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Tandem 1,4-Addition Reactions with Benzene and Alkylated Benzenes Promoted by Pentaammineosmium(II)

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Abstract: Electrophiles such as dimethoxymethane and 3-penten-2-one react with the complex $[Os(NH_3)_5(\eta^2\text{-benzene})]^{2+}$ in the presence of triflic acid to form metastable benzenium intermediates. These benzenium intermediates further react with carbon nucleophiles including silyl ketene acetals, (silyloxy)alkenes, and phenyllithium in an overall tandem 1,4-addition sequence. The metal fragment controls the relative stereo- and regiochemistry for both electrophilic and nucleophilic addition steps. Upon oxidative demetalation with silver triflate, *cis*-1,4 cyclohexadienes are formed in yields ranging from 16 to 82%. This methodology can also be used to dearomatize toluene and *ortho*- and *meta*-xylene with unexpectedly high regio- and stereocontrol.

Introduction

Aromatic hydrocarbons are attractive as possible reagents for organic syntheses,[1] having the potential to form highly substituted alicyclic and polycyclic compounds if properly activated.[2] Given the abundance and stability of arenes, several methodologies have been developed to convert them into cyclohexadienes. When catalyzed by the bacterium *Pseudomonas putida*, benzene and toluene can be oxidized to *cis*-dihydrodiols with high stereoselectivities.[3] The Birch reduction is often used to dearomatize benzenes to 1,4-cyclohexadienes with good regioselectivity.[4] Alkylation under Birch reduction conditions has been developed into a useful method but has been mostly limited to arenes with electron-withdrawing substituents.[5] Alternatively, coordination by transition metals has been used to promote the addition of electrophiles or nucleophiles to arenes.[6,7]

Relative to functionalized arenes such as anisoles, anilines, phenols, and phenones, the dearomatization of benzene and alkylbenzenes is a much greater challenge due to their higher degrees of aromatic stability. In addition, control of the regiochemistry is highly problematic given the relatively weak electron-donating abilities of alkyl groups. While coordination to an electron-deficient transition metal, as in $Cr(CO)_3$ or $[Mn(CO)_3]^+$, sufficiently activates an arene to the addition of organometallic nucleophiles, regioselectivity is typically low, with alkylation often occurring at both *ortho* and *meta* positions.[8] Regioselective deprotonation followed by electrophilic alkylation is also problematic. For example, the lithiation of $Cr(CO)_3$(toluene) occurs at the *ortho* (9%), *meta* (35%), and *para* (35%) positions, as well as at the methyl group (20%).[9] By comparison, Friedel−Crafts alkylation of toluene slightly favors *ortho* and *para* addition but again with practically no selectivity,[10] and these reactions are further complicated by multiple alkylations and cation rearrangements.

The electron-rich pentaammineosmium(II) fragment is known to bind anisole, aniline, and phenol in an η^2 fashion. Once bound they are activated toward electrophilic addition,[6] and the resulting arenium intermediates may be treated with nucleophiles to form 1,3-diene complexes. The electrophilic addition occurs for these reactions at C4 with excellent regio- and stereocontrol.[11,12] Benzene, toluene, and xylenes have previously been shown to form stable complexes with the pentaammineosmium(II) fragment,[13] but owing to the lack of electron-releasing substituents, these complexes are less thermally stable and less nucleophilic than their heteroatom-substituted counterparts. Consequently, the benzenium intermediates resulting from electrophilic addition are highly acidic (the pK_a of the parent benzenium complex is -8.9)[14] and not stable enough to isolate. Nonetheless, we hoped that by forming these intermediates in situ at low temperature and trapping them with a suitable nucleophile, tandem addition reactions could be carried out.

Results

Triflic acid (HOTf) and dimethoxymethane (DMM) were combined with the $[Os(NH_3)_5(\eta^2\text{-benzene})]^{2+}$ complex (**A,**

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(1) Hendrickson, J. B. *J. Am. Chem. Soc.* **1977**, *99*, 5439.
(2) Mander, L. N. *Synlett* **1991**, 134.
(3) Carless, H. A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 795.
(4) Krapcho, A. P.; Bothner-By, A. A. *J. Am. Chem. Soc.* **1959**, *81*, 3658.
(5) Loewenthal, H. J. E.; Gottlieb, L. *J. Org. Chem.* **1992**, *57*, 2631.
(6) Harman, W. D. *Chem. Rev.* **1997**, *97*, 1953.
(7) Pape, A. R.; Kaliappan, K. P.; Kündig, E. P. *Chem. Rev.* **2000**, *100*, 2917.
(8) Semmelhack, M. F. *Transition Metal Arene Complexes: Nucleophilic Addition*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Ed.; Pergamon: Oxford, U.K., 1995; Vol. 12, p 979.
(9) Semmelhack, M. F. *Transition Metal Arene Complexes: Ring Lithiation*; Pergamon: Oxford, U.K., 1995; Vol. 12.
(10) Roberts, R. M.; Khalaf, A. A. *A Century of Friedel−Crafts Alkylation Chemistry*; Marcel Dekker Inc.: New York, 1984.
(11) Kopach, M. E.; Kolis, S. P.; Liu, R.; Robertson, J. W.; Chordia, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 6199.
(12) Winemiller, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 7835.
(13) Harman, W. D.; Sekine, M.; Taube, H. *J. Am. Chem. Soc.* **1988**, *110*, 5725.
(14) Winemiller, W. D.; Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1997**, *119*, 2096.

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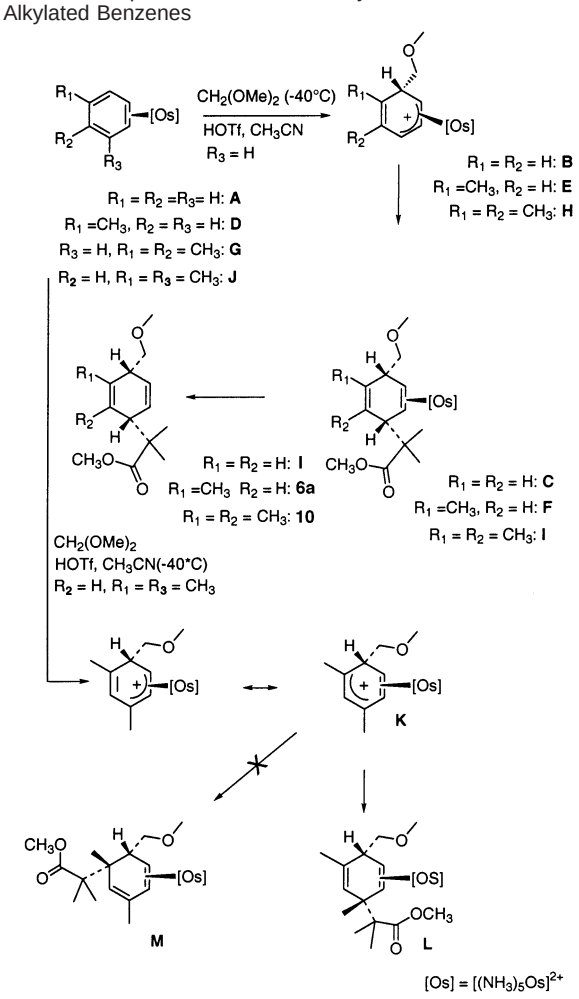
Scheme 1. Proposed Reaction Pathway for the Tandem Addition to Alkylated Benzenes



