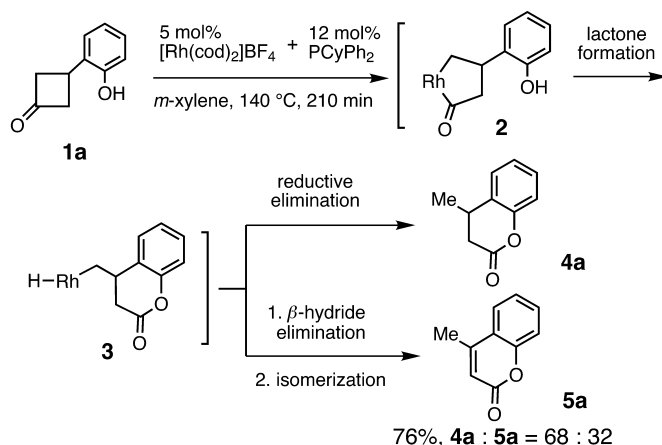


Lactone Formation by Rhodium-Catalyzed C–C Bond Cleavage of Cyclobutanone**

Masahiro Murakami,* Takuo Tsuruta, and Yoshihiko Ito*

Of the variety of synthetic transformations mediated by transition metals, catalytic processes involving cleavage of C–C single bonds are among the most difficult to achieve.^[1] Hence, their development remains an important challenge in organic chemistry. We recently found that the bond between the carbonyl carbon and the α -carbon atom of a cyclobutanone can be catalytically cleaved by a rhodium(I) complex.^[2] Phenolic hydroxy groups have also been reported to direct intramolecular functionalization of unreactive bonds such as C–H bonds.^[3] Thus we anticipated that C–C bond cleavage would be facilitated by appropriate placement of a phenol group in the substrate molecule. Here we report new lactone-forming reactions by the rhodium-catalyzed C–C bond cleavage of a cyclobutanone having a pendant phenol group.

Cyclobutanone **1a**, which has an *o*-substituted phenol group at the 3-position,^[4] was heated to 140 °C in *m*-xylene in the presence of a rhodium complex prepared in situ from [Rh(cod)₂]₂BF₄ (5 mol %, cod = 1,5-cyclooctadiene) and cyclohexyldiphenylphosphane (PCyPh₂, 12 mol %)^[5] under an argon atmosphere. The substrate **1a** was consumed after 210 min. Chromatographic purification afforded a mixture of saturated and unsaturated six-membered-ring lactones (**4a** and **5a**, 68:32) in 76% combined yield (Scheme 1).^[6] The reaction occurred at 140 °C even under an atmosphere of carbon monoxide to give an analogous result.^[7]



Scheme 1. Reaction of **1a** to give six-membered-ring lactones and the postulated mechanism for this reaction.

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The following mechanism explains the formation of the six-membered-ring lactones from **1a**. Rhodium initially undergoes insertion between the carbonyl carbon and the α -carbon atom to afford the five-membered (acyl)rhodium intermediate **2**. The phenolic hydroxy group then reacts with the acyl group on rhodium to form the six-membered-ring lactone **3**.^[8] Direct reductive elimination produces the saturated lactone **4a**. The other product, unsaturated lactone **5a**, is formed from **3** through β -hydride elimination and subsequent isomerization to an α,β -unsaturated system.

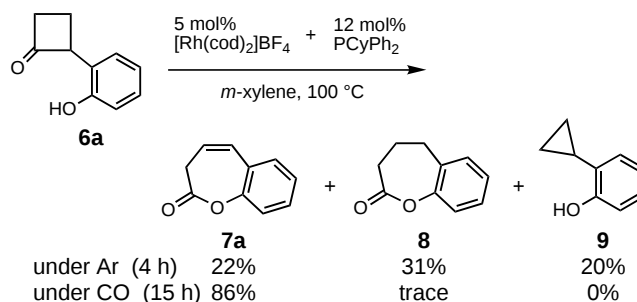
Other examples of the rhodium-catalyzed six-membered ring lactone formation are listed in Table 1. Both substrates having methyl (entry 1; Table 1) and chloro (entry 2; Table 1)

Table 1. Rhodium-catalyzed six-membered-ring lactone formation.

