation or the thermodynamic stabilites of the diastereomeric metallacycles.

Experimental Section

General Considerations. All manipulations involving air-sensitive compounds were carried out under nitrogen either in a glovebox or using standard Schlenk line technique. Diethyl ether solutions of dialkylmagnesium compounds were prepared via the method of Saheki.[47] Solvents were distilled or vacuum transferred from Na/benzophenone prior to use. GC analyses were obtained on a Hewlett-Packard 5890 chromatograph equipped with an SE-54 column (5% phenylmethylsilicone, 95% methylsilicone, 0.33μm × 0.2 mm × 25m). NMR experiments were performed on Varian Gemini 200, Gemini 300, and XL-400 spectrometers. Elemental analyses were performed by Microlabs, University of California at Berkeley, or E+R Microanalytical Laboratory, Inc. High-resolution mass spectroscopy was performed by the facility at the Department of Chemistry, University of California at Berkeley.

9,9-Diallylfluorene (7). In a 500-mL round-bottomed flask equipped with an addition funnel and stir bar, a 16.24-g portion of fluorene was dissolved in 200 mL of THF under nitrogen and cooled in a dry ice/acetone bath. A 39-mL portion of a hexane solution of *n*-butyllithium (2.5 M), was added dropwise over 10 min. The reaction mixture was warmed to room temperature, and the solution turned bright red, after which the reaction mixture was cooled again in the dry ice/acetone bath. An 8.5-mL (0.98 mol) portion of allyl bromide in 30 mL of THF was added slowly to the reaction mixture, warmed to room temperature, and stirred for 2 h. The reaction mixture was then cooled in the dry ice/acetone bath, and a second 39-mL portion of the 2.5 M *n*-butyllithium solution was added. After warming and stirring for 2 h, followed by cooling in a dry ice/acetone bath, a second 8.5-mL portion of allyl bromide was added via the addition funnel. The reaction was allowed to stir for several hours, at which time it was quenched with a 50-mL portion of water and washed with water 3× in a separatory funnel. The organic layer was separated and dried over Na_2SO_4 and concentrated on a rotary evaporator. The resultant oil was filtered through silica gel with hexanes, concentrated, and distilled under vacuum at 90 °C. ^{1}H NMR: ($CDCl_3$) δ 2.72 (d, J = 7 Hz, 4H), 4.7–4.9 (m, 4H), 5.15–5.4 (m, 2H), 7.2–7.5 (m, 4H), 7.7–7.8 (m, 4H). ^{13}C NMR: δ 42.8, 53.5, 116.8, 119.1, 123.0, 126.3, 126.4, 133.1, 140.0, 148.6. Anal. Calcd: C, 92.63; H, 7.37. Found: C, 92.41; H, 7.43.

Synthesis of Metallacycle 8c. A 250-mL flask was charged with 2.93 g of zirconocene dichloride, 2.4 g of 9,9-diallylfluorene, and 150 mL of THF, under nitrogen, and cooled to −78 °C in a dry ice/acetone bath. An 8-mL portion of *n*-BuLi was added to the stirring solution, dropwise via syringe. The reaction mixture turned bright yellow and was allowed to stir at this temperature for 20 min. The reaction vessel was slowly warmed to room temperature and allowed to stir for 3 h. The solvent was removed under vacuum, and the residue was extracted with warm toluene and filtered through a coarse frit. Toluene was removed under vacuum, and the resultant brown solid was washed three times with diethyl ether. Recrystallization from toluene afforded yellow crystals suitable for X-ray analysis. ^{1}H NMR: (benzene-d_6) δ 1.14 (dd, J = 5.1, 11.8 Hz, 2H), 1.30 (dd, J = 11.2, 11.3 Hz, 2H), 1.3–1.7 (m, 2H), 1.94 (dd, J = 10.6, 12.8 Hz, 2H), 2.41 (dd, J = 5.9, 12.9 Hz, 2H), 5.80 (s, 10H), 7.2–7.35 (m, 4H), 7.5–7.7 (m, 4H). ^{13}C NMR: δ 38.2, 42.1, 51.1, 56.7, 109.9, 119.8, 123.1, 126.6, 127.7, 140.1, 156.8.

