Influence of Halide Ion and Lewis Acid in the Demetalation of a Spirolactam Cyclohexadienyl Ruthenium Complex

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Demetalation of an electron-rich spirolactam-based (cyclohexadienyl)Ru(II) complex is achieved upon treatment with boron trifluoride and a source of chloride ion. The cyclohexadienyl ligand is converted to a cyclohexadienone, cyclohexenone, or cyclohexenone epoxide derivative as a function of the specific reaction conditions. Stable (cyclohexadienyl)ruthenium substrates potentially suitable for demetalation under these conditions are prepared via intramolecular spirocyclization of (η^6-arene)Ru precursors; thus, demetalation completes a net Ru-mediated dearomatization sequence. Moreover, the functionalized spirolactam products obtained are structurally distinct from those produced via direct oxidative demetalation.

Introduction

Arene metal complexes are valuable synthetic intermediates in organic and organometallic chemistry. Arene ligands coordinated to a metal center in an η^6 fashion often acquire electrophilic character and so participate in normally unfavorable reactions such as nucleophilic aromatic addition and substitution.[1] The process of nucleophilic aromatic addition usually entails reaction of the nucleophile with the arene ligand from the face opposite the metal center. Initial adducts produced in this process are metal coordinated cyclohexadienyl complexes. Further manipulation of the cyclohexadienyl ligand at the expense of re-aromatization provides a means for conversion of aromatic precursors into functionalized alicyclic materials in a stereocontrolled manner.[2]

(η^6-Arene)Cr(CO)$_3$ complexes have been used extensively in the context of metal-mediated dearomatization. Cyclohexadienyl adducts obtained via nucleophilic addition to arene chromium complexes are anionic and generally quite labile, readily undergoing additional reactions with electrophiles (H$^+$, alkyl and acyl halides).[1,2] Recently, analogous arene molybdenum complexes have been shown to exhibit similar reactivity.[3] Cationic (η^6-arene)Mn(CO)$_3$ complexes possess an even more activated arene ligand relative to their Cr(0) and Mo(0) counterparts. Consequently, neutral cyclohexadienyl adducts obtained from aromatic addition reactions still retain electrophilic character and can be further functionalized by treatment with additional nucleophilic reagents to produce metal-free 1,3-dienes.[4] Alternatively, replacement of one CO ligand with NO$^+$ affords cationic Mn(I) cyclohexadienyl complexes that are even more susceptible to nucleophilic addition.[5]

Cationic (η^6-arene)Fe(II) and (η^6-arene)Ru(II) complexes each possess electrophilic arene ligands that readily participate in nucleophilic addition reactions as well.[1,6] In many instances, stable cyclohexadienyl derivatives may be isolated.[7] In general, however, it has proven difficult to convert these species into metal-free alicyclic products, and extensive investigations of potential Fe- and Ru-mediated dearomatization processes have not been reported. Arene iron and ruthenium complexes (especially (arene)Ru(cyclopentadienyl) complexes) are easily prepared, and these materials represent attractive building blocks in preparative organic and organometallic chemistry.[6a,8] Thus, establishing methods suitable for liberating cyclohexadienyl ligands

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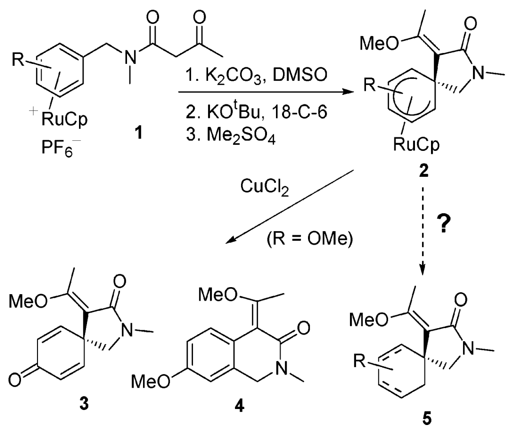
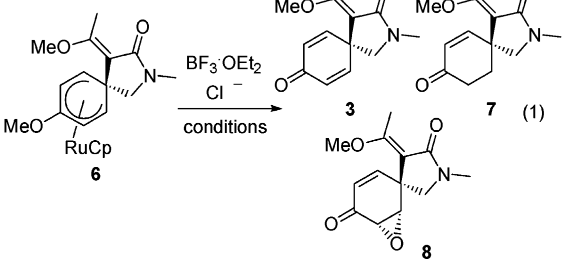
Scheme 1



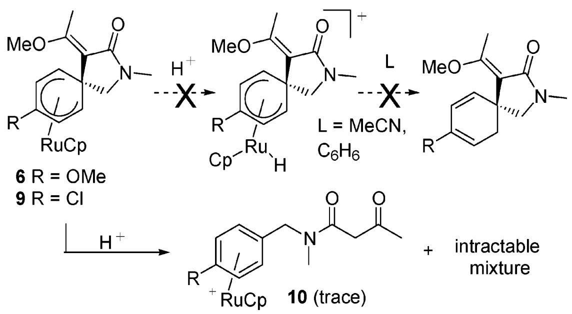
from Ru(II) (or Fe(II)) metal fragments without rearomatization would significantly expand the utility of these organometallic compounds in organic synthesis.

