Highlight Review

Ruthenium-catalyzed Reconstructive Synthesis of Functional Organic Molecules via Cleavage of Carbon–Carbon Bonds

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Abstract

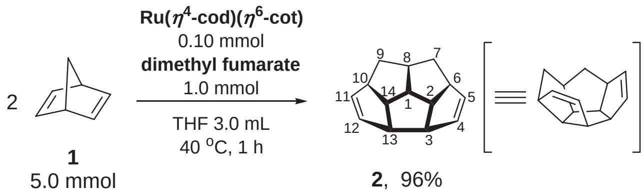
Characteristic aspects of ruthenium-catalyzed reconstructive synthesis of functional organic molecules via carbon–carbon bond cleavage are discussed. Most of the compounds obtained in this study are hard to be prepared by the simple combination of traditional synthetic methods. These ruthenium-catalyzed reactions require highly qualified tuning of reaction conditions with substrates to attain high yields and selectivities of the products.

♦ Introduction

Cleavage of cartbon–carbon bonds by transition metal complexes under homogeneous conditions has recently received much scientific and technological interest, and has opened the door to a new field of synthetic organic chemistry.[1] Since this topic has been well reviewed until up to 1999 with the focus mainly on stoichiometric reactions, we shall consider the *catalytic* carbon–carbon bond cleaving reactions in this review. Except for the alkene and alkyne metatheses,[2] most of the catalytic carbon–carbon bond cleaving reactions so far reported have been classified into the reactions due to ring strain,[3] chelation assistance,[4] incipient aromatic stabilization,[4f,5] skeletal rearrangement,[6,7] β-carbon elimination (vide infra), or combinations of these phenomena.[8–10] Synthesis of novel functional organic molecules that cannot be obtained by the simple combination of traditional synthetic methods is a challenging subject of many recent studies in atom-economical organic, organometallic, and industrial chemistry.[11] Although ruthenium chemistry has lagged somewhat behind that of palladium, a large number of novel, useful, and unique reactions have been developed with ruthenium catalysts.[12] Recently, much attention has been paid to ruthenium-catalyzed characteristic carbon–carbon bond cleaving reactions as well as carbon–carbon bond forming reactions.[2f,13] In this Highlight Review, discussion will be focused on the recent progress of ruthenium-catalyzed reconstructive synthesis of novel functional organic molecules via carbon–carbon bond cleavage, developed mainly by the present authors.

♦ Ruthenium-catalyzed Novel Dimerization of 2,5-Norbornadiene to PCTD

In the course of our study on the codimerization of 2,5-norbornadiene with alkenes, unusual homodimerization of 2,5-norbornadiene involving carbon–carbon bond cleavage was disclosed.[14] The selectivity of the products depended on the kind of catalyst and solvent. 2,5-Norbornadiene (**1**) selectively dimerized to pentacyclo[6.6.0.0.^{2,6}0.^{3,13}0^{10,14}]tetradeca-4,11-diene (PCTD, **2**) in the presence of a catalytic amount of Ru(η^4-cod)(η^6-cot) [cod = 1,5-cyclooctadiene, cot = 1,3,5-cyclooctatriene] and dimethyl fumarate in THF at 40 °C in 96% yield (Scheme 1).[13c,14] Formation of the known *endo–endo* dimer, heptacyclo[6.6.0.0.^{2,6}0.^{3,13}0.^{4,11}0.^{5,9}0^{10,14}]tetradecane (HCTD)[15] was suppressed. PCTD is a novel half-open cage hydrocarbon, possessing five five-membered rings and two olefinic groups on both sides, which may be a candidate as a new industrial raw material.



Scheme 1.

PCTD reacted with AgOTf to give [AgOTf (PCTD)]$_n$ **3**. An X-ray analysis showed that **3** is a two-dimensional polymer (Figure 1).