Collection of X-ray Diffraction Data. A yellow crystal of approximate dimensions 0.30 × 0.33 × 0.47 mm was oil-mounted on a glass fiber and transferred to the Syntex $P2_1$ diffractometer (Siemens R3m/V system), which is equipped with a modified LT-1 low-temperature system. Subsequent setup operations (determination of accurate unit cell dimensions and orientation matrix) and collection of low-temperature (168 K) intensity data were carried out using standard techniques similar to those of Churchill.[48,49] All 2875 data were corrected for absorption and for Lorentz and polarization effects and placed on an approximately absolute scale. The diffraction symmetry was *mmm* with systematic extinctions $0kl$ for $k + l = 2n + 1$ and $hk0$ for $h = 2n + 1$. The two possible orthorhombic space groups are the centrosymmetric *Pnma* [D^{16}_{2h}, no. 62] or the noncentrosymmetric $Pna2_1$ [C^9_{2v}, no. 33] (standard setting of $Pn2_1a$). The centrosymmetric space group was determined to be correct by successful refinement of the model.

Solution and Refinement of the Crystal Structure. All crystallographic calculations were carried out using either our locally modified version of the UCLA Crystallographic Computing Package or the SHELXTL PLUS program set.[50] The analytical scattering factors for neutral atoms were used throughout the analysis; both the real ($\Delta f'$) and imaginary ($i\Delta f''$) components of anomalous dispersion[51] were included. The quantity minimized during least-squares analysis was $\Sigma w(|F_o| - |F_c|)^2$, where $w^{-1} = \sigma^2(|F_o|) + 0.0005(|F_o|)^2$. The structure was solved by direct methods (SHELXTL PLUS) and refined by full-matrix least-squares techniques. Hydrogen atoms were included using a riding model with d(C–H) = 0.96 Å and U(iso) = 0.08 Å^2. The molecule lies on a crystallographic mirror plane at (x, 1/4, z). The zirconium atom and carbon atoms C(6), C(7), C(9), C(10), and C(11) are fixed at $y = 1/4$ with site-occupancy factors of 0.50. Carbon atoms C(8) and C(12) lie above and below the mirror plane, requiring them to be disordered. These atoms and their associated hydrogen atoms were also assigned site-occupancy factors of 0.50. Refinement of positional and thermal parameters led to convergence with R_F = 3.9%, R_{wF} + 4.6%, and GOF = 1.38 for 155 variables refined against those 2162 data with $|F_o| > 2.0\sigma(|F_o|)$. A final difference Fourier map was devoid of significant features, p(max) = 0.39 e Å^{-3}.

Cyclomagnesiation (Representative Procedure): 1,2-Dimethylcyclopentane. Under nitrogen, zirconocene dichloride (0.17 mmol, 0.025 equiv) was dissolved in 30 mL of a 0.34 M solution of dibutylmagnesium (10 mmol, 1.5 equiv) in diethyl ether. 1,6-heptadiene (7.4 mmol) was added dropwise to this solution. The solution was stirred for 24 h, at which time it was quenched with 10% HCl. The organic layer was separated and washed with a saturated solution of $NaHCO_3$. The yield and isomer ratio were determined by GC relative to a toluene internal standard based on converted olefin (92%, 89% conversion, 36:64 cis:trans). The products, *cis*-1,2-dimethylcyclopentane and *trans*-1,2-dimethylcyclopentane, were confirmed by GC coinjection with known samples and by GC/low-resolution mass spectroscopy.

Monitoring Catalysis by NMR (Representative Procedure). In the glovebox under nitrogen, a 10-mL vial was charged with 25 mg of dibutylmagnesium (0.18 mmol) and 30 mg of 9,9-diallylfluorene. This was dissolved in a 0.5-mL portion of perdeuterated ether. The reaction was initiated via the addition of a 0.15-mL portion of a 0.85 M solution of zirconocene dichloride containing 0.02 M mesitylene in C_6D_6. The reaction was monitored hourly by NMR. Relative ratios of intermediates were taken from the comparison of the integrations of cyclopentadienyl singlets at δ 6.13 (metallacycle) and δ 5.96 (dibutylzirconocene). ^{1}H NMR: δ −0.455 (t, J = 8 Hz, Bu_2Mg), 0.32 (m, Cp_2ZrCH_2*-Pr), 1.00 (t, J = 7 Hz, Bu_2Mg), 1.40 (m, Bu_2Mg), 1.93 (m, Bu_2Mg), 4.5–4.8 (m, diene), 4.97–5.22 (m, diene), 5.96 (s, $C_5H^*{}_5ZrBu_2$), 6.13 (zirconacycle Cp), 7.15–7.3 (m, zirconacycle aromatic), 7.2–7.3 (m, zirconacycle aromatic), 7.4–7.4.5 (m), 7.5–7.6 (m), 7.75–7.85 (m, organomagnesium product aromatic).