We have recently developed a general route to cyclohexadienyl ruthenium complexes of the type **2** that involves intramolecular nucleophilic aromatic addition of an (η^6-arene)RuCp complex followed by enolate O-alkylation.[9] This procedure affords stable (cyclohexadienyl)RuCp complexes in which the cyclohexadienyl ligand is incorporated into a larger 2-azaspiro[4.5]-decane ring system (Scheme 1). We subsequently found that certain derivatives of **2** (specifically those possessing electron-releasing substituents on the cyclohexadienyl ligand) could be demetalated by treatment with oxidizing agents (e.g., $CuCl_2$) to give products such as **3** and/or **4** according to the substrate employed.[10] Significantly, **3** and its congeners represent the culmination of a net Ru-mediated dearomatization sequence. We therefore were interested in further exploring the chemistry of cyclohexadienyl complexes **2** with the aim of uncovering truly general nonoxidative demetalation procedures that would deliver metal-free spirolactams of the type **5**. While this overall goal remains elusive, we have found that methoxy-substituted complex **6** can be converted to metal-free cyclohexadienone **3**, cyclohexenone **7**, or epoxide **8** in synthetically useful yields under similar reaction conditions (eq 1). We report herein the details of the transformations shown in eq 1, which all occur most efficiently in the presence of $BF_3\cdot OEt_2$ and a source of chloride ion.



(1)

Scheme 2



Results and Discussion

There are relatively few reports describing the demetalation of cyclohexadienyl ligands from Ru(II) metal fragments. Maitlis and co-workers have examined the reactivity of (η^5-cyclohexadienyl)(η^6-arene)Ru(II) cations in the course of developing methods for the partial reduction of benzene to cyclohexene,[11] while DiMauro and Wolczanski have described the acid-mediated transformation of a bis(η^5-cyclohexadienyl)Ru(II) complex to a metal-free diene.[12] By comparison, the reactivity of various open (η^5-pentadienyl)Ru(II) complexes has been extensively investigated by Ernst[13] and others.[14] In general, pentadienyl ligands can be converted to agostic Ru hydrides upon treatment with strong Brønsted acids (e.g., HBF_4). Exposure of the agostic complexes to monodentate ligands (e.g., phosphines, phosphites, CO) then results in complete proton transfer to afford Ru-coordinated dienes.[13a,d,14] In many instances the dienes can be removed from the metal via simple ligand exchange reactions. In initial attempts to demetalate spirocyclic cyclohexadienyl complexes of the type **2**, we sought to apply the literature precedents described above. Unfortunately, treatment of both **6** and **9** with either HBF_4 or TFA in benzene, CH_2Cl_2, or CH_3CN returned intractable mixtures, sometimes accompanied by small amounts of the corresponding η^6-arene complex **10** (Scheme 2). Presumably the arene complex is generated via enol ether hydrolysis and spirocycle ring opening triggered by the presence of adventitious water.

Operating under the assumption that unwanted acid lability of complexes such as **6** would be greatly reduced if the enol ether functional group could be modified, we attempted to reduce the olefin using catalytic hydroge-

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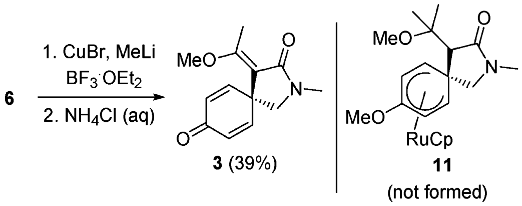
nation (1 atm H_2, Pd/C or PtO_2) and electron transfer (Mg^0, SmI_2) methods. In each case, unreacted starting material was recovered. Alteration of the enol ether via conjugate addition was also attempted using reaction conditions reported by Yamamoto to be effective for sterically crowded and/or unreactive enones.[15] As shown in eq 2, the reaction did not lead to the conjugate addition product **11** but instead produced the demetalated dienone **3** in moderate isolated yield. The structure of **3** was assigned on the basis of spectroscopic comparison with an authentic sample prepared by direct oxidative demetalation of **6** with $CuCl_2$.[10] Interestingly, systematic modification of the reaction conditions shown in eq 2 revealed that the combination of $BF_3{\cdot}OEt_2$ and NH_4Cl was responsible for the observed transformation and that neither CuBr nor MeLi was necessary for successful decomplexation.



(2)

Intrigued by this outcome, a more thorough investigation of the reaction was initiated using cyclohexadienyl complex **6** as the test substrate. Simply stirring a mixture of **6** (50 mg, 0.12 mmol) in THF with an excess of saturated aqueous NH_4Cl (5.6 M, 0.25 mL, ~10-fold excess) under argon at room temperature overnight returned unreacted starting material (88% recovery). Likewise, unreacted starting material was also recovered when cold (−78 °C) THF solutions of **6** were treated with $BF_3{\cdot}OEt_2$ (2 equiv), allowed to warm to room temperature, and quenched with deionized water, NH_4OH, or NH_4OAc. However, when **6** (in deoxygenated THF) was treated with $BF_3{\cdot}OEt_2$ at −78 °C, then allowed to warm to room temperature over 15 min before being opened to the air and quenched with an excess of saturated aqueous NH_4Cl, dienone **3** was obtained in 34% isolated yield (eq 3). Thus, it was concluded that the Lewis acid in conjunction with a source of chloride anion act in concert to effect the observed demetalation. It is also noteworthy that upon addition (via syringe) of aqueous NH_4Cl under argon, the reaction mixture remained homogeneous and turned a deep green color. Exposure to air then resulted in discharge of the green color and precipitation of a reddish-brown solid. Quenching the reaction with aqueous NaCl in place of NH_4Cl produced similar color changes and afforded the dienone product **3** in 57% isolated yield. Likewise, addition of saturated aqueous KBr also resulted in formation of **3**, but addition of aqueous KI led to a complex reaction mixture and generation of what appeared to be I_2. Tetrahydrofuran proved to be the solvent of choice for this transformation, although reactions performed in CH_2Cl_2 were also successful. Benzene, $CHCl_3$, and CH_3CN were not effective solvents. Reactions run in diethyl ether were sluggish, perhaps due to the insolubility of **6** in this medium.