Furthermore, PCTD was converted into a series of novel half-open cage compounds. For example, bromination of PCTD with an excess amount of bromine gave a sole tetrabromide **4** which was formed to avoid the steric hindrance between two bromine atoms (Scheme 2).[14a]

Catalytic oxidation of PCTD gave **5**, tetraol **6**, and diepoxides **7**, depending on the catalyst systems (Scheme 3).[16]

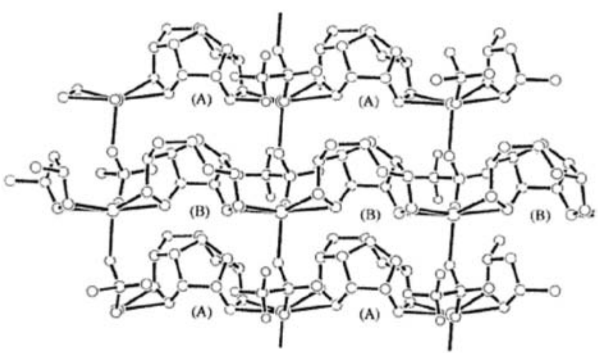


Figure 1. ORTEP drawing of polymeric **3**.

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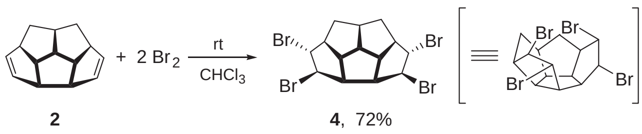
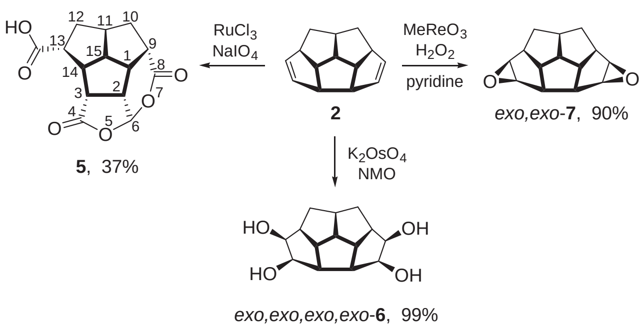


Scheme 2.



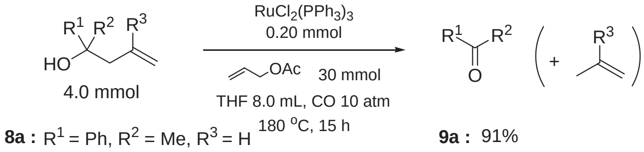
Scheme 3.

As for the mechanism, PCTD and HCTD were not interconverted into each other under the present catalytic reaction conditions. In addition, the dimerization of 7-*tert*-butoxy-2,5-norbornadiene gave the corresponding 4,9-di-*tert*-butoxy-substituted PCTD. These results suggest that the formation mechanism of PCTD would involve the cleavage of two carbon–carbon bonds via oxidative addition of a carbon–carbon bond and β-alkyl elimination reactions.[14] However, further mechanistic investigation is apparently needed.

♦ *Ruthenium-catalyzed Deallylation of Homoallyl Alcohols*

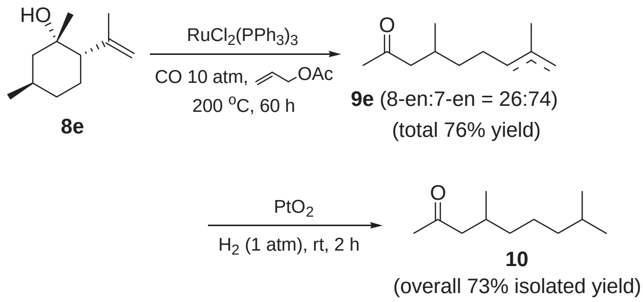
In the course of our studies on π-allylruthenium chemistry,[17] a catalytic deallylation reaction of tertiary homoallyl alcohols was found. General tertiary homoallyl alcohols bearing either an aryl or alkyl substituent (**8a**–**8d**) were smoothly deallylated by the present catalyst system to give the corresponding ketones (**9a**–**9d**) in high isolated yields (Scheme 4).[18] Gas analysis showed the generation of propene (54% yield) in the reaction of **8a**, and isobutene (42% yield) in the reaction of **8d**. The presence of both carbon monoxide and allyl acetate was crucial. Carbon monoxide operates as an effective π-acid. While the role of allyl acetate is not yet clear, it would be required for the generation and stabilization of a catalytically active ruthenium species.

