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Ruthenium-catalyzed ring expansion reaction of allenylcyclobutanols

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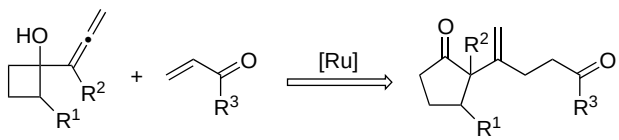
Abstract—A novel method for the synthesis of α-substituted cyclopentanones by the ruthenium-catalyzed rearrangement of allenylcyclobutanols with α,β-unsaturated carbonyl compounds has been developed.

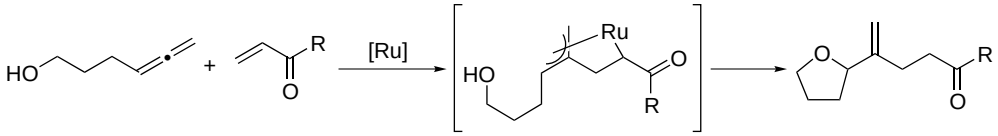
Palladium-promoted ring expansion reactions of alkenyl-,[1] alkynyl-[2] and allenylcyclobutanols[3] are well investigated reactions that are triggered by release in the strain of the four-membered ring systems. These useful methodologies for the construction of five-membered ring systems have been successfully applied to the syntheses of natural products.[4] However, in contrast with these palladium-promoted ring expansion reactions, there is no example of ring expansion reaction of cyclobutanols using other transition metals.

In recent years, Trost et al. reported the ruthenium-catalyzed alkylative cycloetherification reaction of hydroxyallene with enone (Scheme 1).[5] The reaction mechanism postulates the formation of a π-allylruthenium intermediate followed by nucleophilic attack of the internal hydroxyl group. We focused our attention on the formation of the π-allyl species, and applied the reaction to the ring expansion reaction.[6] We report here the first example of the ruthenium-catalyzed ring expansion reaction of cyclobutanols. The reaction enables the one-pot synthesis of α-substituted cyclopentanones from allenylcyclobutanols and α,β-unsaturated carbonyl compounds (Scheme 2).

The reactions of allenylcyclobutanol **1** with MVK (methyl vinyl ketone) were examined (Table 1).[7] Treatment of **1** and MVK with 10 mol% $[CpRu(MeCN)_3]PF_6$ **2**[5,8] and 15 mol% $CeCl_3 \cdot 7H_2O$[5] in CH_3CN at 60°C provided the cyclopentanone **3** and the hemiacetal **4** as a mixture (41% yield, **3**:**4** = 20:80 in entry 1). The reaction also proceeded uneventfully in various solvents (entries 2–5), the yield was increased to 53% when the reaction was carried out in DMF (entry 5). Furthermore, it was made clear that the reaction smoothly proceeded even in the absence of



Scheme 2.



Scheme 1.

Keywords: cyclopentanones; ruthenium and compounds; rearrangements; ring transformations.

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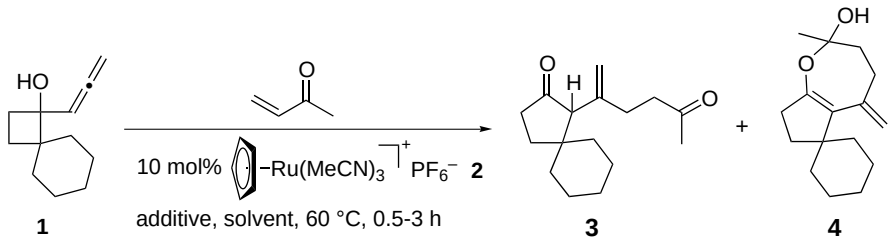
Table 1. Ruthenium-catalyzed ring expansion reactions of allenylcyclobutanol **1** with MVK