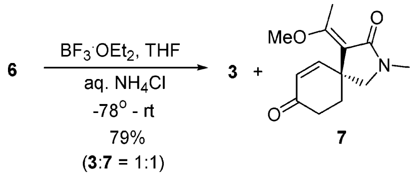
$$\mathbf{6} \xrightarrow[\substack{\text{-78}^\circ\text{ - rt;} \\ \text{then aq. NH}_4\text{Cl} \\ \text{(or aq. NaCl)}}]{\text{BF}_3{\cdot}\text{OEt}_2\text{, THF}} \underset{\substack{34\% \\ (57\%)}}{\mathbf{3}} \qquad (3)$$

Table 1. Effect of Chloride Source on Dienone (3)/Monoenone (7) Ratio (see Eq 4)[a]

entry	chloride source	equiv	ratio 3:7	% yield
1	aq NH_4Cl (5.6 M)	1	1:1	79
2	aq NH_4Cl (5.6 M)	20	1:4	55
3	solid NH_4Cl	1	2:1	47
4	aq NaCl (2.4 M)	1	2:5	59
5	aq NaCl (2.4 M)	20	2:5	34
6	solid NaCl	1	10:1	29

[a] Reactions were performed by combining **6**, $BF_3{\cdot}OEt_2$ (2 equiv) and the indicated chloride source at −78 °C in deoxygenated THF.

Experiments designed to shed some mechanistic insight into the demetalation process revealed that the product composition could be affected by the timing of not only chloride but also proton addition. For example, when **6**, $BF_3{\cdot}OEt_2$, and 1 equiv of aqueous NH_4Cl were all combined in THF at −78 °C and allowed to warm to room temperature before being exposed to air, dienone **3** was obtained along with mono-enone derivative **7** in a 1:1 ratio (eq 4). The two products were easily separated by radial chromatography, and the structure of **7** was assigned on the basis of spectroscopic data. A single-crystal X-ray structure was also obtained (see Supporting Information). As shown in Table 1, the **3**:**7** ratio seems to correlate with the amount of proton/chloride source present in the reaction mixture. While 1 equiv of aqueous NH_4Cl affords a 1:1 product ratio, addition of 20 equiv yields a 4:1 ratio in favor of the mono-enone **7**. In contrast, limiting the protons available by eliminating water from the reaction mixture and employing solid NH_4Cl as an additive gave a product mixture enriched in dienone **3** (Table 1, entry 3). A somewhat similar trend was also observed when NaCl was used in place of NH_4Cl. In this case, the product ratio did not change between 1 equiv and 20 equiv of aqueous NaCl; however, addition of solid NaCl afforded **3** as the major product accompanied by only a trace of mono-enone **7**, albeit in slightly diminished combined yield. A deuterium labeling experiment was performed in order to probe the stereoselectivity of hydrogen incorporation in **7**. Hydrogen addition from the face of the cyclohexadienyl ligand originally occupied by the Ru(II) fragment may be indicative of Ru−H intermediates. Unfortunately, while the use of ND_4Cl in D_2O as a reaction additive did indeed afford **7**-d_2 (as determined from ^1H, ^2H, and 2D NMR experiments), overlapping resonances in the ^1H NMR spectrum precluded stereochemical assignment of the remaining hydrogen substituents. It should also be noted that, in keeping with previous observations, the reaction mixtures turned green upon warming to room temperature under Ar.



(4)

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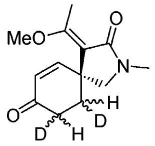
Scheme 3

$$\mathbf{6} \xrightarrow[\text{-78° - rt}]{\text{1. BF}_3\text{·OEt}_2\text{, THF}} \mathbf{3} + \mathbf{7}$$

2. HCl

1 N aq. HCl	1 : 1	(75%)
1.1 equiv anhyd. HCl	0 : 57%	
2.2 equiv anhyd. HCl	0 : 68%	

Opening the reaction vessels to air once again produced a brown precipitate.



