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Rh-Catalyzed Intermolecular Reactions of Alkynes with α-Diazoesters That Possess *β*-Hydrogens: Ligand-Based Control over Divergent Pathways

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One of the challenges for modern synthesis is to create distinct types of complex molecules from identical starting materials based solely on catalyst selection. In this context, Rh(II)carboxylates and Rh(II)carboxamidates are remarkable, as a relatively small body of related catalysts can effect a diverse range of reactivity.[1−3] Herein, we present the first general method for cyclopropenation that tolerates *β*-hydrogens and the first examples of direct,[4a] Rh-catalyzed intermolecular alkyne insertions to generate putative[4b] alkenyl carbene intermediates (Scheme 1). Both of these pathways can be accessed via common starting materials based on ligand selection.

Chiral cyclopropenes are increasingly popular building blocks for asymmetric synthesis.[5] Although the Rh-catalyzed reaction of diazo compounds with alkynes is a particularly powerful tool for the synthesis of cyclopropenes,[6] a major limitation was that simple α-alkyl-α-diazoacetates were not viable owing to a lack of selectivity over *β*-hydride elimination.[7] In elegant studies, Müller[8a] and Padwa[8b] described the Rh_2OAc_4 catalyzed reactions of 1-hexyne with ethyl α-diazopropionate and α-diazopropiophenone, respectively. However, the *β*-hydrogens of these diazo compounds belong to strong (methyl) bonds, and cyclopropenation reactions with weaker *β*-C−H bonds were unknown. As shown in Table 1, the reactivity of ethyl α-diazobutanoate with phenylacetylene was surveyed. Attempts to adapt known[8] conditions (0.5 mol % Rh_2OAc_4) were unsuccessful, as were attempts to apply a variety of rhodium(II) carboxylates,[1,2] Rh(II) carboxamidates,[1,2] and Cu catalysts[9] that have been used previously in cyclopropenation and cyclopropanation reactions (Table 1). However, **1** was obtained in 6% yield along with 50% of ethyl *cis*-crotonate (**2**) with Rh_2Oct_4 at −78 °C. It was reasoned that the difference in reactivity between Rh_2Oct_4 and Rh_2OAc_4 might be steric in origin. In accord with this hypothesis, Rh_2Piv_4 was shown to give **1** in 59% yield with only 11% of crotonate **2** at −78 °C. High selectivity for cyclopropenation over *β*-hydride elimination was also observed with Rh_2esp_2[2e] and catalyst **3**. However, only low yields of **1** were obtained when Rh_2TFA_4 [dirhodium tetra(trifluoroacetate)], Rh_2TPA_4 [dirhodium tetra(triphenylacetate)], or catalyst **4** were utilized. Reaction temperature is a critical parameter for the cyclopropenation reaction. Thus, **1** was obtained in <5% yield when the Rh_2Piv_4 catalyzed reaction was carried out at room temperature instead of −78 °C: the major product was crotonate **2** as a 6:1 *Z*/*E* mixture.

As shown in Table 2, the Rh_2Piv_4 catalyzed cyclopropenation is successful for a range of terminal alkynes with α-diazopropionate, α-diazobutanoate, and α-diazohydrocinnamate. The success of α-diazohydrocinnimate is notable given the susceptiblility of benzylic hydrogens to undergo *β*-hydride elimination. The moderate yields (40−75%) should be considered in the context of known cyclopropenation reactions,[6] which typically proceed in similar yields even without the complications of *β*-hydrogens. The described method is successful for terminal alkynes that are conjugated to an arene or alkene. However, cyclopropene products

Scheme 1. Divergent Reactivity Based on Ligand Selection

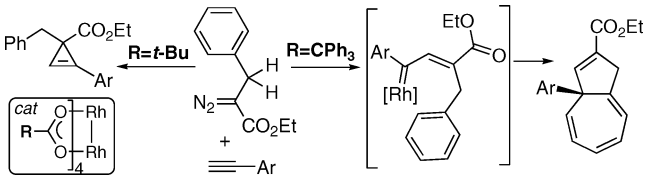
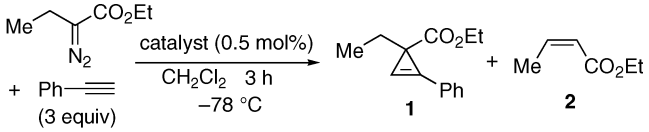
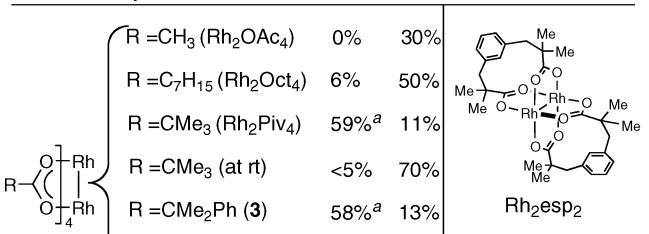


