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Rhodium-Catalyzed Ring Opening of Benzocyclobutenols with Site-Selectivity Complementary to Thermal Ring Opening

Naoki Ishida, Shota Sawano, Yusuke Masuda, and Masahiro Murakami*

Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Katsura, Kyoto 615-8510, Japan

Supporting Information

ABSTRACT: A rhodium catalyst induced ring opening of benzocyclobutenols with selective cleavage of the C(sp^2)–C(sp^3) bond adjacent to the hydroxyl group. The site-selectivity markedly contrasted with that of their thermal ring-opening reaction. The rhodium-catalyzed ring opening led to the development of a new alkyne insertion reaction constructing a dihydronaphthalene framework.

Carbon–carbon single bonds are thermodynamically stable and kinetically inert in general. Nevertheless, transition metal catalysis in organic synthesis has made a significant progress so that a number of unique synthetic reactions in which a carbon–carbon single bond is cleaved in preference to other seemingly more reactive functional groups have emerged in the past decade.[1]

Cyclobutenes undergo thermal and photochemical ring-opening reactions with cleavage of the C(sp^3)–C(sp^3) bond to form 1,3-dienes.[2] An oxy substituent, in particular an anionic one, accelerates the ring-opening reaction and directs its own rotational direction (torquoselectivity).[3] Analogously, benzocyclobutenols undergo ring opening with cleavage of the C(sp^3)–C(sp^3) bond, which we refer as the "distal" bond (Scheme 1). Heating,[4] photo irradiation,[5] and treatment with a base[6−8] induce their ring opening to furnish reactive *o*-quinodimethanes,[9] which subsequently engage in [4 + 2] cycloaddition with dienophiles.[10] This type of [4 + 2] cycloaddition has served for the synthesis of natural products[11] and functional materials.[12] On the other hand, we previously reported a rhodium-catalyzed addition reaction of phenylboronic acid onto 6-chlorobenzocyclobutenone.[13] The resulting rhodium *tert*-benzocyclobutenolate intermediate underwent ring opening with preferential cleavage of the "proximal" bond rather than the distal bond. This preliminary finding led us to examine rhodium catalysts for ring opening of benzocyclobutenols in detail. Herein, we report a rhodium-catalyzed ring-opening reaction of benzocyclobutenols, which is characterized by the site-selectivity complementary to those of the conventional ring-opening reactions, that is, by exclusive cleavage of the proximal C(sp^2)–C(sp^3) bond.[14] A new alkyne insertion reaction was also developed based on this unique ring opening (Scheme 1).[15]

Scheme 1. Ring Opening of Benzocyclobutenols

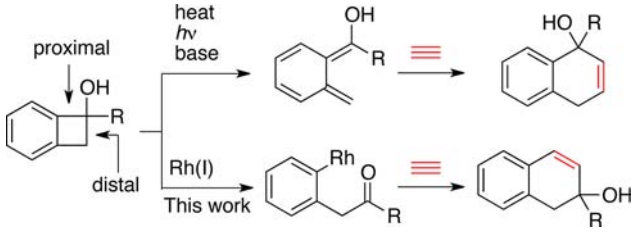
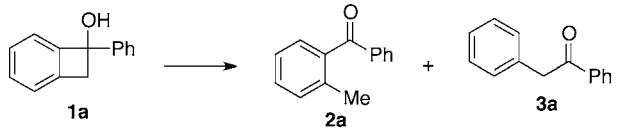


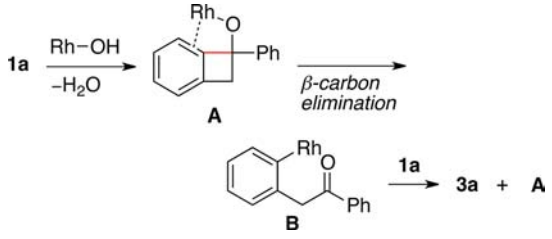
Table 1. Ring Opening of 1a[a]



entry	conditions	yields/%[b] 2a	3a
1	toluene, 100 °C	86	0
2	NaOH aq, dioxane, rt	87	0
3	*hν*, benzene, rt	30[c]	0
4	5 mol % of Rh(acac)(CH_2CH_2)$_2$ 10 mol % of P(*t*-Bu)$_3$, toluene, 100 °C	14	74
5	2.5 mol % of [Rh(OH)(cod)]$_2$, toluene, 100 °C	0	89
6	2.5 mol % of [Rh(OH)(cod)]$_2$, dioxane, 100 °C	20	74
7	2.5 mol % of [Rh(OH)(cod)]$_2$, 12 mol % of IPr, toluene, 100 °C	80	0

[a]Benzocyclobutenol **1a** (0.20 mmol), solvent (1.0 mL). See Supporting Information for details. [b]Isolated yields. [c]NMR yield.

