4170 *Organometallics* **2003,** *22,* 4170−4171

Formation of *o*-Quinone Methides from η^2-Coordinated Phenols and Their Controlled Release from a Transition Metal To Generate Chromans

Sterling M. Stokes, Jr., Fei Ding, Philip L. Smith, Joseph M. Keane,
Michael E. Kopach, Ramiro Jervis, Michal Sabat, and W. Dean Harman*

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22904-4319

Received July 9, 2003

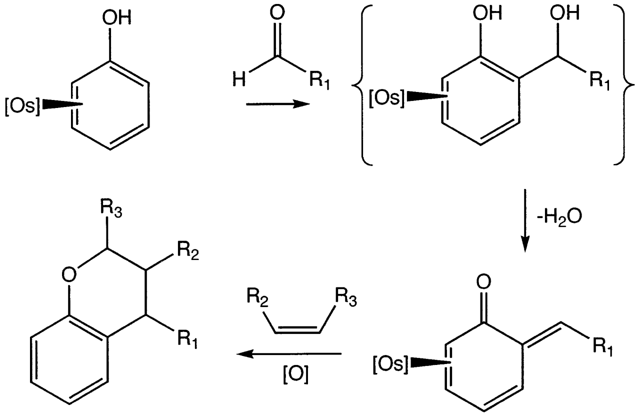
Summary: Phenol or p-cresol is bound to osmium(II) and combined with an aldehyde to generate remarkably stable η^2-coordinated o-quinone methide complexes. When these materials are treated with an oxidant (CAN, Cu(II)), the o-quinone methide is liberated and can be trapped with suitable alkenes to generate chromans.

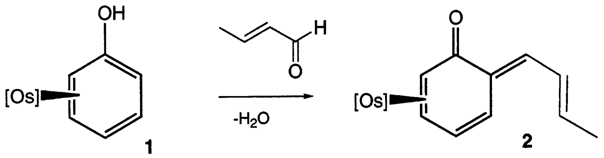
While quinone methides (QMs) are usually far too reactive to be isolated,[1] they represent an important class of intermediates in synthetic chemistry and in biochemistry.[2] In particular, *o*-QMs are valuable as precursors to chromans, serving as heterodienes for both inter- and intramolecular Diels−Alder reactions.[3] One of the most common methods for their generation is from the dehydration of *o*-hydroxybenzyl alcohols, by pyrolysis,[4] photolysis,[5] or catalysis by Lewis acids.[6] Recently, two independent research groups have reported examples of QMs stabilized by coordination to a transition metal.[7,8] If a hydroxybenzyl alcohol bound to a transition metal were to undergo dehydration, the resulting *o*-QM could be stabilized and subsequently released in the presence of a dienophile to form the chroman ring system.

Our longstanding interest in transition-metal-based dearomatization agents[9] led us to investigate the reactivity of η^2-phenol complexes with various carbon electrophiles.[10] Herein we wish to report that phenols, when bound to pentaammineosmium(II), readily react with aldehydes to generate complexes of *o*-quinone methides. While these complexes are remarkably stable, when exposed to air or dissolved in water, treatment with CAN oxidizes the metal and releases the intact QM ligand, which can be trapped by a suitable dienophile (Scheme 1).

Our first experience with this reaction was during an investigation of the Michael reactions with the compound $[Os(NH_3)_5(\eta^2\text{-phenol})](OTf)_2$ (**1**).[10] When **1** was treated with crotonaldehyde under neutral conditions, three osmium complexes were isolated. Although two of these were Michael adducts, the third was the product of an aldol condensation followed by dehydration to form the *o*-QM complex **2**.

Scheme 1. Metal-Promoted Formation of *o*-QM and Its Controlled Release





1 **2**

Repeating this reaction with acetaldehyde in place of crotonaldehyde resulted in the formation of the *o*-QM **3** along with small amounts of the η^2-acetaldehyde complex $[Os(NH_3)_5(\text{acetaldehyde})]^{2+}$.[11] The addition of a small amount of pyridine accelerated the aldol condensation, thus preempting ligand substitution. DEPT and ^1H NMR data for **3** indicate three downfield (6.5−7.1 ppm) and two upfield (4.7−5.2 ppm) methine resonances along with a methyl and two ammine signals, while ^{13}C NMR data include resonances corresponding to a carbonyl (199.8 ppm) and three uncoordinated methine carbons (133, 131, and 118 ppm). Homonuclear decoupling experiments and NOE data support the formation of the *E* diastereomer, as shown in Chart 1. While the NMR spectra indicated only one species present in a sample of **3**, cyclic voltammetry disclosed

---

* To whom correspondence should be addressed. E-mail: wdh5z@virginia.edu.

[1] McIntosh, C. L.; Chapman, O. L. *J. Chem. Soc., Chem. Commun.* **1971**, 771.

[2] Tomasz, M.; Chawla, A. K.; Lipman, R. *Biochemistry* **1988**, *27*, 3182.

[3] Boger, D. L.; Weinreb, S. N. *Hetero Diels−Alder Methodology in Organic Synthesis*; Academic Press: New York, 1987.

