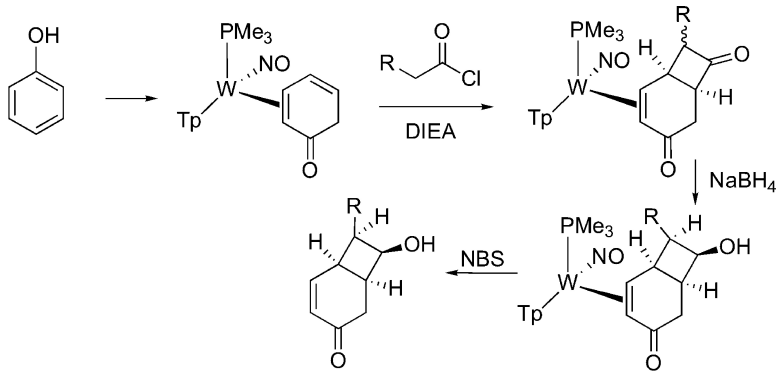
Communication

[2+2] Cycloaddition Reactions with a Tungsten-Stabilized 2*H*-Phenol

Michael A. Todd, Michal Sabat, William H. Myers, and W. Dean Harman

J. Am. Chem. Soc., **2007**, 129 (36), 11010-11011• DOI: 10.1021/ja0739279 • Publication Date (Web): 18 August 2007



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 2 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

J|A|C|S
COMMUNICATIONS

Published on Web 08/18/2007

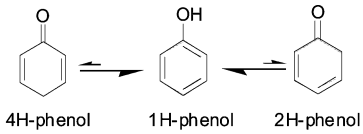
[2+2] Cycloaddition Reactions with a Tungsten-Stabilized 2*H*-Phenol

Michael A. Todd,† Michal Sabat,† William H. Myers,# and W. Dean Harman*,†

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22904-4319, and Department of Chemistry, University of Richmond, Richmond, Virginia 23173

Received June 13, 2007; E-mail: wdh5z@virginia.edu

Phenol exists in solution as three tautomers. Normally, the enol form (1*H*-phenol) is heavily favored (6−10 kcal/mol)[1] because of its aromatic stability. However, the nonaromatic 2*H*- and 4*H*-phenols, both dieneones, are also present, even if their low concentrations make them difficult to observe. As such, the chemistry of phenols is dominated by the 1H isomer or its conjugate base. This typically involves O-alkylation or electrophilic addition to the ortho and/or para positions.[2]



(1)

Coordination of phenol to a transition metal can have a profound effect on this equilibrium. Binding through the oxygen might be expected to enhance the stability of 1*H*-phenol relative to its tautomers. However, coordination through one or more of the π bonds can capture the enone forms.[3,4] We recently reported that the phenolic ligand of TpW(NO)(PMe_3)(η^2-phenol) (**1a**,**b**) is isolated as the 2*H*-phenol tautomer, a species that contains an *uncoordinated and localized* C=C bond.[5] We envisioned gaining access to the chemistry of a dienone isomer of phenol in this manner. To test this hypothesis we sought a reaction type that was general for unactivated alkenes, one which did not depend on an enolate (phenolate) intermediate. The [2+2] cycloaddition reaction of ketenes with alkenes to form cyclobutanones has been well documented,[6,7] and we know of no reports of this cycloaddition with phenol, so this seemed an ideal test case.

The complex TpW(NO)(PMe_3)(η^2-2*H*-phenol) exists in solution as a mixture of two diastereomers differing by which face of the C_5=C_6 bond is coordinated. These isomers can be interconverted in basic solution passing through a purported η^2-phenolate intermediate.[5] In methanol, however, one of the diastereomers, **1b**, selectively precipitates from the solution. We reasoned that stirring a mixture of **1a**,**b** in a basic solution could increase the isomerization rate sufficiently that the insolubility of **1b** could drive the system toward this isomer (Scheme 1).

