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Mechanisms of Allene Stereoinversion by Imidozirconium Complexes

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New routes to enantiopure allenes are important because of their documented utility in organic synthesis.[1−3] We recently reported an efficient kinetic resolution of 1,3-disubstituted allenes using enantiopure ethylenebis(tetrahydroindenyl) (ebthi) imidozirconium compounds.[4] In the course of that investigation, a remarkable selective inversion of allene configuration was observed (Figure 1). Treatment of (*S*,*S*)-**1** with *either* (*R*)- or (*S*)-1,2-cyclononadiene resulted in formation of the *same* diastereomer of [2 + 2] cycloadduct **2**. In both cases, 1,2-cyclononadiene of predominantly (*S*) configuration was isolated upon treatment of **2** with allene (C_3H_4). To rationalize these observations, a stepwise [2 + 2] cycloaddition pathway was proposed, proceeding via an unidentified intermediate in which the original allene stereochemistry was lost.

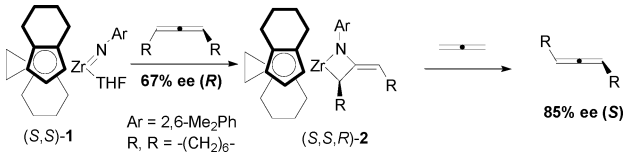

Figure 1. Stereoinversion of allenes by an enantiopure imido complex.

We have now examined the reaction of a wider range of 1,3-disubstituted allenes with both chiral and achiral imidozirconium complexes. Our experiments have provided more extensive information about these transformations, requiring new proposals for both the mechanism of the cycloaddition reaction and the subsequent behavior of the metallacycle products.

To determine whether the cycloaddition proceeds through an intermediate in which the chirality of the allene fragment is destroyed, we interchanged the enantiopurity of the reaction partners and carried out the reaction between *enantioenriched* allenes and *achiral* imidozirconocene complex **3**. In initial experiments with 4,5-nonadiene, circular dichroism (CD) spectroscopy revealed that the resultant azazirconacyclobutane **4** was optically inactive within 30 min (Figure 2). The recovered 4,5-nonadiene was also racemic, in accordance with the original stepwise cycloaddition mechanism.

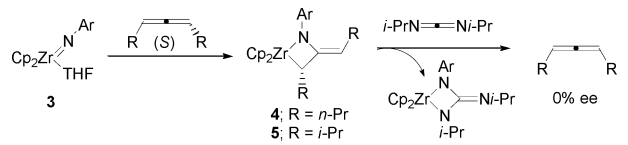

Figure 2. Reaction of dialkylallenes with imidozirconocene complex.

When this reaction was extended to 1,3-diphenylallene, different behavior was observed. In this case, treatment of enantiopure (*R*)-1,3-diphenylallene (>95% ee) with achiral imidozirconocene compound **3** afforded the expected metallacycle **6** (Figure 3). Treatment of **6** with diisopropylcarbodiimide regenerated diphenylallene *with no detectable loss of enantiopurity* (>95% ee (*R*)). Furthermore, CD spectroscopy on metallacycle **6** confirmed that it was optically active, in contrast to dialkylallene-derived metallacycle **4**. Heating a solution of **6** in C_6H_6 at 95 °C for 1.5 d resulted in the disappearance of the CD signal, indicating that under forcing conditions, racemization of the metallacycle could occur. The allene recovered from the sample after heating was also found to be racemic.

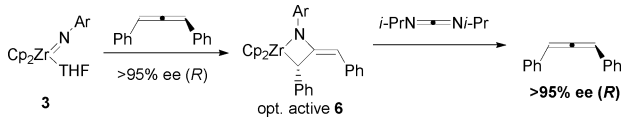

Figure 3. Unexpected retention of diphenylallene stereochemistry.

The diphenylallene observations stimulated an investigation of the reactions of **3** with a wider range of enantioenriched dialkylallenes. This ultimately resulted in the finding that optically active dialkylmetallacycles are, in fact, formed but racemize much faster than their diaryl analogues (Figure 2). For example, a solution of metallacycle **5**, formed from **3** and (*S*)-1,3-diisopropylallene, was initially CD active; however, the metallacycle underwent complete racemization within 24 h at room temperature, and cleavage of the metallacycle with carbodiimide yielded racemic allene.[5] The most economical conclusion from this observation is that 4,5-nonadiene also leads initially to optically active metallacycle **4**, but that racemization occurs even more rapidly under the reaction conditions.

The slow racemization rate of diphenylallene-derived metallacycle **6** prompted an examination of the cycloaddition reaction using both partners in enantioenriched form. This should allow both the initial selectivity of the cycloaddition and the subsequent isomerization processes to be directly observed. Accordingly, treatment of (*R*,*R*)-**1** with (*R*)-diphenylallene resulted in complete conversion to a single metallacycle isomer, **7** (the "matched" isomer). The same compound was also formed when an excess of *rac*-diphenylallene was allowed to react with (*R*,*R*)-**1**. The relative configuration of **7** is the same as that of cyclononadiene adduct **2** and was assigned by NOESY spectroscopy. Cleavage of **7** with carbodiimide regenerated (*R*)-diphenylallene with no detectable loss of enantioenrichment. Complex **7** was stable at lower temperatures; however, heating a solution of **7** for 24 h at 105 °C afforded a 3:1 equilibrium mixture of (*E*) and (*Z*) olefin isomers **7** and **8** (Figure 4, top).