Scheme 1) in CD_3CN at −40 °C. The light red solution was monitored by proton NMR spectroscopy (−40 °C). Peaks at δ 6.51, 6.14, 6.05, 5.95, and 5.13 were compared to the ring protons found for the parent benzenium complex and found to be similar.[14] Carbon data also closely matched, indicating the formation of the alkylbenzenium **B**. No other complex was detectable in the proton or carbon NMR spectrum. Although the benzenium complex **B** could not be isolated due to its thermal instability, subsequent treatment of **B** with 1-methoxy-2-methyl-1-(trimethylsiloxy)propene (MMTP) formed the putative diene complex **C.** Silver triflate was added to oxidize the metal. Heating this solution resulted in liberation of the disubstituted cyclohexadiene **1** in an isolated yield of 82%. The assignment of a 1,4-cyclohexadiene addition product was supported by the splitting pattern of olefinic protons at δ 5.84 and 5.58 and carbons at δ 128.6 and 126.1, indicating mirror symmetry in the product. Following DMM addition to the benzene complex, both 2-(trimethylsiloxy)propene and phenyllithium (with cuprous cyanide) were found to react, giving 1,4 addition products with overall isolated yields of 23% (**2**) and 16% (**3**), respectively. Less sterically hindered silyl ketene acetals were prepared according to the procedure of Mikami et al.[15] The addition of DMM followed by the ketene acetal 1-ethoxy-1-(trimethylsiloxy)ethene generated the 1,4-cyclohexadiene **4** in 31% isolated yield. Careful examination of the ^1H NMR spectra for the crude organic products **1**−**4** shows no indication of any other regio- or stereoisomer (dr > 20:1). Although reactions with methyl vinyl ketone failed to give a clean addition reaction, the Michael acceptor 3-penten-2-one reacted cleanly with the benzene complex (**A**). Subsequent nucleophilic addition by the acetal 1-methoxy-2-phenyl-1-(trimethylsiloxy)ethene, followed by oxidative decomplexation, afforded the corresponding 1,4-cyclohexadiene **5** in 27% overall yield. For the diene **5**, NMR data also suggest that a single diastereomer is formed, but in this case the two stereocenters are sufficiently far removed that it is likely that diastereomers could not be resolved.

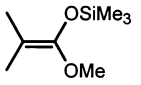
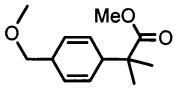
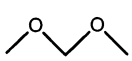
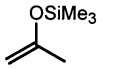
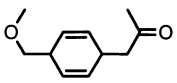
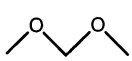
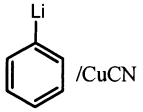
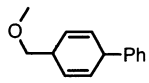
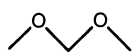
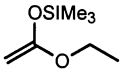
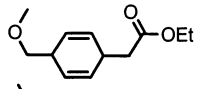
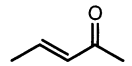
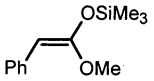
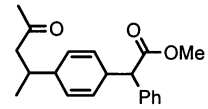
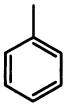
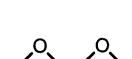
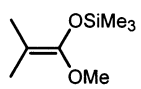
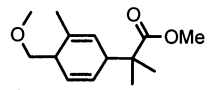
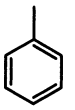
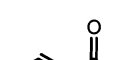
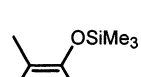
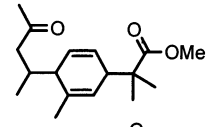
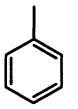
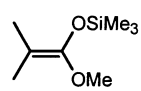
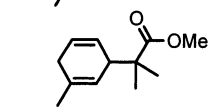
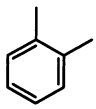
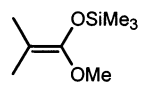
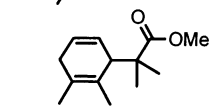
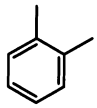
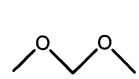
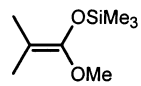
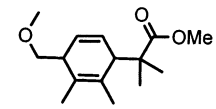
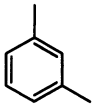
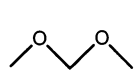
In an earlier study, the toluene complex (**D**) was found to react with HOTf to form a toluenium intermediate **E** in which protonation occurred exclusively *ortho* to the methyl group.[14] This complex was stable enough to be observed at low temperatures but again could not be isolated. However, when a cold solution of **E** was treated with MMTP, followed by silver triflate, a 1,4-cyclohexadiene was formed and isolated in 56% yield. Given that COSY data showed no coupling between the olefinic proton adjacent to the ring methyl group at δ 5.24 and either of the other two olefinic protons at δ 5.85 or 5.54, the product (**8**) is thought to be a 1,4 cyclohexadiene species similar to those formed from benzene (**1**−**5**). When the methyl group on C1 at δ1.70 was irradiated, the methylene protons on C2 at δ 2.52 showed 1.6% NOE enhancement, confirming the protonation occurred on the *ortho* position of toluene.

The tandem addition of DMM and MMTP to the toluene complex gave two isomers (**6**) in a 5:1 ratio when the reaction was carried out at −40 °C, and this ratio improved to 10:1 when the reaction was run at −80 °C. These isomers could not be separated by chromatography. With the aid of COSY data and the results from the analogous reaction with triflic acid, the major isomer (**6a**) was tentatively assigned as the 2,5 addition product with respect to the methyl group of toluene (vide infra). Surprisingly, 3-penten-2-one and MMTP reacted with the toluene complex (**D**) to yield after oxidative decomplexation a single diastereomer of **7**, even though three new stereocenters were formed. The methine proton (δ 2.50) on the methyloxobutyl substituent showed a 10.4% NOE enhancement when the methyl group on the ring at δ 1.68 was irradiated, indicating that the electrophile added to the *ortho* position of toluene exclusively. Attempts to assign the relative configuration of the stereogenic centers for **7** by X-ray diffraction were frustrated by the difficulties in growing high-quality crystals of either the cyclohexadiene complex of pentaammineosmium(II) or the organic product.