This reaction was applicable to a cyclic homoallyl alcohol (**8e**) to provide a novel tool for the ring-opening reaction (Scheme 5).



8a : R^1 = Ph, R^2 = Me, R^3 = H — **9a :** 91%
8b : R^1 = R^2 = Ph, R^3 =H — **9b :** 87%
8c : R^1 = R^2 = Bu, R^3=H — **9c :** 71%
8d : R^1 = Ph, R^2 = Me, R^3= Me — **9d :** 85%

Scheme 4.



Scheme 5.

The reaction is rationalized to proceed via a (homoallylalkoxy)(hydrido)ruthenium complex. β-Carbon (or β-allyl) elimination would liberate a ketone and generate a (π-allyl)(hydrido)ruthenium complex, followed by the reductive elimination to give an alkene. The driving force of this reaction is the formation of a stable (π-allyl)ruthenium complex. This reaction is the first example of the transition metal-catalyzed deallylation reaction.[19]

This type of allylic stabilization is also utilized in the palladium-catalyzed carbon–carbon bond cleavage of 6-vinyl cyclic carbonate to give ω-diene aldehyde.[20] In addition, a unique palladium-catalyzed multiple arylation of 2-hydroxy-2-methylpropiophenone with aryl bromides via successive carbon–carbon and carbon–hydrogen bond cleavages has been reported.[21] β-Alkyl elimination of a strained molecule was represented by Pd-catalyzed oxidative transformations and arylation of *tert*-cyclobutanols.[22] Catalytic deallylation of allyl- and diallylmalonates has recently been reported.[23]

♦ *Ruthenium-catalyzed Synthesis of Cyclopentenones by Unusual Coupling of Cyclobutenediones with Alkenes*

Cyclobutenediones have been recognized as versatile reagents for the construction of various multicyclic compounds.[24] The conversion of cyclobutenediones to quinones[25] and 5-alkylidene-2-cyclopentene-1,4-diones[26] using a stoichiometric amount of transition metal complexes via (maleoyl)metal complexes has been studied in detail. However, neither transition metal complex-catalyzed transformation of cyclobutenediones nor the synthetic reaction via metallacyclopentenedione and/or metallacyclobutenone complexes instead of (maleoyl)metal complexes has been reported. During our study on the catalytic synthesis of cyclopentenones,[27] we found a novel ruthenium-catalyzed reconstructive synthesis of cyclopentenones by an unusual coupling reaction of cyclobutenediones with alkenes involving carbon–carbon bond cleavage.[28]

The results obtained from the reactions of several 3-alkoxycyclobutenediones (**11a**–**11d**) with 2-norbornene (**12a**) under optimum conditions are listed in Table 1. In all cases, the starting cyclobutenediones were completely consumed, and the products detected by GLC were only the corresponding cyclopentenones, **13a**–**13d**.

The carbon monoxide pressure had a dramatic effect. The best result was obtained under 3 atm of carbon monoxide, and either an increase or decrease in the carbon monoxide pressure caused a rapid decrease in the yield of **13a**. Use of ^{13}CO gave the ^{13}C-labeled cyclopentenone (70% scrambling), which sug-

