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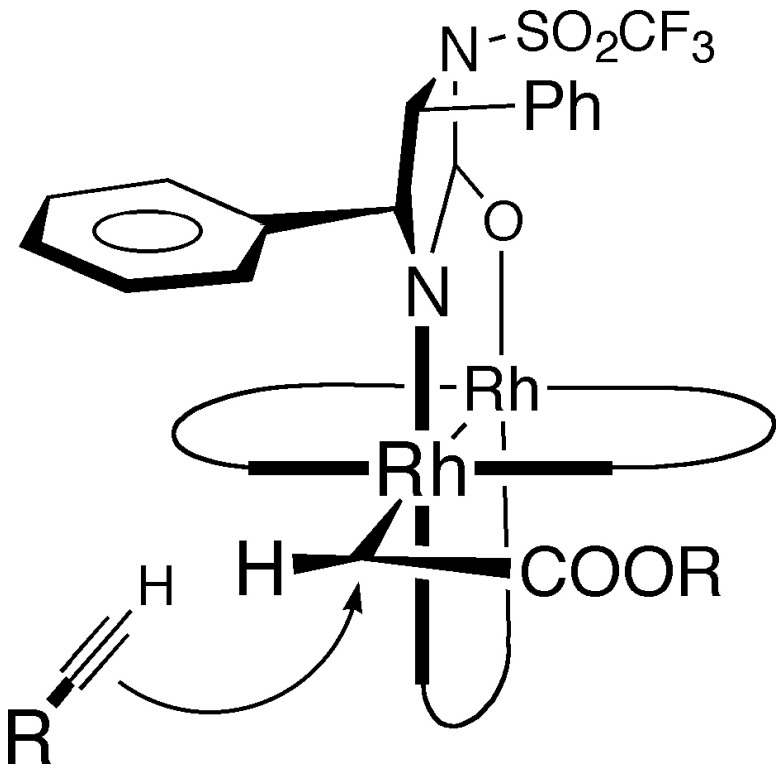

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Mechanism and Origin of Enantioselectivity in the $Rh_2(OAc)(DPTI)_3$-Catalyzed Cyclopropenation of Alkynes

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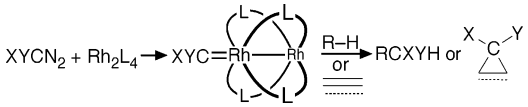
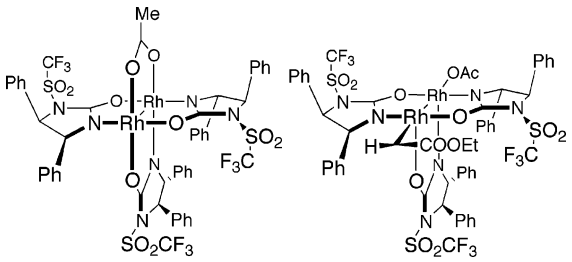
Tetrabridged dirhodium(II) catalysts effect several valuable reactions of α-diazocarbonyl compounds, including C−H and N−H insertions, cyclopropanations of alkenes, and cyclopropenations of alkynes.[1−3] The conventional mechanism for these reactions involves formation of a rhodium carbenoid followed by direct C−H insertion or cycloaddition of the carbenoid to afford products.[2a,4] It has generally been assumed that the tetrabridged framework is intact in the active rhodium carbenoid, and a considerable body of experimental and theoretical results in the literature has been consistent with this mechanism.[5,6]



Corey and co-workers have recently reported that dirhodium tris(diphenyltriflylimidazolidinone)(acetate) [$Rh_2(OAc)(DPTI)_3$, **1**] is a useful catalyst for enantioselective reactions, particularly in cyclopropenations of alkynes with ethyl diazoacetate.[7] To explain the enantioselectivity of these reactions, Corey proposed that the *tribridged* carbenoid **2** is the key intermediate. He further proposed that the cyclopropene products of these reactions are formed by a stepwise process involving a [2 + 2] cycloaddition of the alkyne with **2** followed by reductive elimination. The key evidence for this proposal was that it accounted for the observation of similar selectivity using **1** versus a complex containing only two of the chiral ligands, $Rh_2(O_2C\text{-}t\text{-}Bu)_2(DPTI)_2$.

