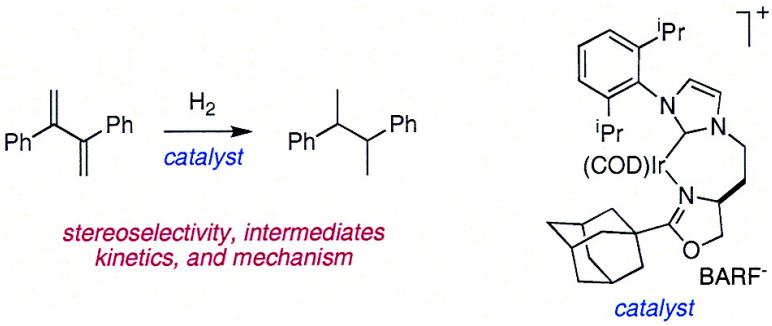
Communication

Iridium-Mediated Asymmetric Hydrogenation of 2,3-Diphenylbutadiene: A Revealing Kinetic Study

Xiuhua Cui, and Kevin Burgess

J. Am. Chem. Soc., **2003**, 125 (47), 14212-14213• DOI: 10.1021/ja037653a • Publication Date (Web): 30 October 2003



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 6 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

J|A|C|S
COMMUNICATIONS

Published on Web 10/30/2003

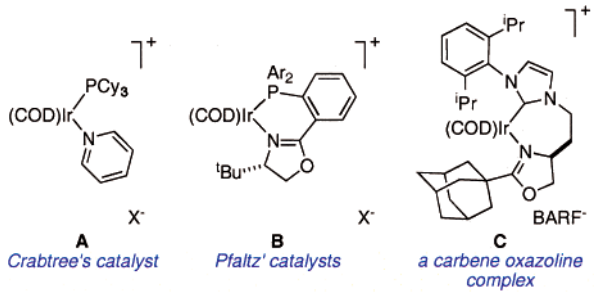
Iridium-Mediated Asymmetric Hydrogenation of 2,3-Diphenylbutadiene: A Revealing Kinetic Study

Xiuhua Cui and Kevin Burgess*

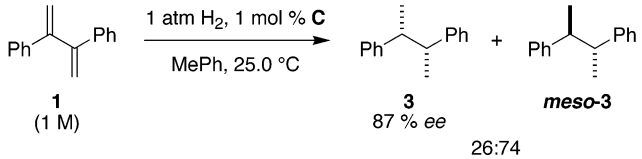
Department of Chemistry, Texas A & M University, Box 30012, College Station, Texas 77842-3012

Received July 30, 2003; E-mail: burgess@tamu.edu

Chiral derivatives of Crabtree's catalyst **A**,[1] including Pfaltz' phosphine oxazoline systems **B**,[2] some related *N*,*P*-complexes,[3−8] and carbene oxazoline complexes like **C**,[9,10] are unusual in that they can be used for asymmetric hydrogenations of arylalkenes that have no other functional groups. However, there are no reports of these catalysts being applied to reduce prochiral dienes or polyenes. Indeed, the literature on asymmetric hydrogenations of dienes of any kind, functionalized or otherwise, with any catalyst, is sparse.[11−13] Consequently, we initiated a program to study asymmetric hydrogenations of dienes with little or no other functionality, beginning here with a kinetic study for 2,3-diphenylbutadiene **1**. While the data obtained in this preliminary work have no immediate synthetic application, they are highly informative for this particular substrate and may illustrate general facets of the mechanism of hydrogenation by iridium catalysts **A**−**C**.



Hydrogenation of **1** to the corresponding 2,3-diphenylbutanes could occur directly or via formation of the alkenes **2**, as indicated in Figure 1a. Authentic samples of compounds **2**−**4** were prepared, the hydrogenation reaction was performed as indicated in reaction 1, and the reaction was followed via GC using a chiral column (Figure 1b).[14]



reaction 1

The initial phase of the reaction (until ca. 475 min in Figure 1b) was characterized by zero-order consumption of diene **1**. Extrapolation of the concentration of **1** to 1 mol L^{-1} indicates there was an induction period of ca. 4 min. Control experiments (NMR) indicate that catalyst **C** in the absence of hydrogen did not exchange 1,5-cyclooctadiene (COD) for excess **1** to any significant extent under the conditions of this experiment. Moreover, pretreatment of **C** with hydrogen in the absence of **1** gave a mixture of complexes that were almost inactive for hydrogenation of **1** added later. Thus, the induction period involved removal of the COD ligand in the presence of **1** and hydrogen to give the initial catalyst species.

