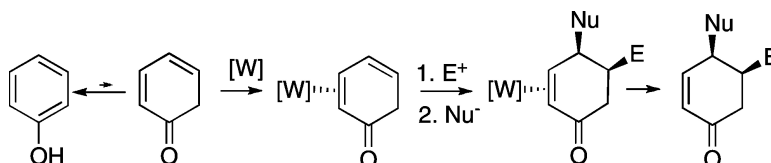


Communication

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Stereoselective Umpolung Tandem Addition of Heteroatoms to Phenol

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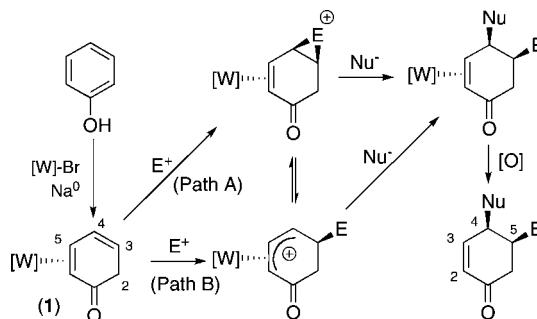
Although phenol normally exists in solution as an enol, when coordinated to a transition metal, its dienone tautomers can become energetically competitive. For example, the dihapto-coordinated phenol complex, $\text{TpW}(\text{NO})(\text{PMe}_3)(5,6\text{-}\eta^2\text{-phenol})$, **1**, can be isolated as a single diastereomer of the 2*H*-phenol tautomer.^{1,2} This nonaromatic form of phenol was recently reported to undergo regioselective [2 + 2] cycloaddition reactions with ketenes.² Interestingly, the electrophilic carbon of the ketene was found to selectively add to C3, suggesting that the meta carbon of the phenol ring was nucleophilic. This observation was an umpolung of the reactivity pattern normally associated with phenol, in which electrophiles add to C2, C4, or oxygen.³ We speculated that this [2 + 2] cyclization occurs sequentially, passing through an allyl cation intermediate that is stabilized by the electron-rich tungsten atom (Scheme 1).² The aim of the present study was to determine if this reaction pattern could be generalized for independent combinations of electrophiles and nucleophiles.

Previously reported tandem addition sequences with dihapto-coordinated arene complexes were initiated by the addition of a proton or carbon-based electrophile.^{4–7} Heteroatomic electrophiles are generally strong oxidants and were found to be incompatible with this electron-rich W(0) system. However, the dienone ligand of complex **1** is an excellent π -acid which has the effect of considerably raising the reduction potential of the metal ($E_{\text{p,a}} = +0.80$ V, cf -0.18 V for the anisole analogue (NHE)).¹ We reasoned that this property would improve the chances that a ligand-centered reaction could pre-empt a reaction occurring at the metal (e.g., oxidation).

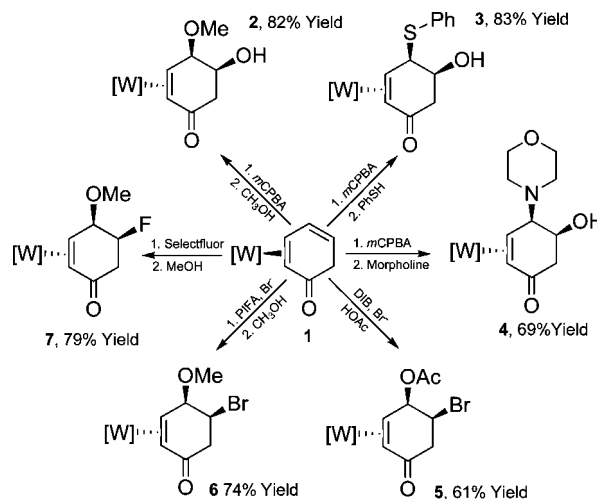
Our initial aim was to oxygenate C3 of the bound phenol of **1**, either directly (see Scheme 1, path B) or through an epoxide intermediate (path A) that could be opened with a suitable nucleophile.⁸ Gratifyingly, when *meta*-chloroperbenzoic acid (*m*CPBA) was added to $\text{TpW}(\text{NO})(\text{PMe}_3)(\eta^2\text{-2H-phenol})$ in CH_2Cl_2 , at 0 °C, followed by methanol, the addition proceeded smoothly to form the alkoxyhydroxyenone **2**, as a single diastereomer, in 82% yield (Scheme 2). Of note, *m*CPBA has previously been used in our laboratories (unpublished observations) to oxidatively decompose alkene and arene complexes of $\{\text{TpW}(\text{NO})(\text{PMe}_3)\}$, but in this case, no metal oxidation was apparent. An analysis of NMR and X-ray crystallographic data (Figure 1) indicates that both electrophilic (OH) and nucleophilic (OMe) additions occur *anti* to the metal fragment. Key spectral features include $J_{3,4}$ and $J_{4,5}$ coupling constants of 3.0 Hz, indicating $\text{HC}^3\text{C}^4\text{H}$ and $\text{HC}^4\text{C}^5\text{H}$ dihedral angles in the range of 60–90°. The X-ray structure also confirms the regiochemistry of the addition.