Entry	Solvent	Additive	Yield (%)	**3**:**4**[a]
1	CH_3CN	$CeCl_3{\cdot}7H_2O$	41	20:80
2	Toluene	$CeCl_3{\cdot}7H_2O$	38	20:80
3	CH_2Cl_2	$CeCl_3{\cdot}7H_2O$	24	50:50
4	DMA	$CeCl_3{\cdot}7H_2O$	20	65:35
5	DMF	$CeCl_3{\cdot}7H_2O$	53	35:65
6	DMF	None	71	**3** only

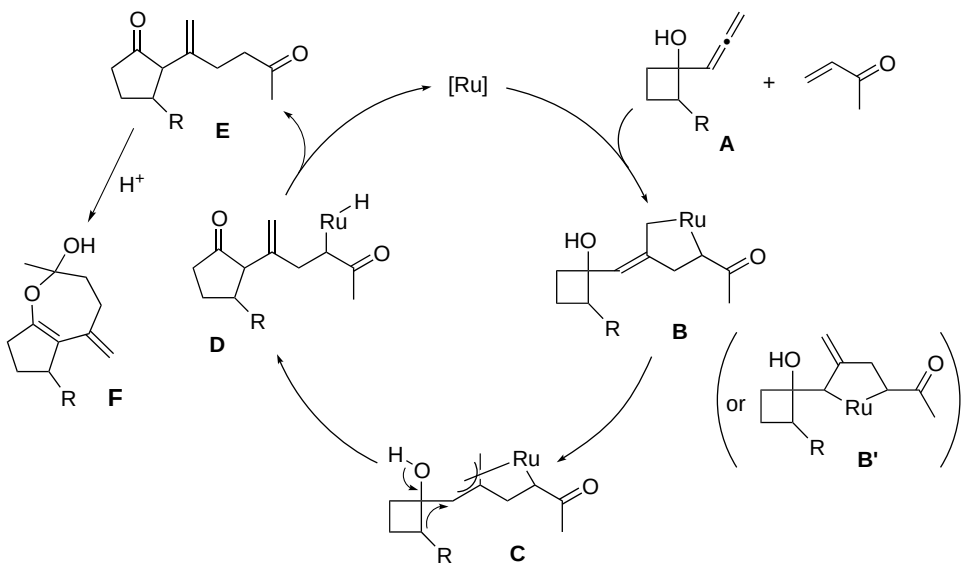
[a] The product ratios were determined by ^1H NMR integration of olefinic methylene signals.

$CeCl_3{\cdot}7H_2O$, and the hemiacetalization was completely suppressed under this condition (71% yield of **3** in entry 6).

A plausible mechanism for the reaction is shown in Scheme 3. The ruthenacycle **B** (or **B′**) would be formed from allenylcyclobutanol **A** and MVK by reaction with a ruthenium catalyst. Complex **B** (or **B′**) would be transformed to π-allylruthenium intermediate **C**, which would cause the ring expansion of the four-membered ring. Finally, ring-expanded product **E** would be produced by the reductive elimination of **D**, which further isomerizes to **F** under the acidic conditions.

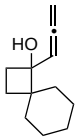
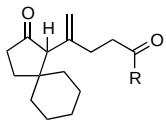
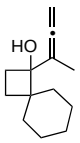
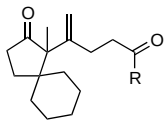
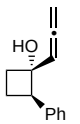
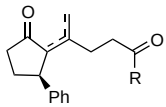
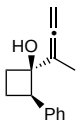
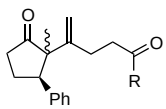
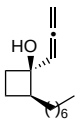
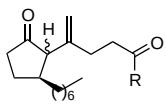
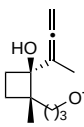
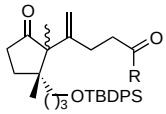
Next, the reactions of various allenylcyclobutanols with MVK and acrolein were examined (Table 2). When the allenylcyclobutanol **5**, which had a methyl group at the allenyl moiety was subjected to the reaction, the cyclopentanone **11** possessing a quaternary carbon center was produced in 84% yield (entry 3). The phenyl-substituted substrate **6** was transformed into the product **13** as a mixture of isomer and diastereomer (entry 5). The reactions of the other substrates **7**,[3b] **8** and **9**[3b] having two stereogenic centers in the molecule also afforded the corresponding products **15**, **17** and **19** in satisfactory yields as mixtures of two stereoisomers (entries 7, 9 and 11). On the other hand, when acrolein was used as an α,β-unsaturated carbonyl compound, all the reactions of **1** and **5**–**9** successfully proceeded to give the corresponding cyclopentanones **10**, **12**, **14**, **16**, **18** and **20** in 63–90% yields (entries 2, 4, 6, 8, 10 and 12).