Thus, a 1:1 mixture of TpW(NO)(PMe_3)(η^2-phenol) (**1a**/**1b**) was stirred in methanol using a catalytic amount of DBU (0.25 equiv) under an argon atmosphere for 72 h. Simple filtration delivered **1b** in 81% yield. The remaining complex in the filtrate was then recycled. This method allowed us to generate a single isomer of the air-stable 2*H*-phenol complex **1b** on a large scale (3−6 g).

Of the methods available for generating ketenes we found the dehydrohalogenation method to be the most convenient:

(2)

True to expectation, the addition of chloroacetyl chloride to a solution of **1b** and diisopropylethylamine (DIEA) in CH_2Cl_2 affords the cycloadduct **2a**,**b** in 92% yield as a 1.4:1 mixture of diastereomers (Scheme 2). These isomers were found by NMR studies to vary by the relative stereochemistry at C7. The H7−H6 coupling constant for **2a** (9.0 Hz) indicates a cis relationship between these protons resulting from the endo cycloadduct.[8,9] By comparison the exo cycloadduct, **2b**, has a smaller coupling constant ($J_{H6,H7}$ = 6.9 Hz). The cycloaddition proceeds with complete regioselectively with the C3 carbon of the 2*H*-phenol ligand adding to the electrophilic carbon (C1) of the ketene. We propose that this cycloaddition is sequential, where the tungsten stabilizes the allyl cation intermediate (Scheme 2). A similar two-step mechanism has been proposed for η^4-iron triene complexes.[10] Note that this reaction represents an umpolung for phenol in which a meta carbon of the originating phenol displays nucleophilic character. The reaction is stereoselective at C3 and C4 of **1b**, adding exclusively anti to the bulky tungsten metal fragment. The cyclobutanone (1787 cm^{-1}) and cyclohexenone (1621 cm^{-1}) carbonyl stretches for **2** are well separated, owing in part to the significant backbonding interaction for the latter. ^{1}H NMR spectra also show characteristic doublet of doublets at 5.22 ppm (**2a**) and 4.77 ppm (**2b**) corresponding to H7.

Similar reactivity is seen for 3-methoxyphenylacetyl chloride (generated in situ from 3-methoxyphenylacetic acid and oxalyl chloride),[11] which forms **3a**,**b** in 81% combined yield. While this reaction also generates two diastereomers which are C7 epimers (dr = 2:1 **a**/**b**), they can be easily separated by exploiting their solubility differences in acetone. The less soluble **3b** is conveniently separated from **3a** by filtration of an acetone suspension. Attempts were made to interconvert the diastereomers using various bases, Lewis acids, or combinations thereof, with the hope of generating one isomer (vide supra), but to no avail. Like **2**, these isomers were characterized by IR, NMR, and electrochemistry, and the assignment of **3b** as the endo isomer was confirmed by an X-ray crystal structure of its derivative **5** (vide infra). (The ORTEP diagram of **5** is shown in Figure 1.) The endo/exo ratio observed for both **2a**,**b** and **3a**,**b** is consistent with previous studies that have shown that there is a preference for endo selectivity with respect to bulky substituents.[12]

The dichloroketene generated from dichloroacetyl chloride provided cyclobutanone **4** but in only 90% purity. Stirring the crude product as a suspension in EtOAc for 5 min resulted in crystalline **4** (65%), which was readily characterized through analogy to **2** and **3**. The reaction of chloropropionyl chloride or 2-phenoxyacetyl chloride with base and **1b** resulted in intractable mixtures while diphenylketene failed to react with **1b**.

† University of Virginia.
# University of Richmond.

