

Formal Carbene Insertion into C–C Bond: Rh(I)-Catalyzed Reaction of Benzocyclobutenols with Diazoesters

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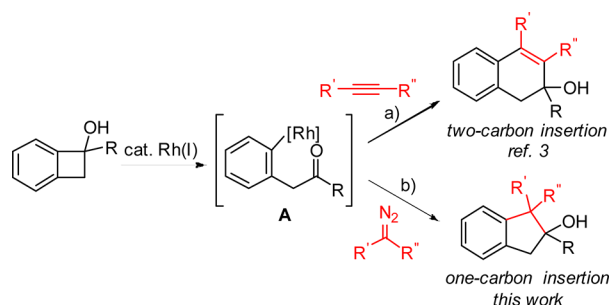
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S Supporting Information

ABSTRACT: A Rh(I)-catalyzed formal carbene insertion into C–C bond of benzocyclobutenols has been realized by employing diazoesters as carbene precursors. The product indanol derivatives were obtained in good yields and in diastereoselective manner under mild reaction conditions. All-carbon quaternary center is constructed at the carbenic carbon. This catalytic reaction involves selective cleavage of C–C bond, Rh(I) carbene insertion, and intramolecular aldol reaction.

Carbon–carbon bonds constitute the fundamental frameworks of organic compounds. The selective C–C bonds cleavage and subsequent functionalization are important issues in organic chemistry from both mechanistic investigations and practical synthetic applications. However, a formidable challenge exists in this area because of the kinetically inert and thermodynamically stable property of C–C bonds. Nevertheless, significant progresses have been made over the past decades, particularly in transition-metal-catalyzed reactions of strained systems such as *tert*-cyclobutanols.^{1,2} In this context, Murakami and co-workers have recently reported Rh(I)-catalyzed reaction between benzocyclobutenols and internal alkynes (Scheme 1a).³ Interestingly, the Rh(I) catalyst induces

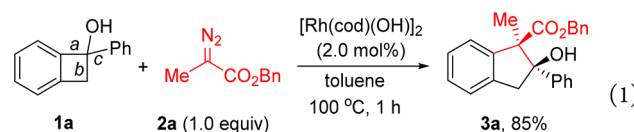
Scheme 1. Rh(I)-Catalyzed Reaction of Benzocyclobutenols through C–C Bond Cleavage: (a) Alkyne Insertion; (b) Carbene Insertion



the four-membered ring-opening with selective cleavage at the C(sp²)-C(sp³) bond adjacent to the hydroxyl group, generating arylrhodium species A.⁴ Further reaction of A with alkyne provides dihydronaphthalene derivatives. The overall transformation is a formal two-carbon insertion into C–C bond.⁵

On the other hand, diazo compounds and *N*-tosylhydrazones have recently emerged as a new class of cross-coupling partners in transition-metal-catalyzed reactions.^{6,7} We have previously demonstrated that this type of cross-coupling reaction can be explored in the construction of two separate C–C bonds on the same carbenic carbon center through a sequence of palladium carbene migratory insertion–transmetalation–reductive elimination.^{8,9} As the continuation of our interest in catalytic carbene transformation and also inspired by Murakami's recent report,³ we further conceived the combination of transition-metal-induced C–C bond cleavage with the catalytic carbene migratory insertion process. As shown in Scheme 1b, by replacing the alkyne substrate with diazo compound,¹⁰ we expect that a one-carbon insertion may be realized,¹¹ generating an all-carbon quaternary center at the carbenic carbon. Herein we report the investigation along this line.

At the outset, benzocyclobutenol **1a** and diazoester **2a** (1 equiv) were treated with [Rh(cod)(OH)]₂ (2.0 mol %) as catalyst in toluene (0.1 M) at 100 °C for 1 h. To our delight, the anticipated product indanol **3a** was cleanly obtained in 85% isolated yield (eq 1). Moreover, the reaction showed excellent



regioselectivity and diastereoselectivity, as only one product was observed. The structure of the product was unambiguously established by X-ray crystallography, which shows the hydroxyl group and the ester group are in the *cis*-configuration (Figure 1). Same as Murakami's reaction,^{3,4} C(sp²)-C(sp³) bond *a* is exclusively cleaved, and the other two C–C bonds *b* and *c* remain intact in this transformation.