In conclusion, we have developed a novel type of ring expansion reaction of allenylcyclobutanols catalyzed by ruthenium. Efforts to extend the scope of this reaction are currently under progress.



Scheme 3.

Table 2. Reactions of allenylcyclobutanols with MVK and acrolein[a]

entry	substrate	α,β-unsaturated compound	time (h)	product		yield (%)
1	 **1**	MVK	0.5		**3** R=Me	71
2		acrolein	0.5		**10** R=H	65
3	 **5**	MVK	0.5		**11** R=Me	84
4		acrolein	0.5		**12** R=H	90
5	 **6**	MVK	2		**13** R=Me	71
6		acrolein	2		**14** R=H	69
7	 **7**	MVK	2		**15** R=Me	83 (*dr*=1.3:1)[b]
8		acrolein	2		**16** R=H	81 (*dr*=2:1)[b]
9	 **8**	MVK	0.5		**17** R=Me	64 (*dr*=1.2:1)[b]
10		acrolein	0.5		**18** R=H	63 (*dr*=1.4:1)[b]
11	 **9**	MVK	1.5		**19** R=Me	68 (*dr*=1.2:1)[b]
12		acrolein	1.5		**20** R=H	68 (*dr*=1.1:1)[b]

[a]Reactions were carried out in the presence of 10 mol % $[CpRu(MeCN)_3]PF_6$ **2** and 1.5 equiv of MVK or acrolein in DMF at 60 °C. [b]The product ratios were determined by ^{1}H-NMR integration of olefinic methylene signals.

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5. Trost, B. M.; Pinkerton, A. B. *J. Am. Chem. Soc.* **1999**, *121*, 10842.
6. It is known that ring expansion reactions are caused by the formation of the π-allylpalladium species, see Refs. 1f, 2c, 3a and 3b.
7. General procedure for the ruthenium-catalyzed ring expansion reaction (entry 3 in Table 2). To a stirred solution of the allenylcyclobutanol **5** (61.8 mg, 0.321 mmol) and MVK (33.8 mg, 0.482 mmol) in DMF (1 ml) was added $[CpRu(MeCN)_3]PF_6$ **2** (14.0 mg, 0.0321 mmol)

at room temperature in a sealed tube. After stirring was continued for 0.5 h at 60°C, the reaction mixture was filtered through Celite, then washed with water and extracted with Et_2O. The combined organic layer was washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by chromatography on silica gel with hexane–AcOEt (85:15 v/v) as eluent to give the cyclopentanone **11** (70.4 mg, 84%) as a colorless oil. IR (neat) 1732, 1716, 1629 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (3H, s), 1.10–1.18 (1H, m), 1.21–1.27 (1H, m), 1.34–1.50 (5H, m), 1.55–1.72 (3H, m), 1.73–1.85 (1H, m), 1.98–2.07 (1H, m), 2.16 (3H, s), 2.21–2.32 (4H, m), 2.52–2.63 (1H, m), 2.68–2.77 (1H, m), 4.75 (1H, s), 4.96 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.3, 22.1, 22.3, 25.7, 25.8, 28.1, 29.8, 31.2, 32.6, 35.5, 43.4, 46.2, 62.6, 113.0, 148.5, 208.5, 223.0; MS m/z 262 (M^+); anal. calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.53; H, 10.00.

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