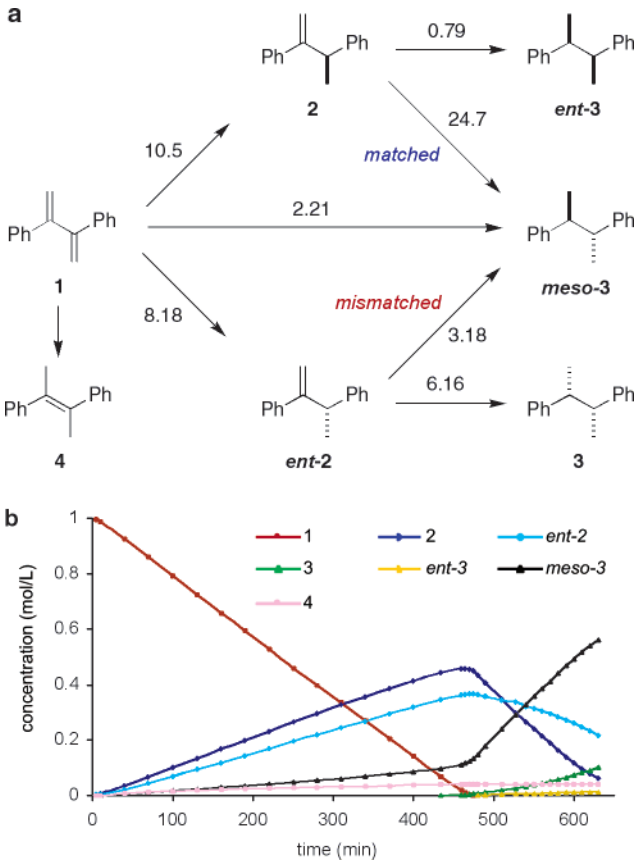


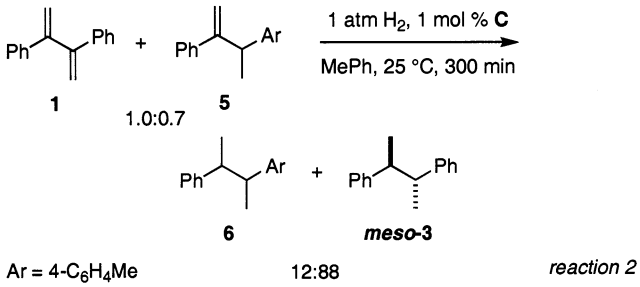
Figure 1. (a) Hydrogenation of 2,3-diphenylbutadiene, with relative rate constants in units of 10^{-4} mol L^{-1} min^{-1} from the slopes in part b. (b) Concentrations of the reaction components as the reaction proceeds.

Four products formed during the initial phase of reaction 1. Prevalent among these were the alkene **2** and its enantiomer, *ent*-**2**. The rate ratio for formation of these two products was only 1.28; i.e., the enantioselectivity was low at that stage. The third product was *meso*-**3**. It formed more slowly (rate of formation of {**2** + *ent*-**2**}:*meso*-**3** = 8.45), while the stereoisomeric products **3** and *ent*-**3** were conspicuously absent during this phase of the reaction.

A series of experiments were performed to test the origin of *meso*-**3** in the first phase of the reaction. To facilitate this, a racemic sample of compound **5** was prepared. Hydrogenation of an equimolar solution of **5** and racemic **2** with catalyst **C** demonstrated that the former substrate reacted slightly faster. Then, in the key experiment, reaction 2, a mixture of **1** and racemic **5** was reduced. Product **6** (as a mixture of stereoisomers) should prevail in reaction 2 if in reaction 1 *meso*-**3** was formed in the initial stages of the reaction via addition of one molecule of hydrogen, dissociation of **2** from the metal, recomplexation, and then a second reduction. Conversely, the dominant product would be *meso*-**3** if that same

10.1021/ja037653a CCC: $25.00

material in the featured reaction 1 was formed via delivery of both molecules of hydrogen to **1** without dissociation from the iridium center. In the event, *meso*-**3** was the major product of reaction 2, implying that direct addition of two molecules of H_2 is the dominant pathway. Formation of *meso*-**3**, rather than **3**, is consistent with two additions of hydrogen to the diene coordinated in a *syn* conformation.

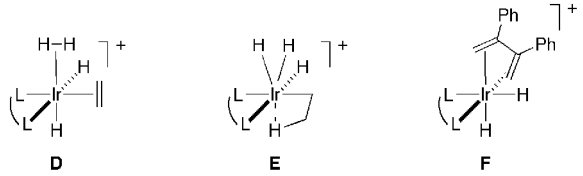


Tetrasubstituted alkene **4** (Figure 1a), the fourth product of the initial phase of the reaction, forms in the first stage, and then its concentration remains nearly constant. Control experiments indicate that alkene **4** is not consumed under the conditions of this experiment. Its *cis* isomer is not formed in the reaction.

After approximately 475 min, *when all the diene **1** is consumed*, the reaction profile changed markedly. The fastest transformation after that point was conversion of **2** into *meso*-**3**; this occurred 31.3 times faster than conversion of **2** into *ent*-**3**. Conversely, *ent*-**2** was reduced to the chiral product **3** 1.94 times faster than to *meso*-**3**. Thus, a significant stereochemical bias to the second hydrogenation step is imparted by the chiral center of the substrates **2** and *ent*-**2**, but the reaction is still catalyst-controlled. Even though alkene **2** was the major product after 475 min, the stereochemical outcome was reversed at the end of the process such that **3**, not *ent*-**3**, prevailed. The overall enantioselectivity for formation of **3** was the combined effect of the two steps: rapid conversion of **2** into *meso*-**3**, where the substrate and catalyst stereoselectivities are matched,[15] and preferential conversion of *ent*-**2** into **3**, where the catalyst stereoselectivity prevails over substrate control.