7-d$_2$

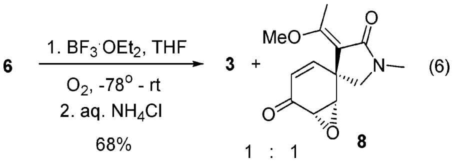
On the basis of the results described above, we speculated that a stronger proton donor in combination with a chloride ion source may provide additional amounts of **7** at the expense of dienone **3**. As indicated in Scheme 3, this does, in fact, seem to be the case. In these reactions, HCl was introduced to a mixture consisting of **6** and $BF_3·OEt_2$ that had warmed to room temperature from −78 °C to produce a deep green solution, which could be maintained until exposure to air. Addition of excess aqueous HCl afforded a mixture of **3** and **7**. Significantly, however, addition of anhydrous HCl (1.0 M in ether) gave mono-enone **7** as the exclusive product in synthetically useful yields. A larger excess of anhydrous HCl (>2.2 equiv) did not result in a further increase in yield. Thus, it does appear that **7** is produced via a protonation event, either of the cyclohexadienyl ligand directly or through formation of a ruthenium hydride intermediate (as has been observed in reactions involving open pentadienyl complexes, vide supra).[7c,13a,b,e,14] Somewhat surprisingly, inclusion of anhydrous HCl from the start of the reaction resulted in a mixture of **7** and dienone **3** in a 3:1 ratio, respectively. In an effort to detect a Ru−H species, the reaction (in THF-d_8) was monitored by variable-temperature ^1H NMR. At no time, however, was a signal attributable to a ruthenium hydride (0 to −10 ppm) detected in the temperature range 198−298 K. Finally, treatment of **6** with anhydrous HCl alone (1.1 equiv, THF, rt, 1 h) was also found to effect demetalation, but the reaction was not as efficient when compared to transformations performed in the presence of $BF_3·OEt_2$. Monoenone **7** was produced in 24% isolated yield, accompanied by dienone **3** (11%) and unreacted **6** (8%). Thus, the inclusion of $BF_3·OEt_2$ seems to be important for clean decomplexation.

On the basis of the experiments described above, it appears that key features of this demetalation procedure include the availability of chloride ion, the presence of a Lewis acid ($BF_3·OEt_2$), and, for generation of **7**, the availability of a proton source. Furthermore, the observation of green intermediates in all the reactions discussed thus far may indicate generation of common reactive species. The appearance of an insoluble brown precipitate upon exposure to air (O_2) also seems significant, as this certainly accounts for the fate of the CpRu fragment. Presumably, exposure to O_2 liberates the spirolactam moiety with concomitant formation of some type of oligomeric Ru complex. Attempts to characterize the brown precipitate were thwarted by its extreme insolubility in most solvents (CH_2Cl_2, acetone, H_2O, acetonitrile). The material proved to be sparingly soluble in DMSO, and X-ray quality crystals were obtained upon slow evaporation over several months. The crystal structure, however, revealed a $Ru(II)Cl_2$ fragment coordinated to four DMSO molecules (three via the S atom and the fourth through the O atom; see Supporting Information).[16] The fate of the Cp ligand remains obscure. In contrast, tractable Ru complexes could be recovered from demetalation reactions upon exposure to CO (1 atm, 30 min) in place of O_2 (eq 5). In this instance, the known dicarbonyl adduct **12** was isolated in an amount identical to the quantity of metal-free spirolactam.[17] Similarly, treatment of green reaction mixtures obtained after addition of HCl with $P(OEt)_3$ afforded $CpRuCl[P(OEt)_3]_2$ as a byproduct[18] along with **7**, although the efficiency of the demetalation was significantly reduced.

$$\mathbf{6} \xrightarrow[\text{-78° - rt}]{\text{1. BF}_3\text{·OEt}_2\text{, THF}} \underset{35\%}{\mathbf{7}} + \underset{\underset{35\%}{\mathbf{12}}}{\text{CpRu(CO)}_2\text{Cl}} \qquad (5)$$

2. anhyd. HCl
3. CO

The apparent role O_2 plays in completing the demetalation process prompted us to examine the effect of performing reactions in the presence of O_2. A solution of **6** and $BF_3·OEt_2$ in THF was cooled to −78 °C and placed under an O_2 atmosphere (1 atm). Upon warming to room temperature, the reaction mixture became a homogeneous brown solution. After quenching with aqueous NH_4Cl two products were isolated: dienone **3** and epoxide **8** (1:1 ratio, eq 6) in 68% combined yield.



The structure of **8** was initially assigned on the basis of 1D and 2D NMR spectroscopy and subsequently confirmed by X-ray crystallography (see Supporting Information). Consideration of the stereochemistry present in **8** is strongly indicative of a Ru-mediated epoxidation. A number of Ru-oxo complexes have been prepared and characterized,[19] including some that are capable of oxygenating other ligands within the Ru coordination sphere.[20] Thus, epoxidation may occur via an intramolecular process. Indirect evidence in support of this notion was obtained by performing the reaction depicted in eq 6 in the presence of excess (4 equiv) 2-cyclohex-

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(19) (a) Gemel, C.; Mereiter, K.; Schmid, R.; Kirchner, K. *Organometallics* **1997**, *16*, 5601. (b) Lindner, E.; Haustein, M.; Fawzi, R.; Steimann, M.; Wegner, P. *Organometallics* **1994**, *13*, 5021. (c) Fan, L.; Turner, M. L.; Hursthouse, M. B.; Malik, K. M. A.; Gusev, O. V.; Maitlis, P. M. *J. Am. Chem. Soc.* **1994**, *116*, 385. (d) Rao, K. M.; Day, C. L.; Jacobson, R. A.; Angelici, R. J. *Organometallics* **1992**, *11*, 2303.

enone. In the event, only **3** and **8** were isolated and cyclohexenone remained unchanged. This result would seem to indicate that a discrete Ru-based oxidizing agent capable of epoxidizing exogenous substrates (i.e., cyclohexenone) is not formed. Reactions performed under argon in the presence of excess 30% aqueous H_2O_2 were also found to produce mixtures of **3** and **8**, with **3** predominating (**3**:**8** = ~3–4:1). Interestingly, if **6**, $BF_3 \cdot OEt_2$ and an excess of aqueous NH_4Cl were combined in cold (−78 °C) THF and then allowed to warm to room temperature under an O_2 atmosphere, only **3** was obtained, in 76% isolated yield. Hence, the presence of chloride ion appears to promote direct oxidative demetalation at the expense of epoxidation.