Next we proceeded to study the scope of this Rh(I)-catalyzed C–C bond carbene insertion reactions. As shown in Scheme 2, the reaction proceeded successfully with a variety of combinations of benzocyclobutenols **1a–i** and diazoesters **2a–i**, affording the corresponding indanol derivatives **3a–x**, which bear all-carbon quaternary center, in regioselective and diastereoselective manner. A series of alkyl substituted diazoesters were found to react with benzocyclobutenol **1a** under the standard reaction conditions, and the indanol derivatives were obtained in 61–87% yields (**3a–f**). When R²

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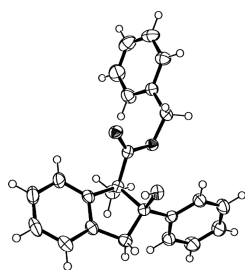


Figure 1. X-ray structure of 3a.

is aromatic group, the substituents on the aryl ring show essentially no effect on the reaction (3g–i). Besides, the naphthyl substituted benzocyclobutenol affords the product in 90% yield (3j). The structure of 3b is confirmed by X-ray crystallography.

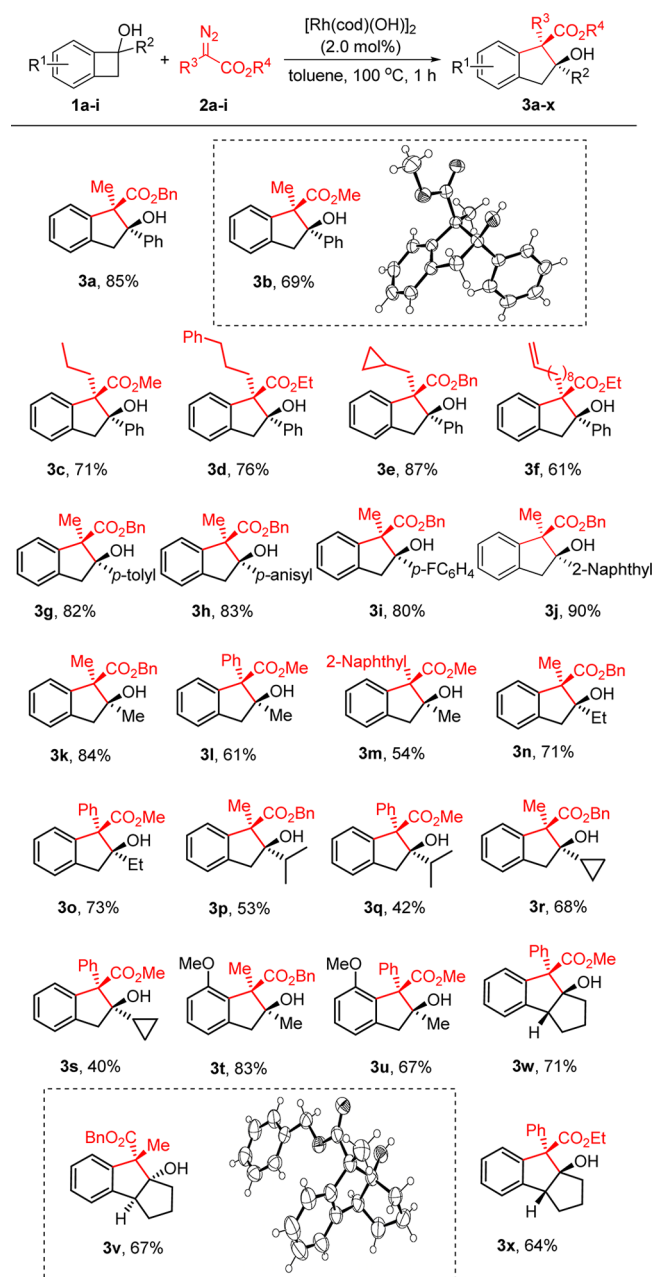
Substrates bearing aliphatic group adjacent to the α -carbon of the tertiary alcohol can participate in this reaction smoothly (3k–s). It is noteworthy that the donor/acceptor diazo compounds can also be employed as carbene precursors in this transformation, albeit with slightly diminished yields (3l, 3m). For the isopropyl substituted benzocyclobutenols, only moderate yields can be obtained, which indicates that the steric hindrance of the aliphatic substituents may affect this reaction (3p, 3q). Interestingly, cyclopropyl moiety tolerates the reaction conditions and remains intact in the reaction (3r, 3s).

Notably, the *ortho*-substituent on the phenyl ring of benzocyclobutenol does not interfere with the regioselectivity of the reaction, giving the products derived from exclusive C(sp²)-C(sp³) cleavage (3t, 3u). Finally, the ring-fused benzocyclobutenols are also suitable substrates for this reaction, affording the corresponding products bearing three fused rings in good yields and excellent diastereoselectivity (3v–x).¹² The relative configuration of product 3v is confirmed unambiguously through X-ray crystallography.