Protonation of the *o*-xylene complex (**G**) with HOTf occurred at a carbon adjacent to one of the methyl groups.[14] When this xylenium complex is treated with MMTP, a 1,4-cyclohexadiene again is isolated in 67% yield after demetalation. The assignment of **9** as a 1,2,3-trialkyl-1,4-cyclohexadiene was made on the basis of the coupling between the methylene protons at δ 2.56 and one olefinic proton at δ 5.88. On the basis of similar coupling patterns of the olefinic protons, similar regiochemistry was assigned for the tandem addition of DMM and MMTP to *o*-xylene to generate **10** in overall 28% yield. A CD_3CN solution of the xylene complex **G** was then treated with DMM and HOTf at −40 °C. Proton signals recorded at −40 °C for the putative

(15) Mikami, K.; Matsumoto, S.; Ishida, A.; Takamuku, S.; Suenobu, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 11134.

Table 1. Products and Yields of the Tandem Additions to Benzene, Toluene, and Xylenes

Arene	Electropile	Nucleophile	Product	Overall yield	
				**1**	82%
				**2**	23%
				**3**	16%
				**4**	31%
				**5**	27%
				**6a** (major)	34%
				**7**	43%
	HOTf			**8**	56%
	HOTf			**9**	67%
				**10**	28%
				**11**	32%

xylenium intermediate at δ 6.75, 6.51, 6.13, and 2.14 and carbon signals at δ 187.9 (C), 166.3 (C), 130.0 (CH), 69.7 (CH), 62.9 (CH), and 50.0 (CH) corresponding to the ring carbons indicated that the carbon electrophile added exclusively to C6 in a manner similar to that observed for protonation.

The *m*-xylene complex (**J**) can be protonated,[14] but subsequent treatment with MMTP followed by silver(I) oxidation failed to yield any of the expected diene products. However, when triflic acid and DMM were combined with the *meta*-xylene complex followed by MMTP and silver triflate, diene **11** was isolated in 32% yield. Diene **11** had a quaternary carbon in the ring and three alkene protons, but this situation did not distinguish between the nucleophile adding at C1 (a 1,3-cyclohexadiene) or at C3 (a 1,4 cyclohexadiene). Ultraviolet absorption spectroscopy showed a λ_{max} of 238 nm with the ϵ_{max} of 78 M^{-1} cm^{-1}. Note that isolated dienes normally absorb below 200 nm, which is out of the range of the spectrometer, so the absorption could be attributed to either the carbonyl n $\rightarrow$ π^* transition or the conjugated diene $\pi \rightarrow \pi^*$ transition. However, a conjugated diene would be expected to have a very high extinction coefficient ($\sim 2 \times 10^5$). On this basis, ϵ_{max} of the sample was attributed to ester absorption,[16] and **11** was assigned as the 1,4-cyclohexadiene shown in Table 1.

Several experiments were carried out in an attempt to extend this methodology to *para*-dialkylated benzenes. In particular, the *para*-xylene complex was synthesized and isolated. Several attempts were made to add a carbon electrophile to this complex, but none were successful.

Previous studies of tandem addition reactions with naphthalene were shown to consistently produce *cis*-disubstituted products with both the electrophile and nucleophile adding *anti* to the face of metal coordination. To confirm this expectation for benzenes, the osmium complex (**N**) of the diene **7** was isolated and characterized (Figure 1). When the cis ammine

(16) Silverstein, R. M.; Bassler, G. C.; Morril, T. C. *Spectrometric Identification of Organic Compounds*; John Wiley & Sons: New York, 1991.

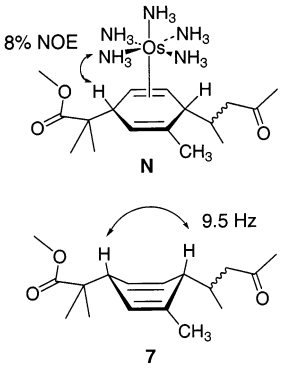


Figure 1. Assignment of regio- and stereochemistry for cyclohexadiene **7** and its complex **N**.

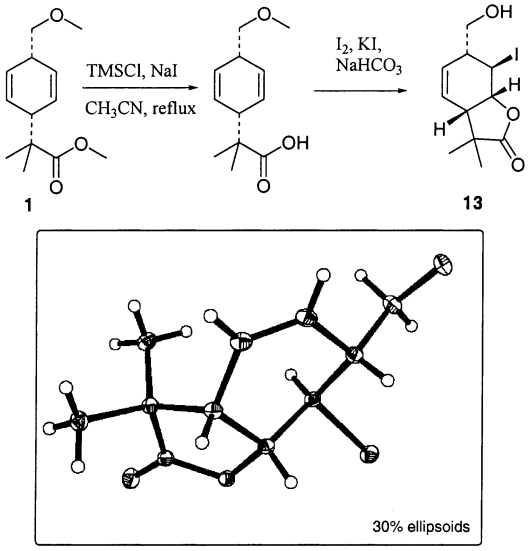


Figure 2. Preparation of a 3*H*-benzofuran-2-one ring system from cyclohexadiene **1**.

resonance of the metal fragment was irradiated, the proton (δ 2.39) at the nucleophilic addition site (C5) showed an 8.0% NOE enhancement, indicating that nucleophilic attack was *anti* to the metal. The overlap of the methyloxobutyl methine proton and the C2 ring proton hampered the identification of the relative stereochemistry on C2. However, the C2 and C5 protons of the organic diene **7** show unusually strong homoallylic coupling with each other ($J = 9.5$ Hz), supporting the hypothesis that they are in a *syn* relationship.[17]

Because both olefin and ester functional groups are present in some of the tandem addition products to benzenes, we considered coupling the tandem addition sequence with iodolactonization as a possible new route to partially saturated benzofuranones**.** Compound **1** was hydrolyzed by iodotrimethylsilane, formed in situ from chlorotrimethylsilane and NaI, and iodolactonization proceeded in an aqueous I_2 and $NaHCO_3$ solution, concomitant with the demethylation of the methoxymethyl substituent, to afford the β-iodo-δ-lactone with a 62% overall yield (Figure 2). Note that four of the benzene's six carbons have been converted to stereogenic centers with high stereoselectivity. An X-ray structure determination confirms the structure shown in Figure 2 (30% ellipsoids) and confirms that DMM and MMTP were added syn to each other.