In order to test the generality of this reaction with other nucleophiles, *m*CPBA was added, followed by thiophenol, to give complex **3** in 83% yield. NMR data show a triplet at 4.56 ppm

Scheme 1. Stepwise Addition of An Electrophile and A Nucleophile to $\text{TpW}(\text{NO})(\text{PMe}_3)(\eta^2\text{-2H-phenol})$; [W] = $\{\text{TpW}(\text{NO})(\text{PMe}_3)\}$



Scheme 2. The Synthesis of Complexes **2–7**; [W] = $\text{TpW}(\text{NO})(\text{PMe}_3)$



(H4) with 3.0 Hz coupling constants, analogous to that observed for **2**, implying that the tandem addition has similar stereochemistry. A sequential addition of *m*CPBA and morpholine yielded the aminohydroxyenone **4** in 69% yield. The H4–H3 coupling constant of **4** (4.5 Hz) is slightly larger than that for **2** and **3**, but single-crystal X-ray diffraction analysis (Figure 1) reaffirms the *cis*-tandem addition away from the metal.

We endeavored to expand the scope of this reaction to other heteroatomic electrophiles. Recently, Kirschning et al. developed a method for the functionalization of olefins by oxidizing halide anions with diacetoxyiodobenzene (DIB).^{9,10} True to expectation, when a solution of DIB and Ph_3PMeBr (MTPBr) in acetic acid is added to **1**, bromoacetoxylation results in analogue **5** in 61% yield. This complex is water-sensitive both in solution and in the solid state and decomposes to form a paramagnetic material within approximately 1–2 days. While this reaction may be performed in air, the complex should be stored under an inert atmosphere.

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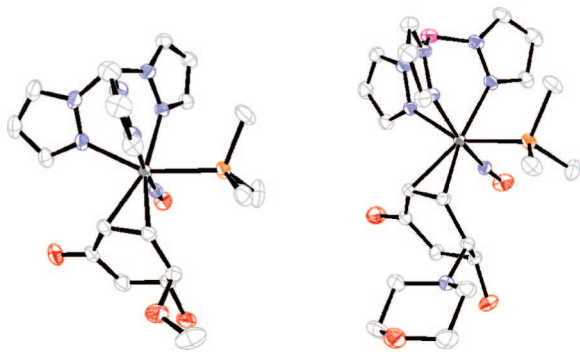


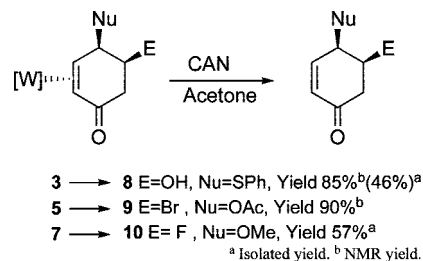
Figure 1. Ortep diagram of complexes **2** and **4**.

Attempts to generalize the DIB-mediated addition of the brominium ion using other nucleophiles failed, yielding either no reaction or mixtures of complexes containing **5**. To circumvent this problem an alternate oxidant, phenyliodobis(trifluoroacetate) (PIFA), was used. The trifluoroacetate groups in PIFA are less nucleophilic than the acetate groups in DIB and do not react with the presumed allyl cation intermediate. A solution of PIFA and MTPBr in methylene chloride was added to **1** at $-40\text{ }^{\circ}\text{C}$, followed by methanol to generate the bromo-methoxy analogue **6** in 74% yield. This reaction must be run at low temperature because the intermediate complex is unstable under ambient conditions. As with **5**, this complex is water-sensitive.

We surmised that the instability of **5** and **6** was likely due to the facile elimination of Br^- . The stepwise addition of Selectfluor (Aldrich) to **1** followed by MeOH produced complex **7**, the fluorinated analogue of **6**, in 79% yield. As with **1–6**, the electrophilic fluorine atom was determined by spectroscopic data ($J_{\text{CF}} = 174\text{ Hz}$) to add to C3 and *anti* to the tungsten. Unlike **5** or **6**, **7** is not water-reactive.

The delicate enone ligands of **1–7** can be liberated from the metal by oxidative decomplexation. For example, the ligand 5-hydroxy-4-(phenylsulfanyl)cyclohex-2-enone, **8**, can be isolated in 46% yield by the action of ceric ammonium nitrate (CAN) on **3** followed by chromatography. A similar procedure allowed for the in situ production of 5-bromo-4-acetoxycyclohex-2-enone, **9**, and 5-fluoro-4-methoxycyclohex-2-enone, **10**. Attempts to purify either of these materials resulted in significant elimination of HX and rearomatization to 4-acetoxy- and 4-methoxyphenol, respectively.

An electron-rich tungsten complex $\{\text{TpW}(\text{NO})(\text{PMe}_3)\}$ has been shown to trap phenol as its *2H*-phenol tautomer and reverse the



polarization of C3 and C4. Thus, oxygen, bromine, and fluorine electrophiles may be combined with oxygen, sulfur, and nitrogen nucleophiles to regio- and stereoselectively convert phenol into *cis*-4,5-disubstitued cyclohex-2-en-1-ones. The versatility of this reaction sequence and its stereofidelity coupled with the ease in handling of synthon **1**¹¹ make this a potentially valuable new method for the preparation of functionalized cyclohexenones.

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Supporting Information Available: Full synthetic details for the preparation of compounds **2–8**, selected spectra of these compounds, and crystallographic information for **2** and **4**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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