Reaction of (*S*)-diphenylallene with (*R*,*R*)-**1** produced a new metallacycle diastereomer, which was assigned as **9** (the "mismatched" isomer) by NOESY spectroscopy. Metallacycle **9** exists in rapid equilibrium with (*R*,*R*)-**1** at room temperature ($K_{eq} = 1$), indicating that it is much less stable than matched diastereomer **7**. Compound **9** has the same double bond geometry as **7** but the opposite configuration at the α-carbon of the metallacycle. Apparently, interaction of the incoming allene with the imido substituent causes more steric repulsion than interaction with the ebthi ligand in the [2 + 2] cycloaddition transition state. Metallacycle **9** isomerizes much more readily than **7**, progressing through mixtures of

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complexes **10** and **8** at 45 °C before finally forming the same 3:1 thermodynamic mixture of **7** and **8**.

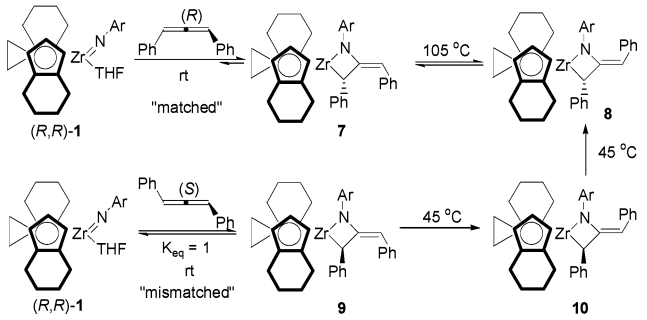

Figure 4. Formation and rearrangement of matched and mismatched diphenylallene metallacycles.

These observations make it clear that the initial cycloaddition takes place with retention of allene stereochemistry, and therefore is almost certainly concerted. Subsequent isomerization of the metallacycles is then responsible for the inversion of allene configuration. The mechanism of this isomerization must account for the observed effect of allene substituent on the racemization rate (*n*-Pr > *i*-Pr ≫ Ph). One possibility is that the rapid racemization of the dialkylallene-derived metallacycles takes place by reversible β-hydrogen elimination. To test this hypothesis, the enantioresolved, deuterium-labeled substrate **5**-d_2 was prepared, and its racemization rate was measured by CD spectroscopy (Figure 5). The racemization followed clean first-order kinetics, and a *normal primary* kinetic isotope effect ($k_H/k_D = 2.9$) was observed.

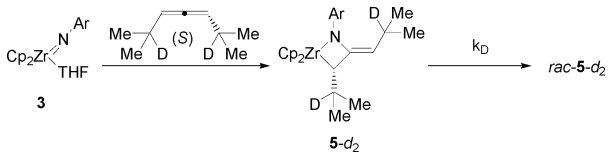

Figure 5. Racemization of deuterated diisopropylallene metallacycle.

The observed primary isotope effect provides strong evidence for racemization of **5** via reversible β-hydride elimination (Figure 6). After initial elimination to form intermediate **11**, hydrozirconation of the opposite enantioface of the newly formed olefin would scramble the stereocenter in **5**. Reversible β-hydride elimination processes are common among early metal alkyl complexes, and isotope effects of similar magnitude have been observed for other β-hydride elimination processes.[6−9] Clearly, this pathway is available only to dialkylallene-derived metallacycles, which explains the large difference in racemization rate between dialkyl- and diarylallene metallacycles.

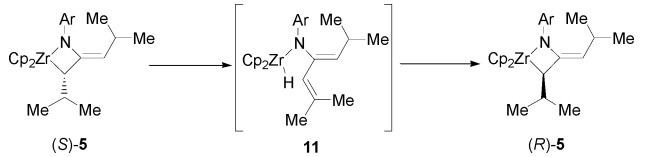

Figure 6. β-Hydride elimination mechanism.

An alternative pathway is required to account for the much slower racemization of diarylallene-derived metallacycles. One possibility is shown in Figure 7. In the limit, puckering of the metallacycle and coordination of the exocyclic double bond would result in the formation of η^4-azatrimethylenemethane complex **12** (a transition state similar to that initially proposed for the cycloaddition reaction). Reversion to η^2-coordination at the opposite terminus of the allylic system would result in overall inversion of the α-stereocenter. To our knowledge, no such η^4-azatrimethylenemethane complexes have been reported to date, but η^4-trimethylenemethane zirconium complexes are known.[10−12]

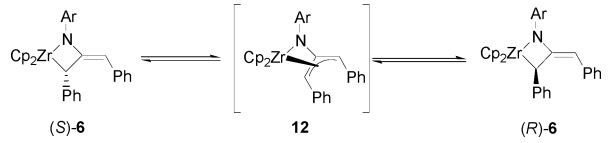

Figure 7. Rearrangement via an azatrimethylenemethane intermediate.

In summary, the above experiments have elucidated several elements of the enantioselective cycloaddition and stereoinversion of allenes mediated by imidozirconium compounds. We propose that the initial [2 + 2] cycloaddition to form the azazirconacyclobutane is concerted and stereospecific, and is therefore not involved in the racemization process. Two distinct pathways can be responsible for metallacycle stereoinversion. For metallacycles possessing β-hydrogen atoms, reversible β-hydride elimination rapidly scrambles the α-stereocenter. For diarylallenes, which do not have that option, slower rearrangement via an η^4-azatrimethylenemethane complex results in stereoinversion. Additional studies of these interesting and potentially useful organometallic transformations are underway.

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Supporting Information Available: Experimental procedures and characterization for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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