(17) Grossel, M. C. *Tetrahedron Lett.* **1980**, *21*, 1075.

Discussion

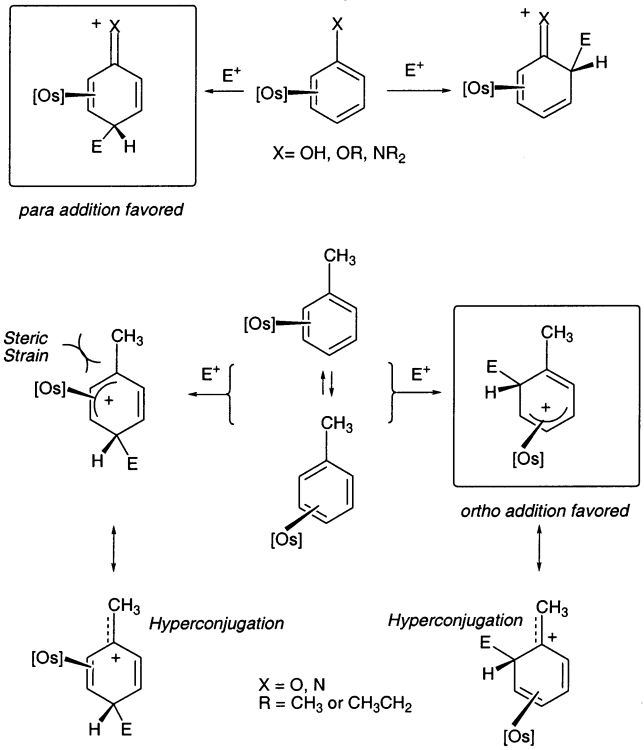
The majority of dearomatization reactions that generate 1,4-alkylated cyclohexadienes already have their carbon skeleton intact prior to reduction.[18,19] Reductive alkylation has been used to introduce one alkyl group; however, to our knowledge, there is no general method available that allows a regio- and stereoselective 1,4-dialkylation of benzenes. Although the methodology described herein is stoichiometric with respect to the metal fragment, it allows the addition of acetals or Michael acceptors, two of the most important classes of carbon electrophiles, in concert with ester- or ketone-derived silylenolates or phenyllithium. The addition sequence is carried out on an unactivated hydrocarbon under relatively mild conditions, with readily predictable outcomes.

One of the most interesting features of this tandem addition sequence is the high degree of regiocontrol expressed in the initial dearomatization step. This is particularly remarkable for toluene given that the only directing influence is a methyl group. In comparison, the regioselectivity for the addition of organolithium reagents for $Cr(CO)_3$ to alkylated benzenes is generally poor unless very bulky nucleophiles are used.[8,20,21] Similarly, the addition of Grignard reagents and ketone enolates to $\{Mn(CO)_3\}^+$ [22] occurs with poor regiocontrol. Because the $\{Mn(CO)_3\}^+$ fragment is more π-acidic than the $Cr(CO)_3$ analogue, double nucleophilic addition is sometimes possible, and it is worth noting that, after methylation of the benzene complex, hard nucleophiles can be added *ortho* and *syn* to the methyl group.[23,24]

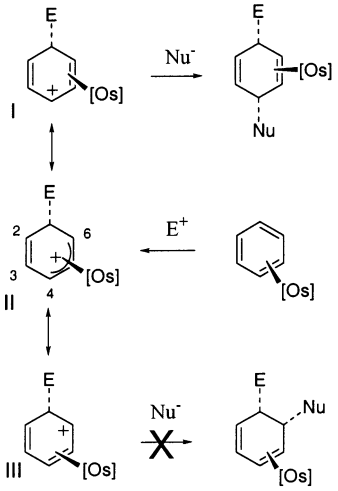
The high regioselectivity observed for the addition of carbon electrophiles to alkylated benzene complexes of pentaammineosmium(II) mirrors that of protonation in all cases that we investigated.[14] Important factors include the ability of the metal fragment to rapidly adjust to different positions in the ring, steric interactions between the metal and alkyl groups that direct the metal away from these substituents, and, most importantly, the stabilization of the resulting arenium intermediate by hyperconjugation with an alkyl group. In an earlier study,[14] we determined that protonation of η^2-bound alkylated benzenes occurs with high selectivity (dr > 25:1) under thermodynamic control. In every case, protonation occurs adjacent to an alkyl group, and as a result, the alkyl group is in a terminal position of the arenium π system where it can stabilize the partial positive charge while minimizing steric strain (Scheme 2). Note the contrast with the regiochemistry typically observed with heteroatom-substituted benzenes such as anisole or aniline.[6] When the arene substituent has a good π donor (e.g., as in anisole), the metal does not need to bind η^3 to stabilize the arenium positive charge and this relieves the steric strain between the metal fragment and the substituent. If the heteroatom itself has

(18) Mander, L. N. *Partial Reduction of Aromatic Rings by Dissolving Metals and Other Methods*; Trost, B. M., Flemming, I., Ed.; Pergamon: Oxford, U.K., 1991; Vol. 8, p 341.
(19) Donohoe, T. J.; Garg, R.; Stevenson, C. A. *Tetrahedron: Asymmetry* **1996**, *7*, 317.
(20) Kündig, E. P.; Desobry, V.; Simmons, D. P.; Wenger, E. *J. Am. Chem. Soc.* **1989**, *111*, 1804.
(21) Kündig, E. P.; Desobry, V.; Simmons, D. P.; Wenger, E. *Organometallics* **1993**, *12*, 3724.
(22) Chung, Y. K.; Willard, P. G.; Sweigart, D. A. *Organometallics* **1982**, *1*, 1053.
(23) Roell, B. C.; McDaniel, K. F.; Vanghan, W. S.; Macy, T. S. *Organometallics* **1993**, *12*, 224.
(24) Chung, Y. K.; Choi, H. S.; Sweigart, D. A.; Connelly, N. G. *J. Am. Chem. Soc.* **1982**, *104*, 4245.

Scheme 2. Comparison of Reaction Mechanisms for the Electrophilic Addition to Alkylated Benzene and Heteroatom-Substituted Arene Complexes



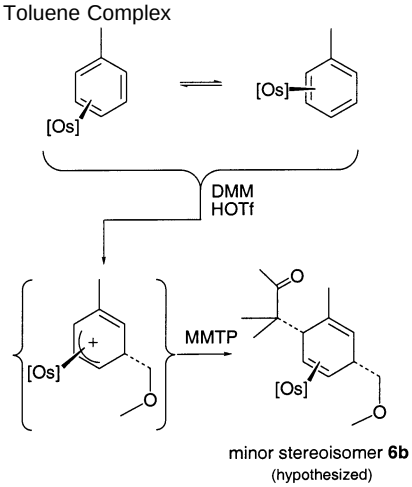
Scheme 3. Comparison of Possible Nucleophilic Addition Pathways



a substituent (e.g., anisole) the *ortho* position is sterically congested as a result of the requirement that R must lie in the plane of the arene to allow for a good π interaction with the heteroatom. The coordinated side of the arene is hence blocked by the pentaammineosmium fragment. Thus, while oxygen and nitrogen substituents are good *para* directors for osmium−benzene complexes, an alkyl group is a good *ortho* director.