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(47) Saheki, Y.; Sasada, K.; Satoh, N.; Kawaichi, N.; Negoro, K. *Chem. Lett.* **1987**, 2299–2300.

(48) Churchill, M. R.; Lashewycz, R. A.; Rotella, F. *J. Inorg. Chem.* **1977**, *16*, 265–271.

(49) Crystallographic details: crystal system, orthorhombic; space group, *Pnma*; unit cell dimensions, a = 18.5111(16) Å, b = 14.4477(14) Å, c = 8.1195(7) Å; V = 2171.5(3) A^3; z = 4; D_{calcd} (mg/m^3) = 1.431; radiation, Mo Kα (0.710730 Å); μ(Mo Kα) (mm^{-1}) = 0.509; 2θ range = 4.0–55.0°. The structure was solved by direct methods, R_F = 3.9%, R_{wF} = 4.6%; 2875 reflections.

(50) UCLA Crystallographic Computing Package, University of California, Los Angeles, 1981. Strouse, C. Personal communication.

(51) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974.

Cyclomagnesiation Kinetics. Reactions were monitored by observing the appearance of cyclized product in hydrolyzed aliquots from the reaction mixture by GC relative to a durene internal standard. For each kinetic run, stock solutions of durene, 9,9-diallylfluorene, zirconocene dichloride, and organomagnesium reagent were prepared and mixed in desired amounts under nitrogen. Reactions were initiated by the addition of catalyst to a stirring solution of the organomagnesium reagent, diene, and standard in diethyl ether. Reactions were maintained at a constant 16 °C. Aliquots were removed at intervals, quenched with aqueous acid, extracted into ether, and analyzed via GC. Characterization data for hydrolysis product **2c:** ^{1}H NMR δ .96 (d, J = 5.2 Hz, 6H), 1.80 (m, 4H), 2.11 (dd, J = 5.6, 5.6 Hz, 2H), 7.19 (d, J = 3.2 Hz, 2H), 7.22 (d, J = 3.2 Hz, 2H), 7.31 (dd J = 3.2, 2.4 Hz, 2H), 7.56 (dd, J = 3.2, 2.4 Hz); ^{13}C NMR δ 17.87, 43.80, 49.22, 55.24, 119.42, 122.80, 126.49, 127.54, 139.18, 155.75. Anal. Calcd: C, 91.9; H, 8.11. Found: C, 92.3; H, 7.97.

Kinetics of Metallacycle Transmetalation (Representative Procedure). In the glovebox, a solution of Bu_2Mg (100 mg, 0.72 mmol) in 1 mL of THF-d_8 was prepared. A solution of metallacycle **8c** (10 mg, 0.021 mmol) was prepared in C_6D_6. To this solution was added 5 mg of mesitylene. A 0.2-mL portion of the dibutylmagnesium solution was transferred to an NMR tube. A 0.8-mL portion of the metallacycle solution was layered above it. The tube was capped, removed from the glovebox, and frozen in liquid nitrogen. The NMR tube was warmed to 19.5 °C, inverted repeatedly to mix its contents, and placed in the spectrometer probe. ^{1}H spectra were taken at 30-min intervals. The reaction progess was monitored by observing the disappearance of the metallacycle Cp peak (δ 5.90) relative to the mesitylene aromatic proton signal (δ 6.68). ^{1}H NMR: δ –0.211 (t, J = 8 Hz, Bu_2Mg), –0.04–0.03 (m), 0.313 (m, Cp_2ZrCH_2*-Pr), 1.16 (t, J = 7 Hz, Bu_2Mg), 1.65 (m, Bu_2Mg), 1.93 (m, Bu_2Mg), 2.28 (dd, J = 6, 13 Hz, zirconacycle methine), 3.15 (s), 3.2–3.4 (m, residual ether), 5.3 (m), 5.77 (s, $C_5H^*{}_5ZrBu_2$), 5.90 (zirconacycle Cp), 7.15–7.3 (m, zirconacycle aromatic), 7.4–7.6 (m, zirconacycle aromatic), 7.55–7.6 (m, organomagnesium product aromatic), 7.75–7.85 (m, organomagnesium product aromatic). ^{1}H NMR for experiments performed by the above procedure using diethyl ether-d_{10} as the solvent: δ –0.455 (t, J = 8 Hz, Bu_2Mg), 0.32 (m, Cp_2ZrCH_2*-Pr), 1.00 (t, J = 7 Hz, Bu_2Mg), 1.40 (m, Bu_2Mg), 1.93 (m, Bu_2Mg), 5.3 (m), 5.96 (s, $C_5H^*{}_5ZrBu_2$), 6.13 (zirconocycle Cp), 6.73 (s, mesitylene), 7.15–7.3 (m, zirconocycle aromatic), 7.2–7.3 (m, zirconocycle aromatic), 7.4–7.4.5 (m), 7.5–7.6 (m), 7.75–7.85 (m, organomagnesium product aromatic).