From the available evidence, it is reasonable to conclude that chloride ions serve as ligands for the Ru fragment during the course of demetalation. Oxygen fulfills a similar role, either at the end of the decomplexation reaction or early in the sequence, thus giving rise to cyclohexadienyl ligand oxidation. Proton donors (NH_4Cl, H_2O, HCl) also react with the cyclohexadienyl ligand under certain conditions to afford the mono-enone product. What role, then, does $BF_3 \cdot OEt_2$ play in this process? Its presence in the reaction is not an absolute requirement for successful demetalation, as treatment of **6** with anhydrous HCl also produced **7**, although the reaction was neither clean nor high yielding. Other Lewis acids proved to be inferior to $BF_3 \cdot OEt_2$ in promoting demetalation of **6** (NH_4Cl quench): $SnCl_2 \cdot 2H_2O$ was the best alternative, yielding a 3:1 mixture of **7**:**3** in 43% combined yield. Aluminum chloride and $ZnBr_2$ afforded only small amounts of **3**, $TiCl_4$ gave an intractable mixture, and $Ti(O^iPr)_4$ elicited no reaction. As it is difficult to imagine any direct interaction between BF_3 and the ruthenium center, we speculate that the Lewis acid serves to coordinate basic sites on the cyclohexadienyl ligand, thereby indirectly increasing the reactivity of the ruthenium fragment toward $Cl^-/H^+/O_2$ reagents. In an effort to shed light on this issue, a variable-temperature ^1H NMR study was performed, the results of which are shown in Figure 1. The bottom trace shows the spectrum of **6** at 200 K. Addition of 2 equiv of $BF_3 \cdot OEt_2$ at this temperature resulted in a splitting of most resonances. Raising the temperature to 260 K, then to 300 K, caused some peaks to coalesce, while others broadened into the baseline. Specifically, signals corresponding to hydrogens adjacent to heteroatoms in the lactam ring (D, E, and F) were absent. Similar results were obtained when the identical experiment was repeated with 1 equiv of $BF_3 \cdot OEt_2$, except that peaks E and F only partially collapsed into the baseline. Thus, it appears that BF_3 enters into a temperature-dependent dynamic relationship with the spirolactam ligand, presumably via formation of Lewis acid/base adducts with the available heteroatoms.

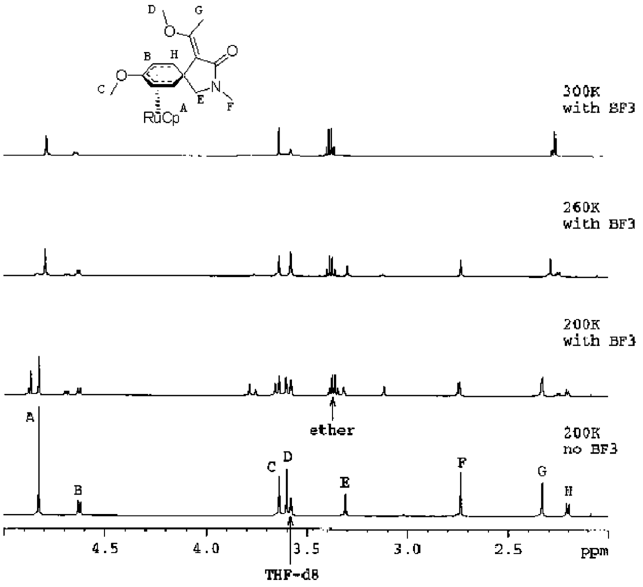

Figure 1. Effect of $BF_3 \cdot OEt_2$ on the variable-temperature ^1H NMR spectra of **6**.

Table 2. Summary of Demetalation Conditions Used to Convert 6 to 3, 7, and/or 8[a]

entry	additive	amount	product(s)	ratio	yield
1	aq NH_4Cl[b]	excess	**3**	na	34%
2	aq NaCl[b]	excess	**3**	na	57%
3	aq NH_4Cl[c]	1 equiv	**3**, **7**	1:1	79%
4	aq NH_4Cl[c]	20 equiv	**3**, **7**	1:4	55%
5	solid NH_4Cl[c]	1 equiv	**3**, **7**	2:1	47%
6	aq NaCl[c]	1 equiv	**3**, **7**	2:5	59%
7	aq NaCl[c]	20 equiv	**3**, **7**	2:5	34%
8	solid NaCl[c]	1 equiv	**3**, **7**	10:1	29%
9	aq HCl[b]	excess	**3**, **7**	1:1	75%
10	anhyd HCl[b]	1.1 equiv	**7**	na	57%
11	anhyd HCl[b]	2.2 equiv	**7**	na	68%
12	anhyd HCl[c]	2.2 equiv	**3**, **7**	1:3	52%
13	anhyd HCl[d]	1.1 equiv	**6**, **3**, **7**	1:1.4:3	43%
14	anhyd HCl, CO[b]	2.2 equiv, 1 atm	**7**[e]	na	35%
15	aq NH_4Cl[b,f]	excess	**3**, **8**	1:1	68%
16	aq NH_4Cl[c,f]	excess	**3**	na	76%
17	30% H_2O_2[c], aq NH_4Cl[b]	excess	**3**, **8**	3.4:1	58%