Table 1. The Effect of Ligand Choice on Rh-Catalyzed Cyclopropenation



catalyst	1	2
R =CH_3 (Rh_2OAc_4)	0%	30%
R =C_7H_{15} (Rh_2Oct_4)	6%	50%
R =CMe_3 (Rh_2Piv_4)	59%[a]	11%
R =CMe_3 (at rt)	<5%	70%
R =CMe_2Ph (**3**)	58%[a]	13%
R =$CMePh_2$ (**4**)	29%	40%
R =CPh_3 (Rh_2TPA_4)	12%[a]	12%
R =CF_3 (Rh_2TFA_4)	0%	80%

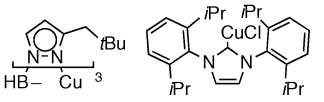


44%[a] (**1**) + 12% (**2**)

catalysts screened that did not give **1**

Rh_2(*S*-DOSP)$_4$ Rh_2(5*S*-MEPY)$_4$

Rh_2(*S*-PTPA)$_4$ Rh_2(4*S*-MEOX)$_4$



[a] Isolated yield. Other yields were measured by ^{1}H NMR.

were not obtained when ethyl α-diazobutanoate was reacted with 1-hexyne, diphenylacetylene, or 1-phenyl-1-butyne under Rh_2Piv_4 catalysis.

The reactivity of aryl alkynes with ethyl α-diazohydrocinnamate is altered dramatically by changing the catalyst from Rh_2Piv_4 to Rh_2TPA_4: angularly substituted dihydroazulenes of structure **5** are formed (Scheme 2), and cyclopropenes are not observed. Ethyl 1-benzyl-2-phenylcyclo-prop-2-ene carboxylate does not react when treated with Rh_2TPA_4, and therefore is unlikely to be an intermediate in the formation of **5**.[10] It is proposed that the formation of **5** takes place via a tandem alkyne insertion/Büchner ring expansion[11] (Scheme 2) via intermediates **6**−**8**.

Rh-catalyzed intramolecular alkyne insertions to generate putative alkenyl carbene intermediates are known,[3,4b] but the reactions in Scheme 2 represent the first solely[4a] intermolecular examples. These reactions rapidly build molecular complexity, and other intermo-

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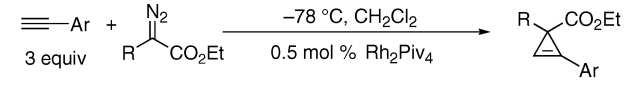
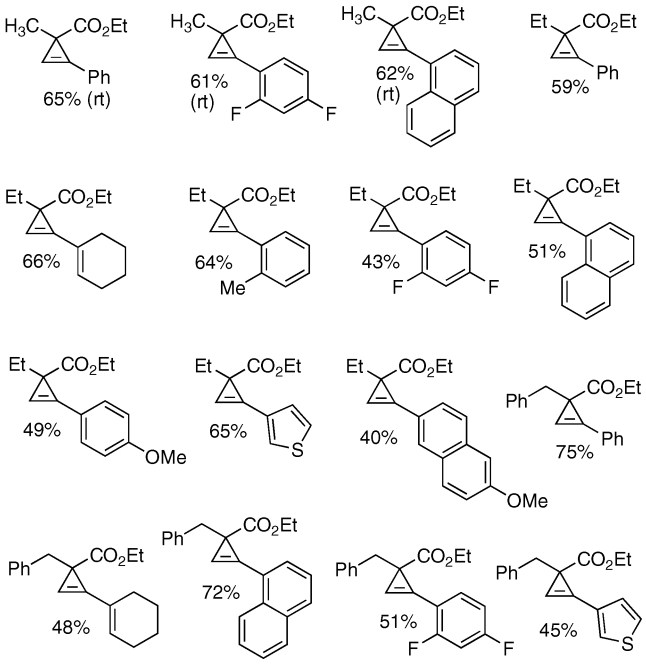
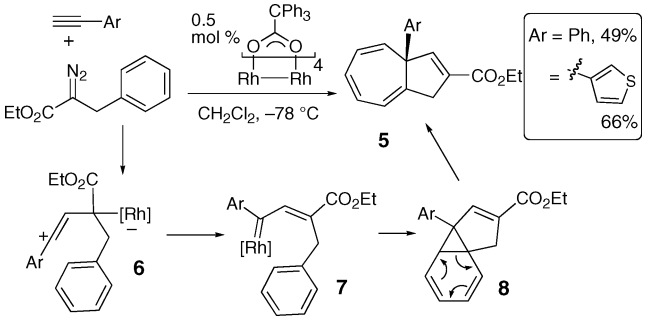
Table 2. Cyclopropenation of Arylalkynes by Diazoesters with β-Hydrogens





Scheme 2. Divergent Reactivity Based on Catalyst Selection



lecular alkyne insertion cascade reactions (e.g., CH insertion) should also be feasible.

In earlier studies that compared β-hydride elimination to C−H insertion[12] or O−H insertion,[13] only minor improvements were observed when Rh-catalysts with sterically demanding carboxylate ligands were compared to Rh_2OAc_4 or Rh_2Oct_4. Currently, it is unclear why hindered carboxylate ligands lead to such dramatic improvements in cyclopropenation and dihydroazulene formation. Several distinct mechanisms for cyclopropenation have been proposed in the literature.[14] A goal of future studies will be to develop a rationale to explain why different ligands lead to divergent reaction pathways and to design new catalyst systems accordingly.

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Supporting Information Available: Full experimental details and ^1H,^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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