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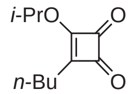
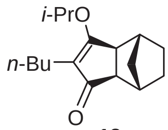
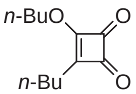
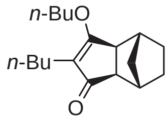
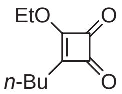
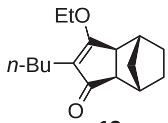
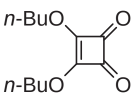
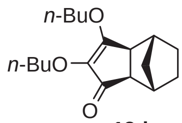
Table 1. $Ru_3(CO)_{12}/PEt_3$-catalyzed synthesis of cyclopentenones (**13**) from cyclobutenediones (**11**) and 2-norbornene (**12a**)[a]

Run	Cyclobutenedione	Product	Isolated Yield/%
1	 **11a**	 **13a**	75
2	 **11b**	 **13b**	60
3	 **11c**	 **13c**	47
4[b]	 **11d**	 **13d**	46

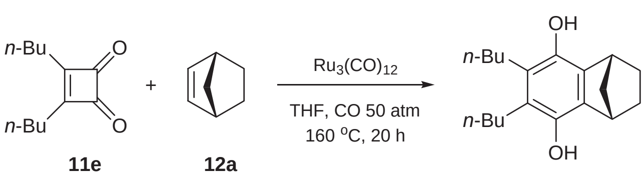
[a]Cyclobutenedione (**11**) (1.0 mmol), 2-norbornene (**12a**) (3.0 mmol), $Ru_3(CO)_{12}$ (0.050 mmol), PEt_3 (0.15 mmol), and THF (1.0 mL) under CO (3 atm) at 160 °C for 20 h. [b]CO 15 atm.

gests that the external carbon monoxide is needed to suppress complete decarbonylation of cyclobutenediones to the corresponding alkynes and carbon monoxide, and to stabilize a ruthenacyclobutenone intermediate (vide infra).

The present reaction highly depends upon the substituents of the cyclobutenediones. For example, 3,4-dialkylcyclobutenedione, such as 3,4-dibutylcyclobut-3-ene-1,2-dione (**11e**), gave the corresponding hydroquinone **14a** instead of the cyclopentenone, probably via a (maleoyl)ruthenium intermediate (Scheme 6).[29]

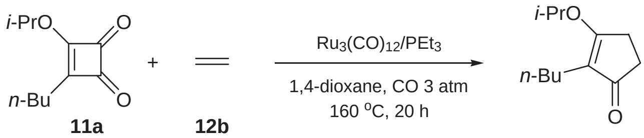
Besides 2-norbornene, the reaction of ethylene (**12b**) with **11a** in 1,4-dioxane also gave the corresponding cyclopentenone **13e** in 65% yield (Scheme 7).

The present reaction is rationalized to proceed via regioselective cleavage of a carbon–carbon bond. First, oxidative addition of cyclobutenedione **11** to an active ruthenium center would occur at the C2–C3 bond selectively under the direction of an alkoxy substituent to give a ruthenacyclopentenedione intermedi-



11e **12a** **14a**, 74%

Scheme 6.



11a **12b** 10 atm **13e**, 65%

Scheme 7.

ate.[30] Appropriate carbon monoxide pressure (3 atm) is needed to control selective *mono*-decarbonylation of a ruthenacyclopentenedione to a ruthenacyclobutenone intermediate, as well as to suppress complete decarbonylation to an (alkoxy)alkyne and CO. Subsequent stereoselective *cis*-carboruthenation of 2-norbornene (**12a**) and reductive elimination with retention of stereochemistry gives the corresponding cyclopentenones **13a**–**13d** exclusively in an *exo* form.[31]

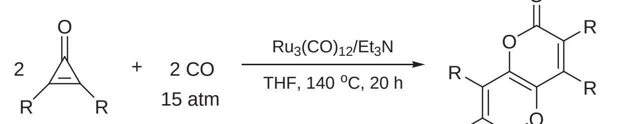
♦ *Ruthenium-catalyzed Synthesis of Pyranopyrandiones by Reconstructive Carbonylation of Cyclopropenones*