Entry	1	Time [h]	4:5	Yield of 4+5 [%]
1		9	81:19	68
2		4	85:15	82
3		24	100:0	57

groups as the phenol substituent afforded the corresponding six-membered-ring lactones as a mixture of saturated **4** and unsaturated **5** in good combined yield. In the case of **1d**, which is equipped with an additional methyl group at the 3-position, β -hydride elimination is inaccessible in the intermediate corresponding to **3**, and hence the saturated lactone was the sole product (entry 3; Table 1).

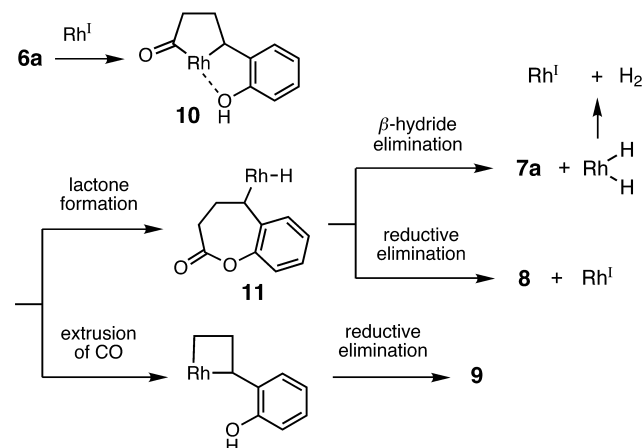
A cyclobutanone possessing an *o*-substituted phenol group at the 2-position (**6a**)^[9] was also examined. The reaction of **6a** proceeded under milder conditions (100 °C), and more interestingly, a mixture of the seven-membered-ring lactones **7a** and **8** was obtained together with the cyclopropane **9** (Scheme 2). When an analogous reaction was carried out under



Scheme 2. Rhodium-catalyzed reaction of **6a** under Ar and CO atmospheres.

an atmosphere of carbon monoxide instead of an argon atmosphere, the unsaturated lactone **7a** was selectively obtained in 86 % yield,^[10] and only a trace of **8** was formed. The decarbonylation to **9** was completely suppressed under these conditions. In addition, nearly quantitative evolution of dihydrogen from the reaction mixture was detected by GC analysis.

A mechanistic scheme postulated to explain these results is shown in Scheme 3. Initially, the phenolic hydroxy group of **6a** coordinates to the rhodium atom, bringing it into proximity to



Scheme 3. The postulated mechanism for the formation of **7a**, **8**, and **9** from **6a**.

the α -C-C bond of the carbonyl group. Insertion of the rhodium atom into this bond is thus facilitated and affords the five-membered (acyl)rhodium intermediate **10**, which can react in two ways. Extrusion of the carbonyl group from the rhodacycle followed by reductive elimination affords cyclopropane **9**. It seems reasonable that this process is disfavored in a CO atmosphere. Alternatively, the hydroxy group of **10** can react intramolecularly with the (acyl)rhodium group to form the seven-membered-ring lactone **11**. Direct reductive elimination forms the saturated lactone **8**, while β -hydride elimination yields **7a**. The resulting rhodium(III) dihydride complex evolves dihydrogen by reductive elimination to regenerate the rhodium(I) catalyst. It is plausible to assume that the β -hydride elimination from **11** is intrinsically reversible and that carbon monoxide acts as a ligand for rhodium expelling the produced **7a** from the coordination sphere, and promoting this process forward irreversibly. Thus, the reaction under a CO atmosphere gives **7a** selectively.

The different rates of reactions of the substrates **1a** and **6a** are noteworthy. The reaction of **1a** at 100 °C was much slower (6 % conversion under Ar after 4 h, no conversion under CO) than that of **6a**. Although the rate-determining step of the lactonization reaction has not been elucidated, it is assumed that, in the case of **6a**, the transition state of the rate-determining step is stabilized more efficiently by the phenolic hydroxy group located closer to the inserting metal, and therefore, the reaction proceeds faster.