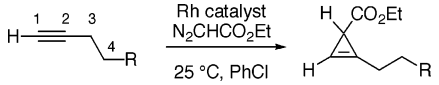


1 **2**

We describe here a study of these reactions using a combination of experimental kinetic isotope effects (KIEs) and theoretical calculations. The results support the conventional tetrabridged carbenoid mechanism and suggest an explanation for the enantioselectivity with DPTI ligands, and they do not support a [2 + 2] cycloaddition of **2**.

The experimental ^{13}C KIEs for cyclopropenations were determined by NMR methodology at natural abundance.[8] Cyclopropenations of 1-pentyne or 1-hexyne with ethyl diazoacetate catalyzed by 0.2 mol % of $Rh_2(OAc)(DPTI)_3$ or 0.1 mol % of $Rh_2(OAc)_4$ were carried out in chlorobenzene at 25 °C. Under these conditions, the conversion of the alkynes to cyclopropene was approximately quantitative, and the enantiomeric excess observed in the $Rh_2(OAc)(DPTI)_3$-catalyzed reactions was 92−93%. Reactions of the alkynes were taken to 71−83% conversion, and the unreacted alkyne was recovered by a vacuum transfer followed by distillation. The samples of recovered alkyne were analyzed by ^{13}C NMR, along with standard samples that had not been subjected to the reaction conditions. The change in isotopic composition in each position was determined relative to the C_4 carbon of the alkyne in each case, with the assumption that isotopic fractionation of this carbon was negligible. From the percentage conversions and the changes in isotopic composition, the KIEs were calculated as previously described.[8]

Table 1. Experimental ^{13}C KIEs for Cyclopropenations versus Predicted KIEs for Tetrabridged Mechanism[a]



	C1	C2	C3
experimental[b,c] $Rh_2(OAc)_4$			
exp 1 (R = Me)	1.012(3)	1.001(3)	0.999(4)
exp 2 (R = Me)	1.012(3)	1.003(3)	1.000(2)
predicted for **3**, saddle point	0.999	1.000	1.001
predicted for **3**, CVTS	1.011	1.004	1.000
experimental $Rh_2(OAc)(DPTI)_3$			
exp 1 (R = Me)	1.008(3)	1.003(1)	1.000(2)
exp 2 (R = Me)	1.007(4)	0.999(2)	0.999(3)
exp 3 (R = Et)	1.010(4)	1.003(4)	1.000(4)
predicted for **4**, saddle point	1.008	1.006	1.005
predicted for **4**, CVTS	1.009	1.003	1.000

[a] The experimental and predicted KIEs are relative values of k_{12C}/k_{13C} versus the C_4 KIE. The calculated absolute isotope effect at C_4 was slightly greater than unity, and the predicted KIEs have been corrected to allow for this. [b] Numbers in parentheses are standard deviations on the last digit (n = 6). [c] The KIEs obtained for the terminal methyl carbon of 1-pentyne and the terminal ethyl carbons of 1-hexyne were within experimental error of unity.

The results are summarized in Table 1. The terminal acetylenic carbon in each case exhibits a significant normal KIE, with a slightly larger KIE observed for $Rh_2(OAc)_4$ than for $Rh_2(OAc)(DPTI)_3$. The internal acetylenic carbon KIE is probably greater than unity based on the preponderance of results, but only very slightly so. These KIEs qualitatively suggest an early, asynchronous transition state in which bond formation to the terminal carbon is proceeding but little bond formation has occurred at the internal acetylenic carbon. The similarity of KIEs for the two catalysts suggests analogous mechanisms.

To interpret these isotope effects in greater detail, the conventional cyclopropenation mechanism involving an intact tetrabridged rhodium carbenoid and the Corey mechanism were explored in DFT calculations using the B3LYP functional.[9] A complication in the reaction of pentyne with tetrabridged rhodium carbenoids is that the energy surface is nearly flat as the alkyne approaches. Under these circumstances, the potential energy saddle point is a flawed

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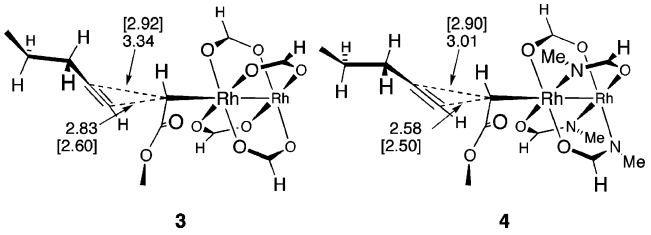