A second important difference between alkylated benzene and heteroatom-substituted benzene complexes of pentaammineosmium(II) is found in the regioselectivity for the addition of the nucleophile.[6] In Scheme 3, three resonance contributors are shown for the η^3-arenium intermediate resulting from electrophilic addition. Form I could be considered to have slightly higher weighting in that it allows the positive charge on C4 to interact with the double bond of C2 and C3. This interpretation

Scheme 4. Formation of the Minor Diastereomer **6b** from the Osmium(II) Toluene Complex



suggests that the actual structure of the arenium ion is slightly distorted from a true η^3-allyl system where the metal is closer to C6 than to C4. This distortion should predispose the allyl to react with a nucleophile at C4 over C2. In addition, if an alkyl electrophile was added, its steric interaction with the nucleophile could inhibit C6 addition. Interestingly, earlier studies have shown that the osmium forms more stable complexes with 1,3-dienes than with isolated alkenes as ligands;[25] thus, the regioselectivity observed in the present study is strictly a kinetic phenomenon. A similar observation was made with 1,4-tandem addition reactions with osmium naphthalene complexes.[12]

Two products (**6a,b**) were observed in a 5:1 ratio for the tandem addition of DMM and MMTP to toluene. Due to the obscurity of the minor product in the proton spectrum, UV spectroscopy was also used and the maximal absorption was found at 242 nm, with the ϵ_{max} of 63 M^{-1} cm^{-1}, assuming the two isomers have similar absorption wavelengths. As mentioned earlier, since the absorption of a typical 1,3-diene is 3 orders of magnitude stronger than that of the ester carbonyl, the minor product almost certainly is a 1,4-cyclohexadiene species (note the NMR ratio). Given the proton NMR signal corresponding to the ring methyl group has a chemical shift consistent with being attached to an alkene carbon, we tentatively assign the minor isomer according to Scheme 4. This would come about by the electrophilic addition of the acetal to the *meta* carbon of toluene. This side reaction becomes less significant (10%) when the temperature is dropped to −70 °C.

In all examples of this study, both the electrophile and the nucleophile add to the side of the ring opposite metal coordination, similar to what has been observed with other aromatic complexes of pentaammineosmium(II).[6] As previously discussed,[14] this represents a departure from most other metal-promoted addition sequences to arenes in that the electrophile adds *directly* to the ligand without the intervention of the metal.

The tandem reactions to benzenes involving 3-penten-2-one deserve special comment. As best as we are able to determine, cyclohexadienes **5** and **7** are formed as single diastereomers. The two side-chain stereocenters in **5** are far removed from each other, making it difficult to resolve hypothetical diastereomers in the proton or carbon NMR spectrum. However, for **7** the high diastereoselectivity is unmistakable. The surprising feature

(25) Harman, W. D.; Hasegawa, T.; Taube, H. *Inorg. Chem.* **1991**, *30*, 453.

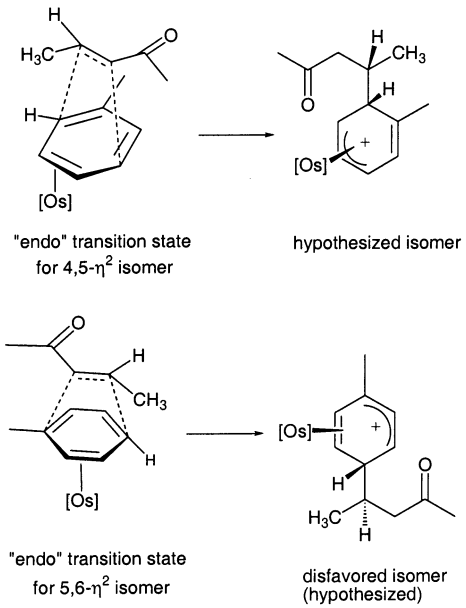


Figure 3. Proposed transition states for the electrophilic addition of 3-penten-2-one to the toluene complex **D**.

is the control of the newly formed benzylic center. We have seen high stereocontrol of this position in Michael additions with other aromatic systems for both osmium and rhenium and have attributed it to a Diels−Alder-like transition state or intermediate similar to that depicted in Figure 3. Evans et al. have recently invoked a similar explanation for high stereochemical fidelity observed in Mukaiyama−Michael addition (note that regular Michael additions do not demonstrate such stereoselectivity).[26] Apparently this mechanism is operative for unfunctionalized η^2-benzene complexes as well.

The same principles outlined above for toluene explain the regiochemistry for *ortho*- and *meta*-xylene. The electrophilic addition occurs adjacent to a methyl group, and the nucleophile subsequently attacks in such a manner that a 1,4-cyclohexadiene complex results. This holds true even in the case of **11**, where addition of DMM to form **K** (Scheme 1) followed by MMTP results in the formation of adjacent quaternary carbons (**M**). Noteworthy is that protonation followed by MMTP addition only worked for toluene and *o*-xylene, which is consistent with the acidity of coordinated benzenes. At −40 °C, the toluenium (−6.5) and *ortho*-xylene (−6.6) complexes have comparably high pK_a values, but the benzenium and *para*-xylene complexes are considerably more acidic (pK_a, ∼−9).

Conclusion

Coordination of alkylated benzenes with the π base pentaammineosmium(II) provides a means to add in a tandem sequence a carbon electrophile and a nucleophile across the benzene ring to form functionalized 1,4-cyclohexadienes. Addition of both the electrophile and carbon nucleophile is highly regio- and stereoselective, the electrophile adding *ortho* to an alkyl substituent and the nucleophile adding *para* to it, with both additions occurring *anti* to metal coordination. The conditions for tandem addition are sufficiently mild that no isomerization or rearomatization to the arene occurs. The metal fragment also provides complete differentiation of otherwise similar or identical C═C bonds. Thus, one can envision subsequent chemistry at the free alkene site while the other remains protected by metal coordination. The reaction conditions are relatively mild, requiring a Brønsted acid at −40 °C (CH_3CNH^+), and the metal is easily removed by the action of either silver(I) or H_2O_2, thereby exposing the coordinated double bond. Finally, by using a silyl ketene acetal as the nucleophile, following the tandem addition by an iodolactonization sequence, a novel route to a functionalized benzofuranone was demonstrated in which four contiguous stereocenters are set from benzene.

