Communication

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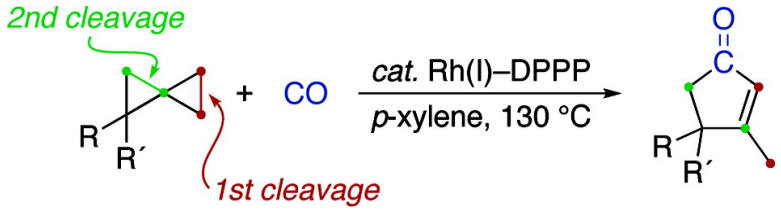

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Rhodium-Catalyzed Carbonylation of Spiropentanes

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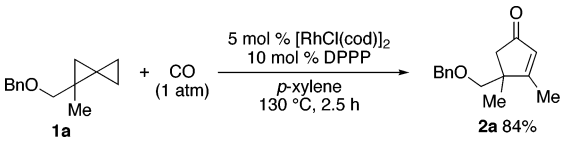
Spiropentanes,[1] the smallest spirocyclic hydrocarbons, possess unique rigid and strained structures and have been the subject of extensive investigation in terms of synthesis,[2] biological activity,[3] and spectroscopy.[4] However, the reactivities of spiropentanes[5] toward transition metals, in particular, are yet to be explored. Hydrogenation of spiropentane occurs in the presence of PtO_2 to produce a mixture of three hydrogenated hydrocarbons.[6] In the cobalt-promoted carbonylation reactions of vinyl- and methylenespiropentanes, one cyclopropane ring was cleaved with the other cyclopropane ring remaining unscathed.[7] Our studies on the C−C bond activation of cyclobutanones[8] led us to target spiropentane substrates for investigation. In this communication, we describe a catalytic carbonylation reaction of spiropentanes forming cyclopentenones through two successive carbon−carbon bond cleavage processes.[8b]

When a solution of 1-(benzyloxymethyl)-1-methylspiropentane (**1a**) in *p*-xylene was heated at 130 °C for 2.5 h under an argon atmosphere in the presence of a rhodium(I) catalyst generated in situ from $[RhCl(cod)]_2$ (5 mol %, 10 mol % Rh) and DPPP (10 mol %),[9] no reaction occurred, and **1a** was largely recovered. In contrast, when the same reaction was carried out under an atmosphere of carbon monoxide, the carbonylation of **1a** took place to afford cyclopentenone **2a** in 84% yield (eq 1).[10,11]



(1)

The formation of cyclopentenone **2a** from spiropentane **1a** is explained by assuming the pathway shown in Scheme 1. Initially, the C4−C5 bond of spiropentane **1a** oxidatively adds to rhodium(I) to form spirocyclic rhodacyclobutane **3**. Insertion of carbon monoxide generates rhodacyclopentanone **4**.[12] Then, the methylene carbon (C2) selectively migrates onto rhodium through a β-carbon elimination[13] to convert the spirocyclic skeleton into six-membered rhodacycle **5**.[14] Finally, reductive elimination furnishes 3-methylenecyclopentanone **6**, which isomerizes to the enone **2a** under the reaction conditions.

Various disubstituted spiropentanes underwent the carbonylation reaction under similar conditions (Table 1). 1,1-Disubstituted spiropentanes **1b**−**e** afforded the corresponding 4,4-disubstituted 3-methylcyclopent-2-enones **2b**−**e** in good yields (entries 1−5). Paraformaldehyde could be used as a carbonyl source instead of gaseous carbon monoxide (entry 2).[15] Cyclopropylspiropentane **1e** reacts only at the spiropentane moiety, leaving the pendant cyclopropyl group untouched, demonstrating the inertness of the isolated cyclopropane ring under the reaction conditions (entry 5). A pair of *cis*/*trans* isomers of 1,2-disubstituted spiropentanes (**1f** and **1g**) was subjected to the carbonylation to test the stereospecificity of the reaction. The secondary carbons migrated onto rhodium with retention of the stereochemistry to furnish the corresponding bicyclic ketones **2f** and **2g**, respectively (entries 6 and 7).