As described above, it has been demonstrated that the explicit cleavage of carbon–carbon bonds of cyclobutenediones leads to the reconstruction of new carbon skeletons, which proceeds via a ruthenacyclobutenone intermediate.[28] Since a similar ruthenacyclobutenone may be formed more directly and efficiently, attention was focused on the reactivity of cyclopropenones.[32] Several stoichiometric reactions of cyclopropenones involving carbon–carbon bond cleavage have been reported,[33] however, few transition metal complex-catalyzed reactions using cyclopropenones directed toward organic synthesis have been reported.[34] Ruthenium-catalyzed unprecedented carbonylative dimerization of cyclopropenones involving carbon–carbon bond cleavage, which gave a novel organic functional monomer, pyranopyrandione, in high yield, is disclosed here.[35]

Treatment of cyclopropenone (**15**) with 3.3 mol % of $Ru_3(CO)_{12}$ and 10 mol % of NEt_3 in THF under 15 atm of carbon monoxide at 140 °C for 20 h gave a novel carbonylative dimerization product, tetrasubstituted pyranopyrandione (**16**), in high isolated yield with high selectivity (Scheme 8).

Furthermore, ruthenium-catalyzed *cross*-carbonylation of cyclopropenones (**15a**–**15d**) with internal alkynes (**17a**–**17c**) was found to be effective for the synthesis of unsymmetrically substituted pyranopyrandiones (**16e**–**16h**) in good to high yields (Scheme 9).

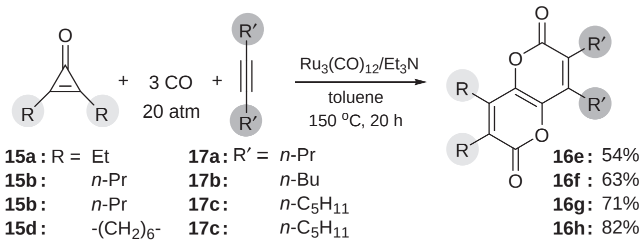
Use of ^{13}CO in the reaction of **15a** with **17a** clearly showed that three equivalents of the external carbon monoxide are incorporated into the product **16e**.



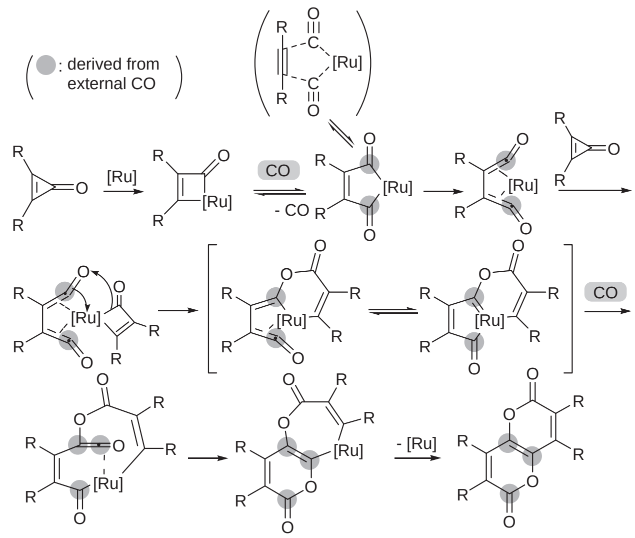
15a : R = Et
15b : n-Pr
15c : n-Bu
15d : -(CH$_2$)$_6$-

16a : 70%
16b : 81%
16c : 86%
16d : 87%

Scheme 8.



Scheme 9.



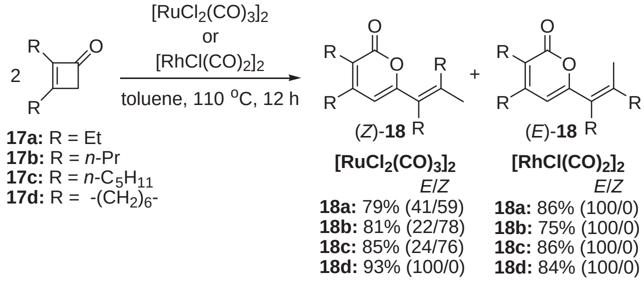
Scheme 10.