Scheme 2. Plausible Mechanism



Initially, ring opening of **1a** was examined under various reaction conditions (Table 1). Simple heating of **1a** in toluene at 100 °C selectively gave **2a** in 86% yield (entry 1). Addition of a base accelerated the ring-opening reaction, which occurred even at room temperature to produce only **2a** again (entry 2). Irradiation with UV light (254 nm) also afforded **2a** albeit in 30% yield along with a number of unidentified byproducts (entry 3). On the other hand, when **1a** was heated at 100 °C in

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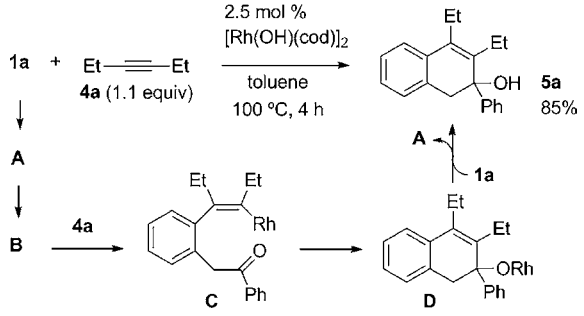
Scheme 3. Rhodium-Catalyzed Reaction of 2a with 3-Hexyne (4a)

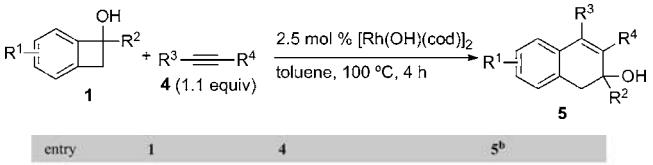


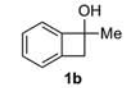
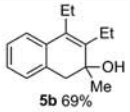
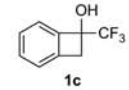
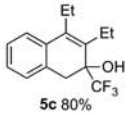
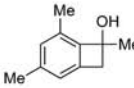
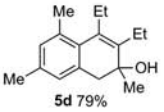
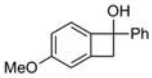
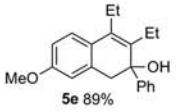
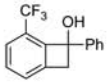
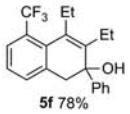
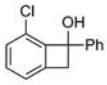
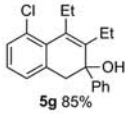
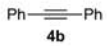
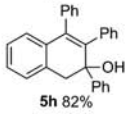
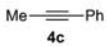
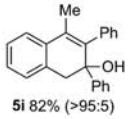
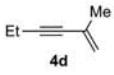
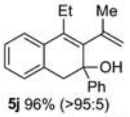
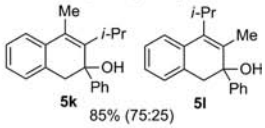
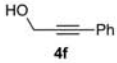
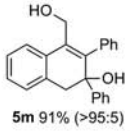
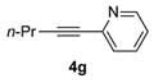
toluene in the presence of $Rh(acac)(CH_2CH_2)_2$ (5 mol %) and $P(t\text{-}Bu)_3$ (10 mol %),[13] a mixture of **2a** and **3a** was formed with the latter predominating by 84:16 (entry 4). Remarkably, **3a** was exclusively obtained in 89% yield when $[Rh(OH)(cod)]_2$ (2.5 mol %) was used in toluene in the absence of any additional ligand (entry 5). No 2-methylbenzophenone (**2a**) was detected in the reaction mixture even by GC analysis. The product selectivity was also subject to a solvent and an additive. The reaction in dioxane under otherwise identical conditions afforded a mixture of **2a** and **3a** with a ratio of 21:79 (entry 6). Only **2a** was formed upon addition of the 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) to $[Rh(OH)(cod)]_2$ (entry 7).