Scheme 1. Mechanism of Spiropentane Carbonylation

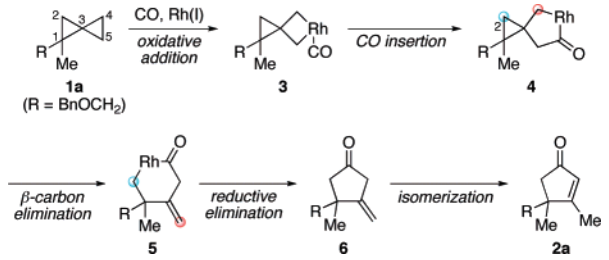
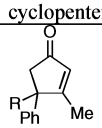
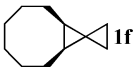
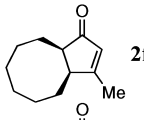
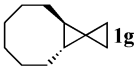
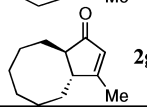
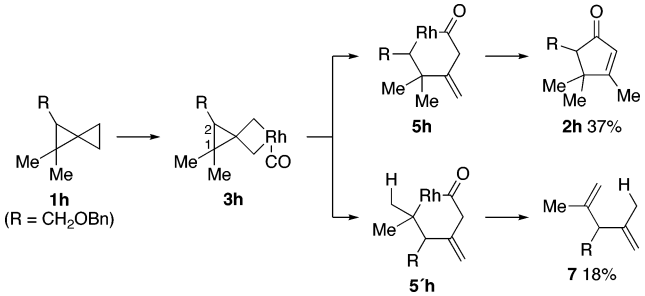


Table 1. Rhodium-Catalyzed Carbonylation of Spiropentanes **1b**−**g**[a]

entry	spiropentane **1** (R)	cyclopentenone **2**	yield[b]
			
1	**1b** ($BnOCH_2$)	**2b**	82%
2[c]	**1b**	**2b**	81%
3[d]	**1c** (Ph)	**2c**	78%
4	**1d** (n-C_5H_{11})	**2d**	76%
5	**1e** (cyclopropyl)	**2e**	82%
6	 **1f**	 **2f**	56%
7	 **1g**	 **2g**	74%

[a] 5 mol % of $[RhCl(cod)]_2$, 10 mol % of DPPP, CO (1 atm), *p*-xylene (0.05 M), 130 °C, 2.5 h, unless otherwise noted. [b] Isolated yield by preparative TLC. [c] **1b** and $(HCHO)_n$ (10 equiv) were reacted for 6 h. [d] 5 h.

Scheme 2. Carbonylation of Trisubstituted Spiropentane **1h**[a]



[a] Conditions: 5 mol % of $[RhCl(cod)]_2$, 10 mol % of DPPP, *p*-xylene, 130 °C, CO (1 atm), 2.5 h.

The carbonylation reaction of spiropentanes with other substitution patterns was also examined. The reaction of trisubstituted spiropentane **1h** was complicated, yielding cyclopentenone **2h** (37%) and diene **7** (18%) as the only identifiable products (Scheme 2). The following pathway accounts for the formation of **2h** and **7**.

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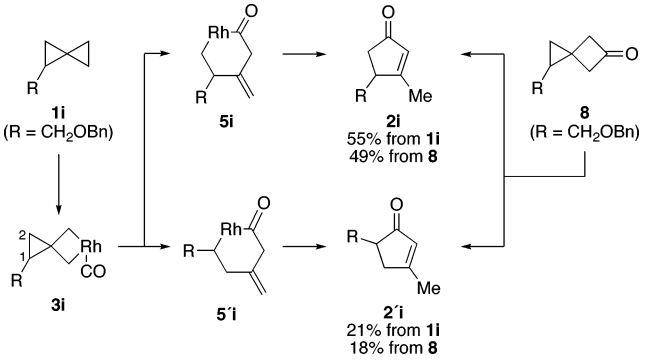
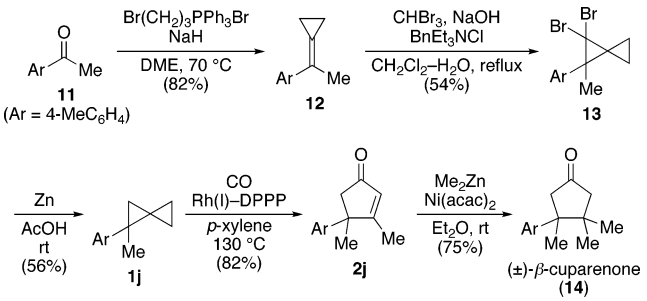
Scheme 3. Carbonylation of Monosubstituted Spiropentane **1i** and Reaction of Spirocyclic Cyclobutanone **8**[a]



[a] Conditions: 5 mol % of $[RhCl(cod)]_2$, 10 mol % of DPPP, *p*-xylene, 130 °C, CO (1 atm), 2.5 h for **1h** and 20 h for **8**.