Kinetics of Dibutylzirconocene Decomposition in the Presence of Excess Bu_2Mg. In the glovebox, a stock solution was prepared containing C_6D_6 (5 mL), mesitylene (80 mg), and 28 mg of Cp_2ZrCl_2. A 0.8-mL portion of this was transferred to an NMR tube and frozen in the glovebox freezer. A 0.2-mL portion of a 1.3 M solution of Bu_2Mg in diethyl ether-d_{10} was layered on top of this, and the tube was removed from the drybox and taken to the spectrometer, where it was warmed to 19.5 °C and mixed by repeated inversion. Spectra were aquired at 10-min intervals for 1 h. The disappearance of the Cp singlet at δ 5.73 was monitored and was correlated to the disappearance of a multiplet at δ 0.32 (Cp_2ZrCH_2*-Pr). ^{1}H NMR: δ –0.121 (t, J = 8 Hz, Bu_2Mg), 0.32 (m, Cp_2ZrCH_2*-Pr), 1.16 (t, J = 7, Bu_2Mg), 1.65 (m, Bu_2Mg), 1.93 (m, Bu_2Mg), 2.13 (s, mesitylene), 2.28 3.15 (s), 3.2–3.4 (m, residual ether), 5.3 (m), 5.77 (s, C_5H_5*$ZrBu_2$), 6.68 (s, mesitylene).

Stereochemical Studies on the Cyclization of 1,6-Heptadiene and 1,7-Octadiene. Solutions of the organomagnesium reagents were prepared in diethyl ether and concentrated while stirring under vacuum to the solid form. The level of residual solvation was determined by NMR in C_6D_6. Portions of the magnesium reagent, diene, zirconocene dichloride, and decane (internal standard) were dissolved (see Tables 6 and 7 for concentration data) in the dibutyl or diethyl ether in a flask equipped with a reflux condenser under nitrogen. This was brought to the appropriate temperature (see Tables 6 and 7) via an oil, ice, or water bath. The reactions were monitored by removing aliquots with a syringe and injecting these into vials containg H_2O and HCl or D_2O and D_2SO_4. The organic layers were analyzed by GC and GCMS, relative to authentic samples of the cyclized products. In each sample quenched with D_2O and D_2SO_4 and analyzed by GCMS, the predominant molecular ion corresponded to the D_2 product.

Stereochemistry of Stoichiometric Cyclization. In the drybox under N_2 a 250-mL round-bottomed Schlenk flask was charged with 585 mg (2.0 mmol, 1 equiv) of zirconocene dichloride, 193 mg (2.0 mmol, 1 equiv) of 1,6-heptadiene, and 235 mg (2.55 mmol) of toluene. To this was added 50 mL of THF. The solution was cooled to 0 °C in an ice bath. A 1.6-mL portion of 2.5 M n-BuLi was added dropwise. The solution turned bright yellow. Aliquots were removed at intervals via syringe and injected into a vial containing 1 mL of diethyl ether layered over 1 mL of dilute aqueous HCl. The vial was capped, shaken, and analyzed via GC. Peaks were identified by GC coinjection with authentic standards and by GC/mass spectroscopy.

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Supplementary Material Available: Tables of crystal data and atomic coordinates (10 pages); listing of calculated and observed structure factors (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.