Thus, it proved possible to completely shift the site of ring opening from the distal $C(sp^3)-C(sp^3)$ bond to the proximal $C(sp^2)-C(sp^3)$ bond. We propose the following mechanistic explanation (Scheme 2). Initially, rhodium hydroxide deprotonates **1a** to form rhodium(I) benzocyclobutenolate **A**. It is assumed that the arene moiety intramolecularly coordinates to the rhodium center in an η^2 fashion, as is the case with $Rh(PEt_3)_2(OCPh_3)$.[16] This coordination would assist the migration of the sp^2 carbon onto the rhodium in preference to the sp^3 carbon migration, thereby releasing the structural strain and forming a carbonyl group. The superior π-accepting character of the 1,5-cyclooctadiene ligand would facilitate the η^2-binding of the arene moiety. The generated arylrhodium species **B** undergoes protonation with **1a** to form the benzyl phenyl ketone (**3a**) together with regeneration of the rhodium alkoxide **A**. On the other hand, the ionic character of the rhodium benzocyclobutenolate is augmented in dioxane to partially cause anion-induced thermal ring opening. The strongly binding IPr ligand would occupy the fourth binding site of rhodium of **A** to discourage the η^2-coordination of the arene, thus suppressing the formation of **3a**.

Next, we examined an alkyne insertion reaction by carrying out the rhodium-catalyzed ring opening of **1a** in the presence of 3-hexyne (Scheme 3). The reaction mixture containing 3-hexyne was heated in toluene at 100 °C for 4 h, and subsequent chromatographic isolation furnished dihydronaphthalene **5a** in 85% yield. Mechanistically, the ring-opened arylrhodium(I) intermediate **B** undergoes not protonation but 1,2-addition across the carbon−carbon triple bond. The resulting alkenylrhodium(I) **C** adds back onto the carbonyl group in a 6-exo mode. Alkoxyrhodium(I) **D** is then protonated with **1a** to give dihydronaphthalene **5a** with regeneration of rhodium benzocyclobutenolate **A**. Overall, the alkyne **4a** is inserted into the proximal $C(sp^2)-C(sp^3)$ bond of **1a**, producing a formal [4 + 2] cycloadduct with site-selectivity which is different from that available via *o*-quinodimethane intermediates.[9,10]

Table 2. Insertion of Alkynes into Benzocyclobutenols[a]



entry	1	4	5[b]
1	 **1b**	**4a**	 **5b** 69%
2	 **1c**	**4a**	 **5c** 80%
3	 **1d**	**4a**	 **5d** 79%
4	 **1e**	**4a**	 **5e** 89%
5	 **1f**	**4a**	 **5f** 78%
6	 **1g**	**4a**	 **5g** 85%
7	**1a**	 **4b**	 **5h** 82%
8	**1a**	 **4c**	 **5i** 82% (>95:5)
9	**1a**	 **4d**	 **5j** 96% (>95:5)
10	**1a**	**4e**	 **5k** 85% (75:25) **5l**
11	**1a**	 **4f**	 **5m** 91% (>95:5)
12	**1a**	 **4g**	 **5n** 89% (>95:5)

[a]Reaction conditions: benzocyclobutenol **1** (0.20 mmol), alkyne **4** (1.1 equiv), $[Rh(OH)cod]_2$ (2.5 mol %), toluene (1.0 mL), 100 °C, 4 h. [b]Isolated yields. Regioisomeric ratios in parentheses.

The six-membered ring forming reaction proceeded successfully with various combinations of benzocyclobutenols

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1 and alkynes **4** to demonstrate the generality of the unique site-selectivity of insertion (Table 2). Even the *ortho*-substituted derivative **1d** showed the same site-selectivity to give dihydronaphthalene **5d** in 79% yield (entry 3). The presence of electron-donating methoxy and -withdrawing trifluoromethyl groups on the benzene ring scarcely affected the reaction (entries 4 and 5). A chloro group remained intact (entry 6). High regioselectivities were observed with unsymmetrical alkynes bearing one aryl or vinyl substituent (entries 8 and 9), which was located at the β-position (next to the hydroxyl group) of the resulting dihydronaphthalene skeleton. On the other hand, the unsymmetrical dialkyl-substituted alkyne **4e** gave a mixture of regioisomers with the ratio of 75:25 (entry 10). The regioselectivities observed with these unsymmetrical alkynes were similar to those of intermolecular 1,2-addition of *o*-carbonyl-substituted arylrhodium species onto alkynes.[17] An unprotected hydroxyl group and a pyridine moiety were allowed in the alkynes (entries 11 and 12). Insertion of terminal alkynes such as phenylethyne failed due to rapid self-oligomerization.

In conclusion, we have demonstrated that $[Rh(OH)(cod)]_2$ induces ring opening of benzocyclobutenols with site-selective cleavage of the proximal $C(sp^2)-C(sp^3)$ bond. The site-selectivity is complementary to that of the conventional ring-opening reactions. A new alkyne insertion reaction constructing a dihydronaphthalene framework was developed based upon the unique ring opening.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and spectral data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

murakami@sbchem.kyoto-u.ac.jp

Notes

The authors declare no competing financial interest.

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