A plausible mechanism is shown in Scheme 10. The initial step in the present reaction consists of oxidative addition of the carbon–carbon bond between a carbonyl and the α-carbon in cyclopropenone **15** to an active ruthenium center to give a ruthenacyclobutenone intermediate (Scheme 10).

Further carbonylation of ruthenacyclobutenone (or carbonylative cyclization of alkynes on the ruthenium) gives a maleoylruthenium intermediate. Subsequent isomerization of a maleoylruthenium intermediate produces an active (η^4-bisketene)ruthenium intermediate,[36a] which reacts with another molecule of cyclopropenone by oxidative addition and insertion reactions to give a (ketene)ruthenium intermediate. Rapid tautomerization would give a ruthenium carbene intermediate, and insertion of carbon monoxide into a carbene–ruthenium bond would give a new ketene intermediate.[36b,36c] Finally, insertion of a carbonyl group of a ketene moiety into an acyl–ruthenium bond and reductive elimination give the desired pyranopyrandione.

♦ *Ruthenium- and Rhodium-catalyzed Carbon–Carbon Bond Cleavage of Cyclobutenones*

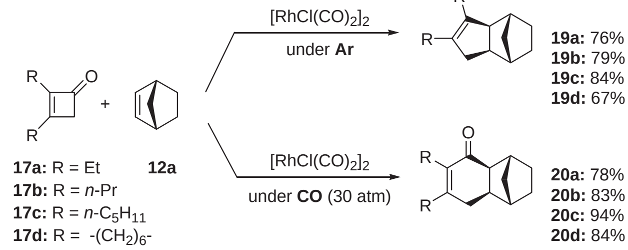
Particular attention has been focused on the thermal ring-expanded reactions of 4-alkynyl- and/or 4-alkenyl-substituted cyclobutenones.[37] However, 4-nonsubstituted cyclobutenones are relatively stable, and only the pioneering work by Liebeskind and co-workers on the transition metal complex-catalyzed



Scheme 11.

synthesis of phenols from 4-nonsubstituted cyclobutenones and alkynes has been reported.[8a,38,39] This methodology is quite attractive, since transition metal vinylketene complexes have been postulated to be important intermediates in reactions leading to a variety of organic ring products, such as phenols, naphthols, cyclohexadienones, cyclopentenones, lactams, furans, α-pyrones, and 2-furanones.[40] As for a catalytic conversion of cyclobutenones, a novel stereoselective synthesis of 2-pyranones **18** via ring-opening dimerization of cyclobutenones **17** catalyzed by ruthenium ($[RuCl_2(CO)_3]_2$) and rhodium ($[RhCl(CO)_2]_2$) complexes (Scheme 11) was developed.[41]

In addition, $[RhCl(CO)_2]_2$ showed high catalytic activity in the decarbonylative and/or direct coupling of cyclobutenones with alkenes via carbon–carbon bond cleavage (Scheme 12).[41]



Scheme 12.

These results indicate that the present reactions likely involve both η^4-vinylketene and metallacyclopentenone intermediates.

♦ *Summary and Outlook*

In spite of the inertness of the carbon–carbon bonds in organic molecules, there have been growing interests in catalytic cleavage of carbon–carbon bonds which realizes rapid and reconstructive synthesis of new functional organic molecules. In this review, some of the strategies for achieving ruthenium-catalyzed carbon–carbon bond cleaving reactions were disclosed. Each of these reactions involves direct oxidative addition of carbon–carbon bonds, β-carbon elimination and/or formation of ruthenacycles, π-allylruthenium complexes, and ruthenium carbene or ketene complexes, respectively, as key steps of the selective carbon–carbon bond cleavage. These ruthenium-catalyzed reactions require highly qualified tuning of reaction conditions with substrates to attain high yields and selectivities of the products. We hope these new findings will offer new methods for synthetic organic chemistry.

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