A series of conclusions about the hydrogenation of diene **1** can be drawn from the data above. First, consistent with our prior observations,[10] removal of the COD ligand requires a significant induction time and the presence of hydrogen. Once the COD group is removed, it is rapidly replaced by 1,3-butadiene **1**. The reduction clearly occurs in two phases, corresponding to reduction of the first diene double bond, and then the second. First, relatively slow, poorly stereoselective hydrogenation of **1** ensues to give mostly **2** and *ent*-**2**, some *meso*-**3** (mainly via a route that does not involve dissociation of an alkene intermediate), and a small amount of alkene **4**. At the end of this first phase, when diene **1** is finally consumed, the overall reaction accelerates by a factor of approximately 1.7. Thereafter, **2** is reduced mainly to *meso*-**3**, while *ent*-**2** is preferentially hydrogenated to **3**; i.e., the enantioface preference is reversed. Thus, the rate and stereochemical data presented here indicate *significant mechanistic differences between the first and second stages of the reaction*.

The assertions outlined above may be pertinent to other systems. Recent theoretical studies on hydrogenation of alkenes using Pfaltz' complexes **B** suggest that the mechanism proceeds via the Ir(III) and Ir(V) intermediates **D** and **E**,[16] i.e., via concomitant migratory insertion of the alkene unit into an Ir−H bond, and oxidative addition of dihydrogen. One straightforward way to explain the experimental data described in this Communication is that, in reaction 1, diene **1** replaces COD as a 4e donor in complex **C**, and then, assuming the carbene oxazoline and diene ligands do not dissociate and the electron count around iridium does not exceed 18, only one H_2 entity could be accommodated around the metal. Thus, while diene is present, the reaction is likely to be restricted to intermediates like **F** and a mechanism that involves cycling between Ir(I) and Ir(III). After the diene is consumed, however,



catalytic cycles that involve Ir(III) and Ir(V) become accessible. In the case of diene **1**, the initial phase of the reaction, possibly involving Ir(I) and Ir(III), is less rapid and selective than the Ir(III)/Ir(V) cycle. This could imply that asymmetric catalysis involving Ir(I)/Ir(III) is limited, and that other metal complexes that cannot undergo redox steps between M(III) and M(V) are unlikely to have the same reactivity as the iridium systems **A**−**C**. Indeed, we have prepared the rhodium analogue of complex **C** and find it is relatively unreactive (see Supporting Information).

Acknowledgment. In memory of Arthur E. Martell; October 18, 1916 − October 15, 2003. Financial support for this work was provided by The Robert Welch Foundation and Johnson Matthey plc. MS spectra were recorded in the TAMU/LBMS-Applications.

Supporting Information Available: Details of the kinetic experiments, syntheses performed to obtain authentic materials, control NMR experiments, and reactions with the rhodium analogue of **C** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Crabtree, R. *Acc. Chem. Res.* **1979**, *12*, 331−337.
(2) Lightfoot, A.; Schnider, P.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 2897−2899.
(3) Blankenstein, J.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4445−4447.
(4) Cozzi, P. G.; Zimmermann, N.; Hilgraf, R.; Schaffner, S.; Pfaltz, A. *Adv. Synth. Catal.* **2001**, *343*, 450−454.
(5) Menges, F.; Pfaltz, A. *Adv. Synth. Catal.* **2002**, *344*, 40−44.
(6) Menges, F.; Neuburger, M.; Pfaltz, A. *Org. Lett.* **2002**, *4*, 4713−4716.
(7) Tang, W.; Wang, W.; Zhang, X. *Angew. Chem., Int. Ed.* **2003**, *42*, 943−946.
(8) Hou, D.-R.; Reibenspies, J. H.; Colacot, T. J.; Burgess, K. *Chem.−Eur. J.* **2000**, *7*, 5391−5400.
(9) Powell, M. T.; Hou, D.-R.; Perry, M. C.; Cui, X.; Burgess, K. *J. Am. Chem. Soc.* **2001**, *123*, 8878−8879.
(10) Perry, M. C.; Cui, X.; Powell, M. T.; Hou, D.-R.; Reibenspies, J. H.; Burgess, K. *J. Am. Chem. Soc.* **2003**, *125*, 113−123.
(11) Muramatsu, H.; Kawano, H.; Ishii, Y.; Saburi, M.; Uchida, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 769−770.
(12) Burk, M. J.; Allen, J. G.; Kiesman, W. F. *J. Am. Chem. Soc.* **1998**, *120*, 657−663.
(13) Beghetto, V.; Matteoli, U.; Serivanti, A. *Chem. Commun.* **2000**, 155−156.
(14) The reaction was repeated many times. It is relatively insensitive to small H_2 pressure changes and the reaction vessel/stirring (i.e., diffusion effects).
(15) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
(16) Brandt, P.; Hedberg, C.; Andersson, P. *Chem.−Eur. J.* **2003**, *9*, 339−347.

JA037653A