Experimental Section

General Procedure. All the tandem addition reactions were performed under nitrogen in a Vacuum Atmospheres Co. glovebox. ^{1}H and ^{13}C NMR spectra were collected on a 300 MHz Varian INOVA spectrometer. Chemical shifts are reported in parts per million relative to tetramethylsilane (TMS) using the deuterated solvents as the internal reference, and coupling constants are reported in hertz. NOE, DQCOSY, and HSQC experiments were carried out using standard parameters. UV spectra were collected on a Hewlett-Packard 8452A diode array spectrophotometer in a quartz cell with the path length of 1 mm using $CDCl_3$ as the solvent and background.

Reagents. The precursor $[Os(NH_3)_5OTf](OTf)_2$ was synthesized as described by Lay et al.[27] Magnesium powder was activated by iodine in DMA (*N*,*N*-dimethylacetamide) under nitrogen with stirring for 30 min and then washed with DMA and Et_2O and dried in vacuo. Benzene, toluene, xylenes, DMA, ether, CH_2Cl_2, and hexanes were purged with nitrogen before being brought into the glovebox.

Typical Procedure for the Preparation of Complexes. To a solution of $[Os(NH_3)_5OTf](OTf)_2$ (400 mg, 0.554 mmol) in 1.5 g of the benzene and 1.0 g of DMA was added 0.8 g of activated magnesium (cleaned with I_2). The reaction mixture was stirred vigorously for 30 min and then quenched into 120 mL of 1:1 Et_2O/CH_2Cl_2 120 mL and washed with 10 mL of CH_2Cl_2. The precipitate was dried in vacuo, giving the complex in 95% yield.

Typical Procedure for the Preparation of the Silyl Ketene Acetals. Silyl ketene acetals were prepared on the basis of the procedure in ref 15, except for MMTP, which is commercially available. A solution of ethyl acetate (352 mg, 4.00 mmol) in 1.0 g of THF was added into a solution of lithium bis(trimethylsilyl)amide (20% in THF, 3.67 g, 4.40 mmol) at −40 °C. The reaction mixture stood for 0.5 h before trimethylsilyl chloride (523 mg, 4.80 mmol) was added. After another 0.5 h, the reaction mixture was warmed to 20 °C and allowed to stand for 1 h. Hexanes (18 mL) and water (8 mL) were then added. The organic layer was washed with 8 mL of brine and dried over Na_2SO_4. Evaporation of the solvents yielded the crude product (481 mg, 75%), which was cooled to −40 °C for use.

Typical Procedure for the Tandem Addition to Arene Complexes and Subsequent Oxidation. The pentaammineosmium benzene complex (**A**, 338 mg, 0.519 mmol), DMM (60 mg, 0.77 mmol), and 2.0 mL CH_3CN were added together, and the solution was cooled to −40 °C. A solution of triflic acid (120 mg, 0.800 mmol) in 0.5 g of CH_3CN was also prepared and chilled. The acid solution was then added into the complex solution, and the mixture was allowed to stand for 1 h. Separately, a solution of phenyllithium (1.8 M in cyclohexane and ether, 1.41 g, 3.06 mmol) and a suspension of copper(I) cyanide (320 mg, 3.55 mmol) in 1.2 g of ether were cooled to −40 °C, mixed together, and briefly allowed to warm to 20 °C and then cooled to −40 °C. The latter reaction mixture was then added into the former, and this mixture was allowed to stand for 12 h. Triflic acid (309 mg, 2.06 mmol) and silver triflate (266 mg, 1.04 mmol) were then added, and the reaction

(26) Evans, D. A.; Scheidt, K. A.; Johnston, J. N.; Willis, M. C. *J. Am. Chem. Soc.* **2001**, *123*, 4480.

(27) Lay, P. A.; Magnuson, R. H.; Taube, H. *Inorg. Synth.* **1986**, *24*, 269.

mixture was then transferred to a pressure tube and put into a 70 °C oil bath for 2 h. After cooling, the solvents were evaporated and 1 mL water was added to dissolve the oil-like residue. The water layer was extracted with 2 × 10 mL ether, and the combination of the two portions of ether layer was washed with 2 mL of brine and dried over Na_2SO_4. Ether was then evaporated, and the residue was dissolved in chloroform and subjected to chromatography. The elution of 10% ethyl acetate in hexanes on silica gel yielded the product (16.3 mg, 16%) (R_f = 0.52, visualized by iodine). For the nucleophiles other than phenyllithium, 1.5 equiv of pyridine with respect to the starting complex was added instead of triflic acid in the demetalation step.

[Os(NH$_3$)$_5$(1α-methoxymethyl-2β,3β,4β-η^3-benzenium](OTf)$_3$ (B). The benzene complex (**A**, 65 mg, 0.11 mmol) was dissolved in CD_3CN (400 mg), dimethoxymethane (8.0 mg, 0.11 mmol) was added, and the reaction mixture was cooled to −40°C. Cold HOTf (30 mg, 0.20 mmol) was added, causing a quick reddening. After 1 h at −40 °C the reaction mixture was frozen with liquid N_2 in an NMR tube and rethawed at −40 °C in the NMR spectrometer. A ^{1}H NMR spectrum then revealed exclusive η^3-arenium formation. ^{1}H NMR (CD_3CN/−40 °C): δ 6.51 (dd, 1H, J = 8.4, 3.3 Hz), 6.14 (br d, 1H, J = 9.0 Hz), 5.95−6.05 (m, 2H), 5.13 (t, 1H, J = 6.0 Hz), 5.07 (br s, 3H, *trans*-NH_3), 3.93 (br s, 12 H, *cis*-NH_3), 3.34 (s, 3H), 1.27 (br s, 1H), 3.90−4.0 (m, 2H-buried in cis NH_3). ^{13}C NMR (CD_3CN/−40 °C): δ 134.1 (CH), 128.0 (CH), 80.7 (CH), 79.4 (CH), 74.2 (CH), 68.3 (CH_2), 58.1 (CH_3), 46.2 (CH).