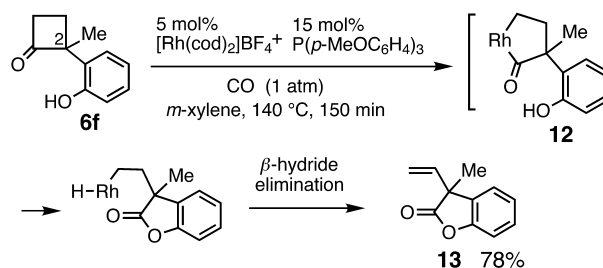
Other examples of the rhodium-catalyzed seven-membered-ring lactone formation are shown in Table 2. The use of tris(*p*-methoxyphenyl)phosphane as the ligand afforded

Table 2. Rhodium-catalyzed seven-membered-ring lactone formation.

Entry	6	Phosphane	Time [h]	7	Yield [%]
1		P(<i>p</i> -MeOC ₆ H ₄) ₃	6		91
2		P(<i>p</i> -MeOC ₆ H ₄) ₃	24		87
3		PCyPh ₂	24		92
4		PCyPh ₂	12		77

better results than PCyPh₂ in some cases. When the pendant phenol group has an additional electron-donating substituent such as methyl and methoxy, the corresponding seven-membered-ring lactone was obtained in high yield (entries 1–3; Table 2). Substrate **6e** with a *p*-chlorophenol group afforded **7e** in slightly lower yield (77 %, entry 4; Table 2).

For comparison, an analogous reaction was carried out using cyclobutanone **6f** which had a methyl substituent in addition to a phenol group at the 2-position. Unlike the case of **6a**, no reaction occurred at 100 °C. The reaction at an elevated temperature (140 °C) afforded the five-membered-ring lactone **13** (Scheme 4). None of the seven-membered-ring lactone was observed. The additional steric constraints



Scheme 4. Reaction of **6f** to give five-membered-ring lactone **13** and the postulated mechanism for this reaction.

introduced by the extra methyl substituent at the 2-position hampered the cleavage of the proximal α -C-C bond. Instead the initial rhodium insertion was transposed to the less substituted C-C bond on the far side, affording rhodacycle **12**. Subsequently, a five-membered-ring lactone linkage is formed. The following β -hydride elimination produces the lactone **13**. It is likely that the assistance of the phenolic hydroxy group of **6f** coordinating to the inserting rhodium center is reduced for geometrical reasons, as with the case of **1a**. Thus, an elevated temperature was required for the insertion.

In summary, new catalytic C-C bond cleaving reactions were developed in which a phenol group serves as a coordinating ligand to facilitate the catalytic activation of a

C–C single bond. Whereas the substrates presently employed benefit from relief of the structural strain,^[11] the construction of seven-membered ring lactone skeletons fused to aromatic rings is of synthetic value because of the presence of these subunits in biologically active compounds.

Experimental Section

7b: To a mixture of [Rh(cod)₂]BF₄ (6.0 mg, 15 μmol) and tris(*p*-methoxyphenyl)phosphane (9.6 mg, 36 μmol) in *m*-xylene (5 mL) under N₂ at room temperature were successively added 2-(2-hydroxy-5-methylphenyl)cyclobutanone (**6b**, 52.9 mg, 0.30 mmol) and *m*-xylene (5 mL). After the N₂ atmosphere was replaced with CO, the mixture was heated at 100 °C for 6 h. The reaction mixture was cooled and then passed through a pad of Florisil to remove the insoluble materials. The eluent was evaporated under vacuum, and the residue was subjected to preparative TLC (silica gel, ethyl acetate/hexane 1/5) to afford **7b** (47.3 mg, 91 %) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz): δ = 2.36 (s, 3H), 3.05 (d, *J* = 6.6 Hz, 2H), 6.03 (dt, *J* = 9.9, 6.6 Hz, 1H), 6.83 (d, *J* = 9.9 Hz, 1H), 7.09–7.20 (m, 3H); ¹³C{¹H} NMR (CDCl₃, 75 MHz): δ = 20.6, 34.2, 120.9, 122.8, 126.7, 129.9, 130.1, 134.5, 148.3, 169.0; IR (neat): $\tilde{\nu}$ = 1752 cm⁻¹; elemental analysis calcd for C₁₁H₁₀O₂: C 75.84, H 5.79; found: C 75.97, H 5.77.