[a] All reactions were performed by combining **6** (50 mg) in deoxygenated THF (5 mL) with 2.0 equiv of $BF_3 \cdot OEt_2$ at −78 °C under Ar. Reactions were then allowed to gradually warm to room temperature. [b] Added after reaction had warmed to room temperature. [c] Additive combined with **6** and $BF_3 \cdot OEt_2$ at −78 °C. [d] Reaction performed at room temperature in the absence of $BF_3 \cdot OEt_2$. [e] $CpRu(CO)_2Cl$ was also obtained in 35% yield. [f] Reaction performed under O_2 (1 atm).

The products obtained and the various reaction conditions employed for the demetalation of **6** are summarized in Table 2. Consideration of these data coupled with the results from the variable-temperature NMR study illustrated in Figure 1 has led to development of a tentative mechanistic rationale to account for the formation of **3**, **7**, and **8** from cyclohexadienyl complex **6** (Scheme 4). Introduction of $BF_3 \cdot OEt_2$ converts **6** to the Lewis acid/base adduct **13**. Reaction with chloride ion then produces an intermediate formulated as the Ru(IV) complex **14**. An intra-complex redox reaction can then give rise to the Ru(II) complex **15**, from which metal-free dienone **3** is obtained upon exposure to air (O_2). Alternatively, **14** can suffer ligand protonation in the presence of a suitable donor to generate the Ru(II) diene complex **16**. Oxygen- or CO-induced decomplexation of the diene and concomitant enol ether hydrolysis then affords mono-enone **7**. Finally, reaction of **13** with O_2 produces some type of intermediate, depicted as the

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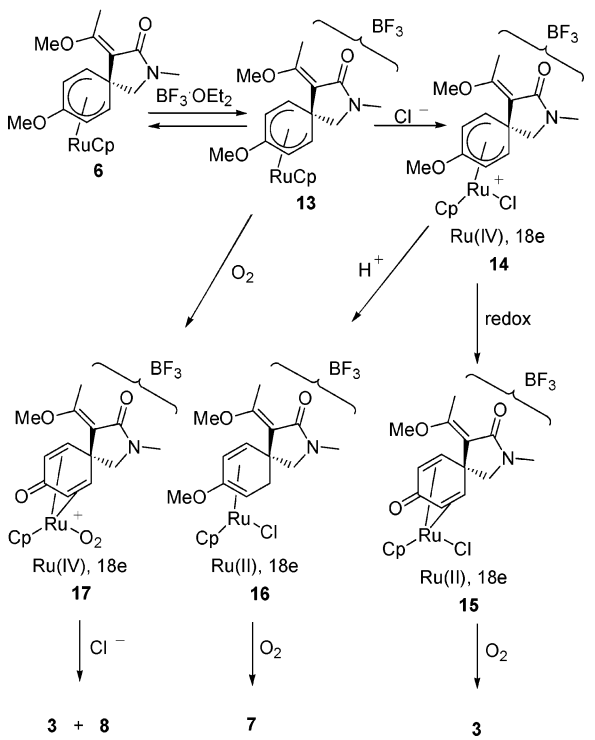
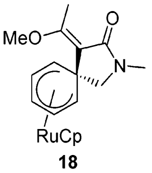
(20) (a) Clemente, M. E. N.; Saavedra, P. J.; Vásquez, M. C.; Paz-Sandoval, M. A.; Arif, A. M.; Ernst, R. D. *Organometallics* **2002**, *21*, 592. (b) Martelletti, A.; Gramlich, V.; Zürcher, F.; Mezzetti, A. *New J. Chem.* **1999**, 199. (c) Jia, G.; Ng, W. S.; Chu, H. S.; Wong, W.-T.; Yu, N.-T.; Williams, I. D. *Organometallics* **1999**, *18*, 3597. (d) de los Rios, I.; Tenorio, M. J.; Padilla, J.; Puerta, M. C.; Valerga, P. *Organometallics* **1996**, *15*, 4565.

Scheme 4

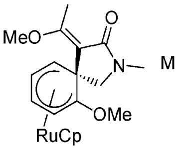


Ru(IV) dioxygen complex **17**. In the presence of chloride ion, **17** is converted to a mixture of **3** and epoxide **8**. Why chloride ion is necessary for this final transformation is unclear, but simply stirring a THF solution of **6** and BF_3 open to the air followed by addition of deionized water returned unreacted starting material.

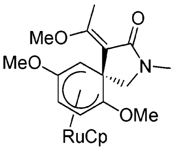
While complex **6** could be successfully demetalated under various reaction conditions, the procedures could not be extended to other spirocyclic cyclohexadienyl substrates. For example, attempted demetalation of the unsubstituted complex **18** using BF_3/anhydrous HCl reaction conditions resulted in extensive decomposition. Likewise, reactions with other methoxy-substituted cyclohexadienyl complexes (e.g., **19** and **20**) also failed to afford isolable products. As shown in eq 7, however, **21** was converted to a mixture of mono-enone **22** and the related borinate ester **23** in 38% combined yield.