[Os(NH$_3$)$_5$(1α-methoxymethyl-2β,3β-η^2-4,6-dimethylbenzenium)](OTf)$_3$ (H). The *meta*-xylene complex (**G**, 48 mg, 0.071 mmol) was dissolved in CD_3CN (500 mg), dimethoxymethane (6.2 mg, 0.081 mmol) was added, and the reaction mixture was cooled to −40 °C. Cold HOTf (30 mg, 0.20 mmol) was then added, which imparted a dark green appearance to the reaction mixture. After 0.25 h at −40 °C a ^{1}H NMR spectrum revealed exclusive η^2-arenium formation. ^{1}H NMR (CD_3CN/−40 °C): δ 6.75 (d, 1H, J = 6.0 Hz), 6.51 (s, 1H), 6.13 (t, 1H, J = 6.3 Hz), 5.08 (br s, 3H, *trans*-NH_3), 4.01 (br s, 12 H, *cis*-NH_3), 3.90−4.0 (m, 2H), 3.72 (s, 3H), 2.14 (br s, 1H), 1.78 (s, 3H). ^{13}C NMR (CD_3CN/−40 °C): δ 187.9 (C), 166.3 (C), 130.0 (CH), 70.0 (CH_2), 69.7 (CH), 62.9 (CH), 58.6 (CH_3), 50.0 (CH), 27.7 (CH_3), 22.6 (CH_3).

Methyl 2-[4-(methoxymethyl)cyclohexa-2,5-dien-1-yl]-2-methylpropanoate (1): R_f = 0.30; yield = 82%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.84 (m, 2H), 5.58 (m, 2H), 3.68 (s, 3H), 3.36 (s, 3H), 3.28 (d, J = 8.2, 2H), 3.16 (m, 1H), 2.96 (m, 1H), 1.12 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 178.10, 128.60, 126.13, 77.40, 59.12, 52.01, 45.59, 43.32, 37.14, 22.26; HRMS calcd for $C_{13}H_{21}O_3^+$ 225.1491, found 225.1492; purity (^{1}H NMR) >99%.

2-[4-(Methoxymethyl)cyclohexa-2,5-dien-1-yl]acetone (2): R_f = 0.27 (for further purification, the compounds were reloaded on silica and eluted with 20% ethyl acetate in hexanes with the R_f of 0.54); yield = 23%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.71 (m, 4H), 3.35 (s, 3H), 3.31 (d, J = 6.5, 1H), 3.23 (m, 1H), 2.96 (m, 1H), 2.50 (d, J = 6.5, 1H), 2.14 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 129.35, 126.83, 77.43, 50.87, 36.89, 31.89, 30.81, CO not observed; HRMS calcd for $C_{11}H_{17}O_2^+$ 181.1229, found 181.1229; purity (^{1}H NMR) 90%.

[4-(Methoxymethyl)cyclohexa-2,5-dien-1-yl]benzene (3): R_f = 0.52; yield = 16%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 7.27 (m, 5H), 5.80 (m, 4H), 3.98 (m, 1H), 3.43 (d, J = 6.6, 2H), 3.41 (s, 3H), 3.06 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 144.44, 129.68, 128.78, 128.30, 126.70, 77.55, 59.26, 42.96, 36.53; MS (FAB) m/z 201.2; purity (H^1 NMR) >90%.

Ethyl [4-(methoxymethyl)cyclohexa-2,5-dien-1-yl]acetate (4): R_f = 0.49; yield = 31%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.74 (m, 4H), 4.15 (q, J = 7.1, 2H), 3.35 (s, 3H), 3.30 (d, J = 6.4, 2H), 3.19 (m, 1H), 2.96 (m, 1H), 2.35 (d, J = 7.5, 2H), 1.26 (t, J = 7.2, 3H); ^{13}C NMR ($CDCl_3$) δ 172.28, 128.99, 127.03, 77.32, 60.62, 59.22, 41.80, 36.92, 33.02, 14.49; HRMS calcd for $C_{12}H_{19}O_3^+$ 211.1334, found 211.1333; purity (^{1}H NMR) >95%.

Methyl [4-(1-methyl-3-oxobutyl)cyclohexa-2,5-dien-1-yl]phenylacetate (5): R_f = 0.52; yield = 27%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 7.30 (m, 5H), 5.58 (m, 4H), 3.69 (s, 3H), 3.50 (m, 1H), 3.36 (d, J = 9.8, 1H), 2.73 (m, 1H), 2.28 (dd, J = 11.0, 7.0, 1H), 2.11 (s, 3H), 2.06 (dd, J = 11.0, 2.2, 1H), 0.85 (d, J = 6.6, 3H); ^{13}C NMR ($CDCl_3$) δ 173.52, 136.68, 128.90, 128.78, 128.50, 128.38, 128.22, 128.11, 127.72, 58.27, 52.25, 47.57, 40.83, 39.33, 32.79, 30.77; HRMS calcd for $C_{20}H_{25}O_3^+$ 313.1804, found 313.1804; purity (^{1}H NMR) >95%.

Methyl 2-[4-(methoxymethyl)-3-methylcyclohexa-2,5-dien-1-yl]-2-methylpropanoate (6b): Rf = 0.39; yield = 34%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.87 (m, 1H), 5.56 (m, 1H), 5.29 (m, 1H), 3.66 (s, 3H), 3.47 (m, 1H), 3.21 (m, 1H), 3.12 (m, 1H), 2.80 (m, 1H), 1.73 (br s, 3H), 1.08 (br s, 6H); purity (^{1}H NMR) >95% (two isomers).

Methyl 2-methyl-2-[3-methyl-4-(1-methyl-3-oxobutyl)cyclohexa-2,5-dien-1-yl]propanoate (7): R_f = 0.21; yield = 43%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.77 (m, 1H), 5.61 (m, 1H), 5.34 (m, 1H), 3.71 (s, 3H), 3.14 (m, 1H), 2.63 (m, 1H), 2.50 (m, 1H), 2.22 (dd, J = 15.3, 2.8, 1H), 2.00 (dd, J = 15.3, 2.8, 1H), 1.68 (s, 3H), 1.14 (s, 3H), 1.13 (s, 3H), 1.02 (d, J = 6.9, 3H); ^{13}C NMR ($CDCl_3$) δ 209.33, 178.12, 135.60, 126.89, 126.46, 122.78, 51.99, 46.41, 46.03, 45.03, 43.99, 30.71, 29.67, 22.73, 22.62, 22.26, 18.26; HRMS calcd for $C_{17}H_{27}O_3^+$ 279.1960, found 279.1960; purity (H^1 NMR) >95%.

Methyl 2-methyl-2-(3-methylcyclohexa-2,5-dien-1-yl)propanoate (8): yield = 56%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.85 (m, 1H), 5.54 (m, 1H), 5.24 (m, 1H), 3.69 (s, 3H), 3.12 (m, 1H), 2.52 (m, 2H), 1.70 (br s, 3H), 1.10 (br s, 6H); ^{13}C NMR ($CDCl_3$) δ 178.40, 134.36, 127.08, 125.12, 119.63, 51.92, 46.91, 43.80, 31.53, 23.70, 21.95, 21.82; HRMS calcd for $C_{12}H_{19}O_2^+$ 195.1385, found 195.1381; purity (^{1}H NMR) >98%.