A plausible mechanism has been proposed for this Rh(I)-catalyzed formal C–C bond carbene insertion reaction (Scheme 3). Initially, [Rh(cod)(OH)]₂ dedimerizes and then deprotonates 1a to give alkoxyl Rh(I) species B. The η^2 -coordination of the arene moiety to the rhodium center leads to the dominant cleavage at C(sp²)-C(sp³) bond through β -carbon elimination process, affording aryl Rh(I) intermediate bearing ketone moiety (A).^{3,4} The arylrhodium(I) species A then reacts with diazoester substrate 2a to generate Rh(I)-carbene complex C, which subsequently undergoes carbene migratory insertion to afford oxa- π -allyl Rh(I) intermediate D.^{9a}

From intermediate D, intramolecular aldol reaction occurs in a diastereoselective manner to produce alkoxyl Rh(I) species E with *cis*-configuration.¹³ Finally, E is protonated with 1a to form the indanol product 3a with regeneration of the alkoxyl Rh(I) species B. Overall, the carbene carbon is inserted into the C–C bond of the benzocyclobutenol, affording a formal C–C bond carbene insertion product with regioselectivity and diastereoselectivity.

The excellent diastereoselectivity of this reaction is attributed to the stereocontrol of the intramolecular aldol reaction step (D to E).¹³ The transition state for the reaction of D to E is proposed as T or T', in which the oxygen atoms of both ketone moiety and oxa- π -allyl moiety are coordinated to the Rh(I) to form chairlike structure (Scheme 4). The *cis*-fused transition state T is favored over the *trans*-fused one T', leading to the

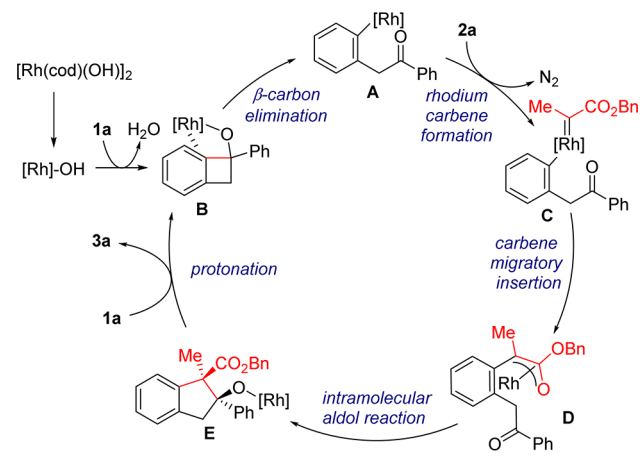
Scheme 2. Scope of Rh(I)-Catalyzed C–C Bond Carbene Insertion Reaction^{a,b}

^aThe reaction was carried out with 1a–i (0.20 mmol), 2a–i (0.20 mmol) in the presence of [Rh(cod)(OH)]₂ (2 mol %) in 2.0 mL of toluene at 100 °C for 1 h. ^bAll the yields refer to the isolated yields by column chromatography. In all the cases, only one of the two enantiomers of the racemic product is shown.

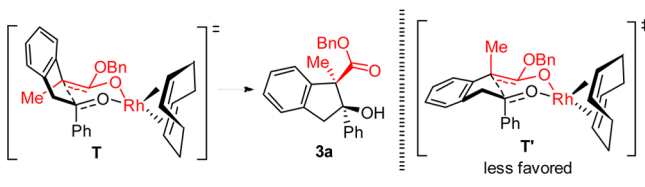
exclusive formation of the product with hydroxyl group and ester group having *cis*-configuration.

In conclusion, we have disclosed a Rh(I)-catalyzed formal C–C bond carbene insertion reaction between benzocyclobutenols and diazoesters. The C–C bond cleavage and rhodium carbene migratory insertion are proposed as the key steps in the catalytic cycle. This reaction shows excellent regioselectivity and diastereoselectivity and provides an efficient approach to indanol derivatives bearing all-carbon quaternary center in the ring. Moreover, this reaction provides the first example of functionalization of C–C bond through metal carbene

Scheme 3. Proposed Mechanism



Scheme 4. Rationalization of Diastereoselectivity



migratory insertion process, which may open up new possibilities in the development of metal carbene related catalytic transformations.

■ ASSOCIATED CONTENT

S Supporting Information

Experimental procedure, characterization data, copies of ^1H and ^{13}C NMR spectra, and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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