10.1021/ja0739279 CCC: $37.00

With several [4.2.0] dione complexes in hand we sought to

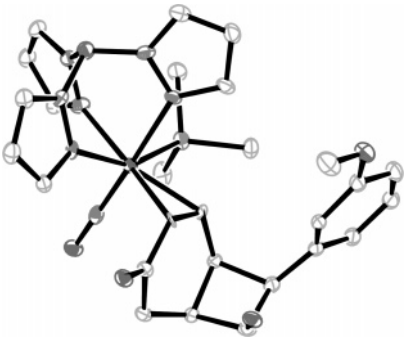
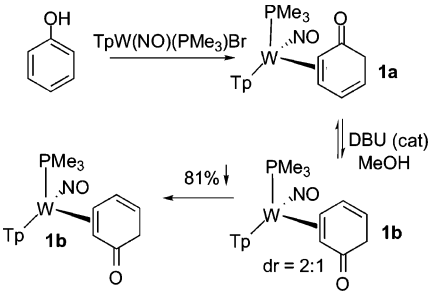
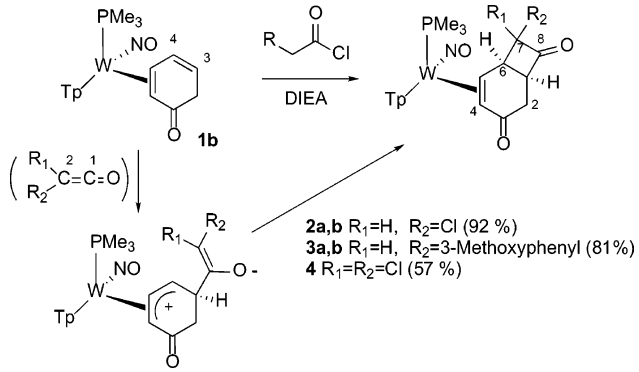


Figure 1. ORTEP diagram of cyclobutanol complex **5**.

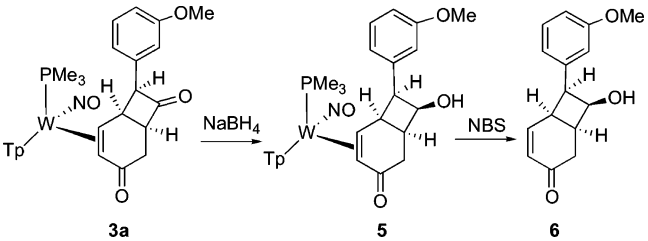
Scheme 1. The Synthesis of One Isomer of TpW(NO)(PMe$_3$)(η^2-Phenol)



Scheme 2. The Regio- and Stereoselective Addition of Ketenes to the 2*H*-Phenol Complex **1b**



Scheme 3. Reduction of the Cyclobutanone Carbonyl and Subsequent Oxidation

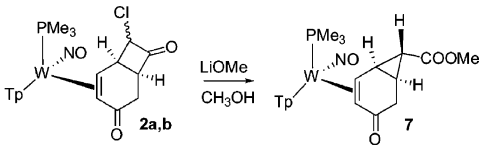


demonstrate how the metal could chemically differentiate the two carbonyls. When $NaBH_4$ was added to a solution of **3a** the reduction of the cyclobutanone proceeded with high stereoselectively, resulting in a single isomer of the cyclobutanol complex **5** (Scheme 3). A crystal structure determination reveals that the addition of a hydride occurs anti to the phenyl group and that the initial cycloaddition generated the endo isomer (**3a**). Even in the presence of an excess of reducing agent, the η^2-bound cyclohexenone resisted reduction, owing to significant electron donation from the tungsten into the enone π system.

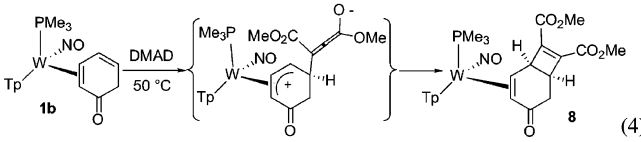
The *endo*-7-arylbicyclo[4.2.0]octane core of **5** is found in the immunosuppressants SNF4435 C and D.[13] Given the potential interest in this ligand by others, we attempted its demetallation with NBS. The free cyclobutanol **6** could be isolated in 48% yield after chromatography.