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Ligand Electronic Effect in Enantioselective Palladium-Catalyzed Copolymerization of Carbon Monoxide and Propene**

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The alternating copolymerization of olefins with carbon monoxide (CO) catalyzed by cationic palladium(II) complexes modified by diphosphane ligands has attracted considerable interest due to the potential use of the produced polyketones as new materials.^[1–7] Recently, a terpolymer derived from ethene, propene, and CO has become commercially available under the trade name of Carilon.

When propene is used as the substrate, control of regio- and stereoselectivity of the olefin insertion is required to obtain stereoregular alternating copolymers.^[8, 9] Recently, a few examples of successful, highly enantioselective CO/propene copolymerizations have been reported, using either in situ or preformed Pd^{II} complexes containing chiral phosphorus ligands.^[10–12] Among the catalysts studied the most active ever reported to date (productivity of about 905 gg(Pd)⁻¹h⁻¹) contained (*R*)(*S*_p)-1-[2-(diphenylphosphanyl)ferrocenyl]-ethyldicyclohexylphosphane (Josiphos) as the modifying ligand.^[13, 14] With this system both a very high regioselectivity (>99 % head-to-tail enchainments) and stereoregularity (>96 % of isotactic diads) were achieved. Thus, despite contrasting proposals,^[15] and a precedent example of a system with low catalytic activity,^[16] the best combination of donor groups in the chelate diphosphane ligand seems to be that of two electronically nonequivalent ligand fragments: a basic PCy₂ group to ensure high regioselective incorporation of propene and a slightly acidic PPh₂ donor.

Since planar-chiral ferrocenyl ligands represent a system that is synthetically easy to modify, and 1) in view of investigating possible electronic effects on both the copolymer structure and the performance of the catalyst, and 2) to gain insight on the role of electronic differentiation of the two binding sites in these ligands,^[17, 18] we prepared a series of related chiral diphosphanes **1a–g** (Scheme 1) according to already published general methods.^[19–22] Here we report extremely active Pd^{II} systems bearing chiral ferrocenyl diphosphanes **1b–d** for highly enantioselective alternating copolymerization of propene and carbon monoxide.

Thus, in typical experiments, in situ Pd^{II} systems prepared by reacting Pd(OAc)₂ with ligands **1a–g** and BF₃·Et₂O in CH₂Cl₂–MeOH were investigated (Scheme 2). In fact, ³¹P

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- [4] The cyclobutanone **1a** was prepared by [2+2] cycloaddition of *o*-(methoxymethoxy)styrene with dichloroketene and the subsequent treatment with zinc in acetic acid.
- [5] A cationic rhodium(I) complex having two PCyPh₂ ligands per rhodium atom is postulated as the catalytic species. No reaction occurred in the absence of the rhodium catalyst.
- [6] The ratio of **4a** to **5a** changed little (68:32 – 75:25), when other catalyst systems like [Rh(cod)₂]BF₄/PPh₃, [Rh(cod)₂]BF₄/P(*p*-methoxyphenyl)₃, and [Rh(cod)(Ph₂PCH₂CH₂CH₂PPh₂)]BF₄ were used.
- [7] The reactions previously reported^[2] normally failed to occur under a CO atmosphere.
- [8] a) M. Hidai, K. Ishimi, M. Iwase, E. Tanaka, Y. Uchida, *Tetrahedron Lett.* **1973**, 1189; b) R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, *Tetrahedron* **1981**, 37, 4313.
- [9] The cyclobutanone **6a** was prepared according to the literature procedure: B. M. Trost, M. J. Bogdanowicz, *J. Am. Chem. Soc.* **1973**, 95, 5321.
- [10] The formation of the corresponding α,β-unsaturated isomer was not observed.
- [11] With less strained substrates like 2-(2-hydroxyphenyl)cyclopentanone, an analogous reaction failed to occur.

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