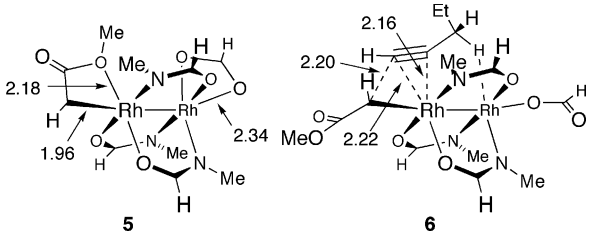
Figure 1. Calculated transition structures for reaction of 1-pentyne with rhodium carbenoids. Distances outside brackets are for the potential energy saddle points, while distances in brackets refer to the approximate canonical variational transition structures.

model for the transition state. For this reason, we also located approximate canonical variational transition structures (CVTS), using entropy estimates at 298 K based on the unscaled harmonic frequencies.

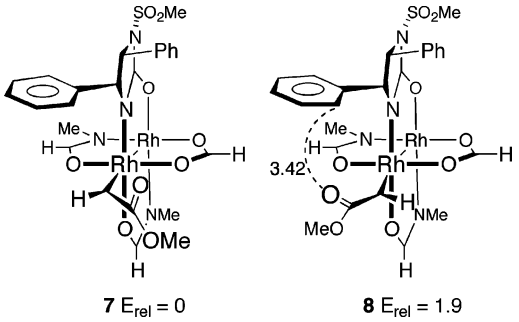
The structures located for reaction of 1-pentyne with model tetrabridged rhodium carbenoids derived from $Rh_2(O_2CH)_4$ and $Rh_2[O(NMe)CH]_3(O_2CH)$ (as a model for **1**) are shown in Figure 1. An anti arrangement of the terminal ethyl group of the pentyne relative to the carbenoid carbon was assumed for simplification. With both systems, the CVTS are significantly later than the potential energy saddle points, as would be expected due to a narrowing of the dynamic entry channel as the alkyne approaches the carbenoid.

^{13}C KIEs based on these transition structures were predicted by the method of Bigeleisen and Mayer,[10] and the results are summarized in Table 1. A striking observation is that the potential energy saddle points lead to poor predictions of the experimental isotope effects. However, predicted KIEs based on the CVTS match quite well with the observed KIEs. From this, we conclude that the experimental KIEs are entirely consistent with cyclopropenation via intact tetrabridged rhodium carbenoids.

In the calculational exploration of models for the tribridged carbenoid **2**, the [2 + 2] mechanism did not appear viable. In contrast to **2**, structure **5** was adopted by a tribridged carbenoid derived from $Rh_2[O(NMe)CH]_3(O_2CH)$. This structure is uphill from the tetrabridged alternative by 21.5 kcal/mol, yet **5** appears resistant to effecting cyclopropenation. Instead, forcing propyne to approach the carbenoid carbon of **5** resulted in a new carbene, $MeCCHCHC(OMe)ORh_2[O(NMe)CH]_3(O_2CH)$. The transition structure **6**, appearing to correspond to the [2 + 2] cycloaddition of the Corey mechanism, was located. However, when **6** is followed forward, it does not afford either a metallocyclobutene or a cyclopropene, but rather affords without barrier the rhodium carbenoid, $MeO_2CCHCHC(Pr)=Rh_2[O(NMe)CH]_3(O_2CH)$, by a process reminiscent of enyne metathesis.



The geometry of **4** suggested an explanation for direction of the enantioselectivity with **1** as well as the observation that two DPTI ligands are sufficient for high selectivity. In **4**, the approximate plane of the carbenoid carbon is oriented perpendicular to the most-donating proximal Rh−N bond, and the alkyne approach anti to the Rh−N bond is unhindered. The enantiomeric product would then be determined by the orientation of the carboalkoxy group of the carbenoid versus the proximal phenyl group of the DPTI ligand (cf. **7** versus **8**). In the model **7**/**8**, conformation **7** is preferred by 1.9 kcal/mol, presumably due to a phenyl/carboalkoxy steric interaction in **8**. Approach of the alkyne anti to the Rh−N bond of **7** would afford the major enantiomeric product.



In summary, we were unable to identify a viable mechanism for cyclopropenation via tribridged structures, but tetrabridged rhodium carbenoids can account for the isotope effects and enantioselectivity of the $Rh_2(O_2CR)_n(DPTI)_{4-n}$ reactions. The tetrabridged mechanism should be the best starting point for ligand design.

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Supporting Information Available: Experimental procedures, and energies and geometries of all calculated structures (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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