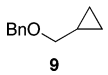
Scheme 4. Synthesis of (±)-*β*-Cuparenone



Rhodacyclobutane **3h** is formed from **1h**, as with the case of **1a**. From this species, two six-membered rhodacycles **5h** and **5′h** result depending on which carbon C1 or C2 migrates. Migration of the secondary carbon (C2) predominates over migration of the tertiary carbon (C1), thus reductive elimination from **5h** gives **2h**. With the six-membered rhodacycle **5′h**, reductive elimination forming a quaternary carbon failed to occur because of the steric reasons. Instead, this species undergoes *β*-hydride elimination prior to reductive elimination to afford **7**.

When monosubstituted spiropentane **1i** was subjected to the reaction conditions, an isomeric mixture of cyclopentenones **2i** (55%) and **2′i** (21%) was obtained (Scheme 3). Product **2i** resulting from migration of the primary carbon (C2) predominated over the product **2′i** resulting from migration of the secondary carbon (C1) (**2i**:**2′i** = 72:28). A control experiment was performed to obtain some mechanistic information. Spirocyclic cyclobutanone **8** isomerized in the presence of the rhodium catalyst to afford a mixture of **2i** and **2′i** (73:27), as previously reported.[8b] This result suggests the possibility of a mechanistic similarity between the reaction of **8** and the carbonylation of **1i**.

For comparison, cyclopropane **9**[16] and spiro[3.2]hexane **10** were subjected to similar reaction conditions. Unlike the case of spiropentanes **1**, no reaction occurred, and after 2.5 h, **9** and **10** remained intact. The contrasting results and the result of the reaction of **1e** indicate that the reactivity toward carbonylation under these conditions is peculiar to the highly strained structure of **1**.



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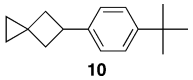

10

The utility of this transformation was demonstrated in a short synthesis of a sesquiterpene, (±)-*β*-cuparenone (**12**) (Scheme 4).[17] Spiropentane **1j**, required for the preparation of cyclopentenone **2j**, was synthesized from commercially available methyl 4-methylphenyl ketone **11** in three steps: Wittig olefination of **11** with cyclopropylidenephosphorane (82%), cyclopropanation of methylenecyclopropane **12** with dibromocarbene (54%), and debromination of **13** with zinc (56%). Carbonylation of **1j** under the standard conditions gave cyclopentenone **2j** (82%). Finally, the nickel-catalyzed conjugate addition of dimethylzinc[17b] furnished **14** in 75% yield.

In summary, we have developed a rhodium-catalyzed carbonylation reaction of spiropentanes involving two different types of carbon−carbon bond cleavage processes. The reaction allows for the synthesis of a series of 3-methylcyclopent-2-enones, one of which was utilized as an intermediate in the concise synthesis of (±)-*β*-cuparenone.

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

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(9) Abbreviations: cod = cycloocta-1,5-diene; DPPP = 1,3-bis(diphenylphosphino)propane.
(10) Results with other conditions: 10 mol % of $RhCl(PPh_3)_3$ (70%); 2.5 mol % of $[RhCl(cod)]_2$ and 5 mol % of DPPP (70%); 10 mol % of $[Rh(cod)_2]$-BF_4 and 10 mol % of DPPP (0%).
(11) The reaction under 10 atm of CO was less productive (29% of **2a** and 54% recovery of **1a**).
(12) Related complexes have been generated from cyclobutanones[8] and cyclopropanes. For the latter examples, see: (a) Roundhill, D. M.; Lawson, D. N.; Wilkinson, G. *J. Chem. Soc. A* **1968**, 845. (b) McQuillin, F. J.; Powell, K. C. *J. Chem. Soc., Dalton Trans.* **1972**, 2129.
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(14) The possibility of occurrence of *β*-carbon elimination from **3** prior to CO insertion cannot be ruled out.
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