α-Chlorocyclobutanones are known to undergo ring contraction under basic conditions,[7] and we were curious what impact the coordinated tungsten would have on this reaction for **2**. When **2a**,**b** was stirred in a mixture of lithium methoxide and methanol the butanone ring smoothly contracted forming the cyclopropyl methyl ester complex **7** in 58% yield (eq 3). Of note, both exo and endo isomers of **2** react to form exclusively the exo isomer of **7** (J_{H7-H6} = 3.6 Hz, J_{H6-H1} = 4.5 Hz).[14]

Finally, we briefly surveyed the reactivity of **1** with electron-deficient alkenes and alkynes. While most[15] failed to react under neutral conditions, dimethylacetylenedicarboxylate (DMAD) reacted over several hours at 50 °C to form **8**. After chromatography, this complex appeared pure by NMR and IR; however, electrochemical measurements revealed an unexpected feature (~40%, $E_{1/2}$ = −1.51 V, NHE) that suggests the presence of a paramagnetic impurity that could not be removed by chromatography or recrystallization.



(3)



(4)

In summary, the η^2-complexation of phenol exposes an isolated alkene fragment of the 2*H*-phenol tautomer, which can undergo a regio- and stereoselective [2+2] cycloaddition with ketenes or DMAD. Reduction or ring-contraction of the (chloro) cyclobutanone occurs without interference from the metal-protected enone.

Acknowledgment. This work was supported by the NSF (Grants CHE-0111558 (U.V.A.), 9974875 (U.V.A.), 0116492 (U.R.) and 0320669(U.R.)).

Supporting Information Available: Full synthetic details for the preparation of cycloadducts **2**−**8** and selected spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Shiner, C. S.; Vorndam, P. E.; Kass, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 5699−5701.
(2) Roberts, R. M.; Khalaf, A. A. *Friedel-Crafts Alkylation Chemistry: A Century of Discovery*; Marcel Dekker Inc.: New York, 184.
(3) Amouri, H.; Le Bras, J. *Acc. Chem. Res.* **2002**, *35*, 501−510.
(4) Kopach, M. E.; Harman, W. D.; Hipple, W. G. *J. Am. Chem. Soc.* **1992**, *114*, 1736−1740.
(5) Todd, M. A.; Grachan, M. L.; Sabat, M.; Myers, W. H.; Harman, W. D. *Organometallics* **2006**, *25*, 3948−3954.
(6) *The Chemistry of Ketenes, Allenes and Related Compounds*; John Wiley & Sons: New York, 1980.
(7) Brady, W. T. *Tetrahedron* **1981**, *37*, 2949−2966.
(8) Sutcliffe, L. H.; Walker, S. M. *J. Phys. Chem.* **1967**, *71*, 1555−1557.
(9) Miller, R. D.; Dolce, D. L.; Merritt, V. Y. *J. Org. Chem.* **1976**, *41*, 1221−1228.
(10) Ito, S.; Yokoyama, R.; Asao, T.; Watanabe, M.; Harada, N.; Morita, N. *J. Organomet. Chem.* **2002**, *648*, 164−175.
(11) Brady, W. T.; Giang, Y. F. *J. Org. Chem.* **1985**, *50*, 5177−5179.
(12) Brady, W. T.; Roe, R. J. *J. Am. Chem. Soc.* **1971**, *93*, 1662−1664.
(13) Beaudry, C. M.; Trauner, D. *Org. Lett.* **2005**, *7*, 4475−4477.
(14) Lambert, J. B.; Chelius, E. C.; Schultz, W. J.; Carpenter, N. E. *J. Am. Chem. Soc.* **1990**, *112*, 3156−3162.
(15) *N*-methylpropialamide, methyl acetylenecarboxylate, phenylacetylene, and 3-butyn-2-one.

JA0739279