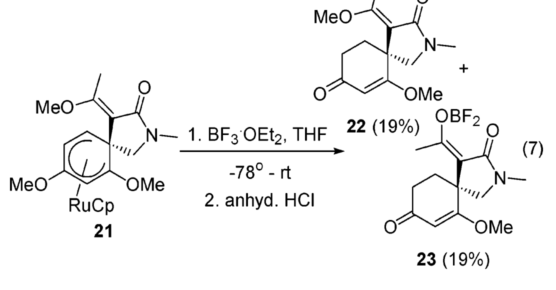
18



19



20



(7)

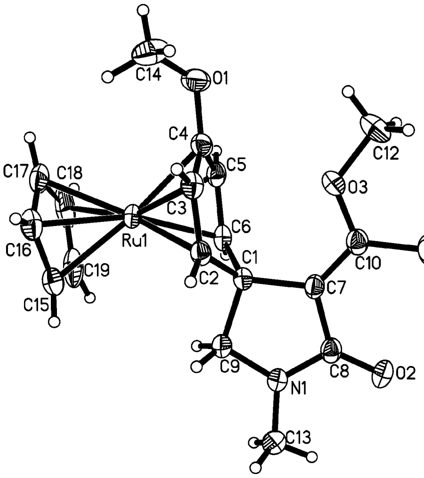


Figure 2. Molecular structure of **6**. Selected bond distances (Å): Ru–C(2) = 2.195, Ru–C(3) = 2.179, Ru–C(4) = 2.190, Ru–C(5) = 2.168, Ru–C(6) = 2.178.

Perhaps the presence of an electron-donating methoxy group directly opposite the spirocyclic linkage (a feature common to **6** and **21**) is important for promoting contolled decomplexation under these reaction conditions. Complex **6** was characterized by X-ray diffractometry in the hope that a structural basis for the observed reactivity might be uncovered. The molecular structure and selected bond lengths are shown in Figure 2.[21] In general, however, the structure exhibits no exceptionally unusual features. The average Ru–C distance to the spirolactam ligand is 2.182 Å, compared to a distance of 2.208 Å to the Cp ligand, indicative of stronger bonding to the cyclohexadienyl moiety. Despite individual variations in the solid-state Ru–C distances to the symmetrical cyclohexadienyl ligand, the average Ru–C bond lengths adopt a pattern similar to that observed in open pentadienyl complexes.[13a,c,d,14e] The average C2,C6–Ru distance is 2.187 Å, whereas the average C3,C5–Ru distance is slightly shorter (2.174 Å). The C4–Ru distance is the longest at 2.190 Å. All the C–C bond distances within the cyclohexadienyl ligand (C2–C6) are virtually identical, falling in the range 1.415–1.418 Å.

In conclusion, this study has demonstrated that a readily prepared cyclohexadienyl Ru(II) complex can be converted to metal-free cyclohexadienone, cyclohexenone, and cyclohexenone epoxide derivatives in synthetically useful yields. The Lewis acid/halide ion mediated decomplexation procedures described above are complementary to our previously disclosed oxidative demetalation protocols and offer access to structurally intriguing and stereochemically rich spirolactam heterocycles. These results also help define the reactivity of this family of cyclohexadienyl ruthenium complex and may ultimately contribute to the development of truly general demetalation procedures of broader scope and applicability. Finally, this work highlights the important and potentially general role halide ions might play in liberating cyclohexadienyl (or other π-coordinated) ligands from organotransition metal fragments.[22]

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[21] Crystal data: fw = 414.45, monoclinic, $P2_1/c$, a = 12.8409(2) Å, b = 12.3144(2) Å, c = 11.4854(2) Å, β = 112.3670(10)°, V = 1679.52(5) Å^3, Z = 4, D_{calc} = 1.639 Mg/m^3, μ = 0.950 mm^{-1}, T(K) = 170, reflections = 22 871, unique reflections = 4046, parameters = 309, R_1 [$I > 2\sigma(I)$] = 0.0272, wR_2 = 0.0676.

[22] Fagnou, K.; Lautens, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 26.

Experimental Section[23]

Cyclohexadienone 3. A solution of **6** (50 mg, 0.12 mmol) in THF (5.0 mL) was deoxygenated by bubbling with a stream of argon for ~15 min. The solution was cooled to −78 °C, and $BF_3 \cdot OEt_2$ (previously deoxygenated with argon, 31 μL, 0.24 mmol) was added via syringe. The reaction was allowed to warm to room temperature over 15−20 min. No visible changes to the reaction mixture were observed. A solution of aqueous NaCl (2.4 M, 0.5 mL) was added via syringe to produce a dark green reaction mixture. After 5 min the reaction was opened to the air, resulting in discharge of the green color and precipitation of a reddish-brown solid. The THF was evaporated and the residue partitioned between CH_2Cl_2 and brine. The layers were separated, and the organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. Purification by radial chromatography (SiO_2, EtOAc) gave **3** (16 mg, 57%) as a white solid whose spectral properties matched those previously reported.[10]