Methyl 2-(2,3-dimethylcyclohexa-2,5-dien-1-yl)-2-methylpropanoate (9): yield = 67%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.88 (m, 1H), 5.71 (m, 1H), 3.67 (s, 3H), 3.14 (m, 1H), 2.52 (m, 1H), 2.45 (m, 1H), 1.65 (s, 3H), 1.56 (br s, 3H), 1.15 (s, 3H), 1.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 179.23, 128.87, 128.09, 126.85, 125.29, 51.83, 49.53, 48.05, 33.86, 23.88, 20.41, 19.44, 18.81; HRMS calcd for $C_{13}H_{21}O_2^+$ 209.1542, found 209.1543; purity (^{1}H NMR) >99%.

Methyl 2-[4-(methoxymethyl)-2,3-dimethylcyclohexa-2,5-dien-1-yl]-2-methylpropanoate (10): R_f = 0.36; yield 28%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.97 (m, 1H), 5.69 (m, 1H), 3.67 (s, 3H), 3.54 (dd, J = 8.7, 4.8, 1H), 3.33 (s, 3H), 3.21 (dd, J = 17.4, 4.2, 1H), 3.17 (d, J = 17.4, 1H), 2.80 (m, 1H), 1.67 (s, 3H), 1.51 (s, 3H), 1.15 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 179.37, 130.24, 128.96, 127.47, 126.08, 77.23, 58.99, 51.91, 49.39, 45.34, 43.71, 25.07, 21.00, 18.58, 18.29; HRMS calcd for $C_{15}H_{25}O_3^+$ 253.1804, found 253.1803; purity (^{1}H NMR) >95%.

Methyl 2-[4-(methoxymethyl)-1,3-dimethylcyclohexa-2,5-dien-1-yl]-2-methyl propanoate (11): R_f = 0.50; yield 32%; ^{1}H NMR (300 Hz, $CDCl_3$) δ 5.81 (dd, J = 10.3, 3.7, 1H), 5.60 (m, 1H), 5.31 (m, 1H), 3.65 (s, 3H), 3.53 (dd, J = 8.8, 4.8, 1H), 3.34 (s, 3H), 3.22 (dd, J = 8.8, 7.7, 1H), 2.75 (m, 1H), 1.76 (s, 3H), 1.11 (br s, 6H), 1.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 177.37, 132.11, 131.15, 127.80, 126.77, 76.36, 59.06, 51.50, 48.27, 42.26, 41.00, 25.20, 22.55, 22.24, 22.17; HRMS calcd for $C_{15}H_{25}O_3^+$ 253.1804, found 253.1803; purity (^{1}H NMR) >95%.

[Os(NH$_3$)$_5$\{methyl 2-methyl-2-[3-methyl-4-(1-methyl-3-oxobutyl)-cyclohexa-2,5-dien-1-yl]propanoate\}](OTf)$_2$ (12). On the basis of the typical procedure, the tandem addition of 3-penten-2-one and MMTP to toluene complex (334 mg, 0.502 mmol) was carried out by allowing 15 min for the electrophilic addition step and 2 h for the nucleophilic attack to optimize the yield of the product complex. The reaction mixture was quenched into 50 mL of 1:1 Et_2O/CH_2Cl_2, and then 100 mL of hexanes was added to afford an ivory precipitate (382 mg, 86%), which was filtered through a fritted funnel, washed with Et_2O, and dried in vacuo. ^{1}H NMR (300 Hz, CD_3CN): δ 5.49 (m, 1H), 3.99 (br s, 3H, trans NH_3), 3.71 (s, 3H), 3.40 (m, 1H), 3.06 (m, 1H), 2.94 (br s, 12H, cis NH_3), 2.59 (m, 2H), 2.39 (d, J = 5.3, 1H), 2.09 (s, 3H),

1.96 (m, 2H, overlapped by CD_3CN), 1.72 (br s, 3H), 1.29 (s, 3H), 1.24 (s, 3H), 1.01 (d, $J = 7.3$, 3H). ^{13}C NMR (CD_3CN): δ 180.61, 139.33, 124.76, 52.97, 50.21, 49.97, 49.22, 47.40, 46.09, 33.45, 30.59, 26.13, 22.85, 2081, 19.01, CO not observed for the ketone substituent. $E_{1/2} = 0.66$ V. Purity (^1H NMR, CV): 73%.

6-(Hydroxymethyl)-7-iodo-3,3-dimethyl-3a,6,7,7a-tetrahydro-1-benzofuran -2(3*H*)-one (13). To a solution of compound **1** (176 mg, 0.786 mmol) in 5.0 g of CH_3CN were added chlorotrimethylsilane (256 mg, 2.36 mmol) and NaI (358 mg, 2.39 mmol), and the reaction was refluxed for 18 h. After CH_3CN was evaporated, the reaction residue was dissolved in 5 mL of water and extracted with 50 mL of ether. The organic layer was dried over Na_2SO_4, and the subsequent evaporation of ether yielded the product acid (141 mg, 85%), which was then dissolved in a saturated $NaHCO_3$ aqueous solution (0.6 g). To the above solution, a solution of I_2 (158 mg, 0.622 mmol) and KI (112 mg, 0.675 mmol) in water (3.0 g) was added over the course of 1 h. The reaction mixture was stirred for an additional 1 h before a 10% $Na_2S_2O_4$ solution was added until the yellow color faded. $CHCl_3$ (30 mL) was added for extraction and then evaporated to yield the crude product which was redissolved in 1:1 $CHCl_3$/ether (1.0 g) and crystallized overnight by solvent evaporation to afford a yellow compound (212 mg, 98%). ^1H NMR (300 Hz, $CDCl_3$): δ 5.82 (m, 2H), 4.95 (t, $J = 7.3$, 1H), 4.51 (dd, $J = 7.7$, 6.6, 1H), 3.81 (m, 2H), 2.96 (m, 1H), 2.82 (m, 1H), 1.33 (s, 3H), 1.19 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 180.78, 128.43, 124.34, 80.38, 65.73, 46.36, 45.33, 43.37, 26.70, 25.73, 22.61. Purity (^1H NMR): >90%.

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Supporting Information Available: Tables of X-ray crystallographic data and an ORTEP diagram. This material is available free of charge via the Internet at http://pubs.acs.org.

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