Cyclohexenone 7. A deoxygenated aliquot of $BF_3 \cdot OEt_2$ (37 μL, 0.29 mmol) was added via syringe to a deoxygenated solution of **6** (60 mg, 0.14 mmol) in 5.0 mL of THF cooled to −78 °C under argon. The reaction was allowed to warm to room temperature, and anhydrous HCl (1.0 M in ether, 0.30 mL, 0.30 mmol) was added by syringe, resulting in formation of a green homogeneous solution. After 5 min the reaction flask was opened to the air, causing deposition of a reddish-brown precipitate. The reaction was worked up as described above. Purification by radial chromatography (SiO_2, EtOAc) afforded **7** (23 mg, 68%) as a colorless solid. Mp: 140−141 °C, R_f = 0.40 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90−1.95 (m, 1H), 2.43−2.55 (m, 3H), 2.50 (s, 3H), 2.89 (s, 3H), 3.12 (d, J = 10.0 Hz, 1H), 3.40 (d, J = 10.0 Hz, 1H), 3.63 (s, 3H), 5.93 (d, J = 10.1 Hz, 1H), 6.78 (dd, J = 10.1, 1.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.3, 30.0, 31.9, 34.6, 40.9, 54.2, 113.8, 127.2, 156.5, 162.1, 169.2, 199.3. IR (KBr, cm^{-1}): ν 1664, 1638. HRMS (EI): calcd for $C_{13}H_{17}NO_3$ 235.1208 [M]$^+$, found 235.1207. Anal. Calcd for $C_{13}H_{17}NO_3$: C 66.36, H 7.28, N 5.95. Found: C 66.17, H 7.37, N 5.79.

Cyclohexenone Epoxide 8. A solution of **6** (52 mg, 0.13 mmol) in THF (6.0 mL) was cooled to −78 °C and placed under an atmosphere of O_2 (balloon). Boron trifluoride etherate (32 μL, 0.25 mmol) was added by syringe, and the reaction was allowed to warm to room temperature over 1 h. Aqueous NH_4Cl (2.4 M, 57 μL, 1.1 equiv) was then added and the reaction maintained for an additional 30 min. The reaction was worked up as described above and the crude product mixture purified by radial chromatography (SiO_2, EtOAc) to yield **3** (10 mg, 34%) and **8** (11 mg, 34%). Colorless solid: mp 148−149 °C, R_f = 0.46 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.50 (s, 3H), 2.93 (s, 3H), 3.28 (d, J = 10.6 Hz, 1H), 3.50 (dd, J = 4.0, 1.9 Hz, 1H), 3.56 (s, 3H), 3.61 (dd, J = 4.0, 2.8 Hz, 1H), 3.69 (d, J = 10.6 Hz, 1H), 5.88 (dd, J = 10.3, 1.9 Hz, 1H), 6.22 (dd, J = 10.3, 2.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.5, 30.1, 42.6, 54.3, 54.9, 55.8, 60.1, 106.9, 123.5, 145.8, 165.1, 168.4, 194.8. IR (KBr, cm^{-1}): ν 1686, 1643. HRMS (EI): calcd for $C_{13}H_{15}NO_4$ 249.1001 [M]$^+$, found 249.1021. Anal. Calcd for $C_{13}H_{15}NO_4$: C 62.64, H 6.07, N 5.62. Found: C 62.57, H 6.19, N 5.54.

Methoxycyclohexenone 22 and Borinate Ester 23. Using the conditions described for the preparation of **7**, cyclohexadienyl complex **21** (53 mg, 0.12 mmol) afforded a mixture of **22** (6 mg, 19%) and **23** (7 mg, 19%) as a yellow oil and a colorless solid, respectively. The compounds were separated and purified by radial chromatography (SiO_2, EtOAc). Cyclohexenone **22**: R_f = 0.29 (EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.86−1.88 (m, 1H), 2.38−2.47 (m, 3H), 2.48 (s, 3H), 2.90 (s, 3H), 3.22 (d, J = 9.6 Hz, 1H), 3.37 (d, J = 9.6 Hz, 1H), 3.60 (s, 3H), 3.66 (s, 3H), 5.36 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.2, 30.0, 31.6, 33.7, 44.1, 54.3, 54.4, 56.2, 102.6, 112.3, 161.1, 168.9, 179.9, 199.0. IR (thin film, cm^{-1}): ν 1679, 1650. HRMS (EI): calcd for $C_{14}H_{19}NO_4$ 265.1314 [M]$^+$, found 265.1314. Borinate ester **23**: R_f = 0.40 (EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.93 (s, 3H), 2.08−2.12 (m, 1H), 2.21−2.28 (m, 1H), 2.46−2.52 (m, 2H), 3.10 (s, 3H), 3.61 (d, J = 10.7 Hz, 1H), 3.72−3.74 (m, 4H), 5.53 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.5, 30.8, 33.1, 33.8, 43.8, 56.8, 59.4, 104.5, 109.6, 169.9, 170.4, 175.3, 196.8. HRMS (EI): calcd for $C_{13}H_{16}BF_2NO_4$ 299.1140 [M]$^+$, found 299.1141.

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Supporting Information Available: General experimental and X-ray crystallographic details, X-ray crystal structures of **7**, **8**, and $Cl_2Ru(DMSO)_4$. Crystallographic information files for all structures. ^{1}H and ^{13}C NMR spectra for **22** and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(23) For general experimental details, see the Supporting Information.