[4] Yato, M.; Ohwada, T.; Shudo, K. *J. Am. Chem. Soc.* **1990**, *112*, 5341.

[5] Diao, L.; Yang, C.; Wan, P. *J. Am. Chem. Soc.* **1995**, *117*, 5369.

[6] Chiba, K.; Hirano, T.; Y., K.; Tada, M. *Chem. Commun.* **1999**, 691.

[7] Milstein, D.; Vigalok, A. *Acc. Chem. Res.* **2001**, *34*, 798.

[8] Amouri, H.; Le Bras, J. *Acc. Chem. Res.* **2002**, *35*, 501.

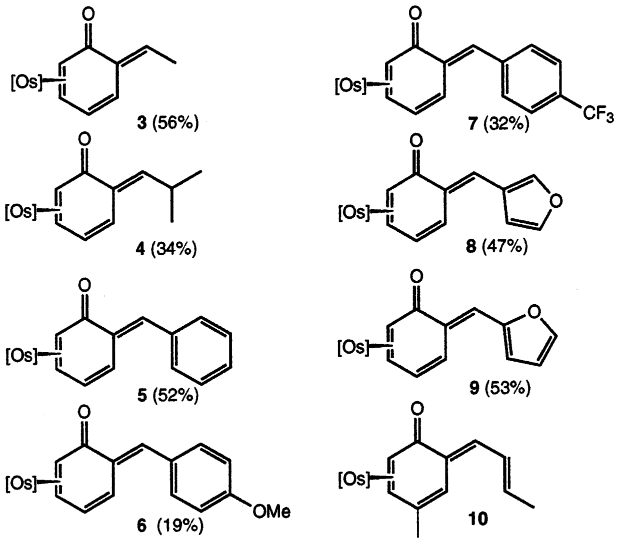
[9] Harman, W. D. *Chem. Rev.* **1997**, *97*, 1953−1978.

[10] Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 6581.

[11] Harman, W. D.; Sekine, M.; Taube, H. *J. Am. Chem. Soc.* **1988**, *110*, 2439−2445.

10.1021/om0305317 CCC: $25.00

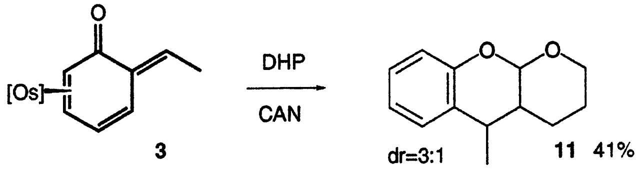
Chart 1



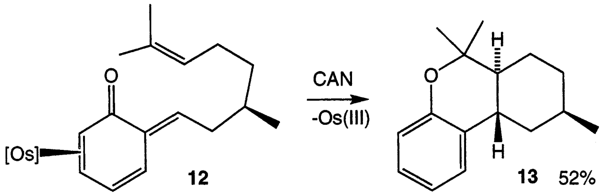
the presence of a significant byproduct (30−40%) characterized by a cathodic wave near −1.0 V vs NHE. Attempts to purify **3** by recrystallization resulted instead in isolation of the impurity, determined by X-ray diffraction (Supporting Information) to be the phenoxide complex $[Os^{III}(NH_3)_5(OPh)]^{2+}$. Attempts to remove this impurity from **3** (as the triflate salt) by recrystallization or chromatography were unsuccessful.

The phenol complex **1** also reacted with isobutyraldehyde, benzaldehyde, *p*-anisaldehyde, 4-(trifluoromethyl)-benzaldehyde, 3-furaldehyde, and 2-furaldehyde to form *o*-quinone methide complexes **4**−**9** (Chart 1). An *o*-QM complex derived from crotonaldehyde (**10**) was prepared by substituting the *p*-cresol complex for **1** in order to block the competing Michael reaction (vide supra). In all cases, ^1H and ^{13}C NMR data indicate formation of only one diamagnetic species, but electrochemical data indicate that the isolated materials contain ~40% Os(III). These *o*-QM complexes can be purified by a laborious procedure involving ion exchange chromatography followed by precipitation from water as the BPh_4^- salts,[11] but for ease we elected to use these materials without purification.

The *o*-QM complex **3** was found to be completely unreactive with electron-rich (e.g., dihydropyran) or electron-deficient dienes (e.g., *N*-methylmaleimide). However, when an acetonitrile solution of **3** was combined with an excess of 3,4-dihydropyran and 1.5 equiv of CAN, the tetrahydropyranochromene **11** was recovered in 41% yield (based on available *o*-QM), as a 3:1 ratio of diastereomers. Although **11** has not previously been prepared, ^{13}C and ^1H NMR data closely correspond to those of the nitromethyl analogue.[12]



An example of an intramolecular Diels−Alder reaction was achieved using the *o*-QM **12,** formed by treating the phenol complex **1** with (*R*)-citronellal and pyridine. Treatment of **12** with CAN effected demetalation and cycloaddition to form the benzo[*c*]chromene **13** in 52% yield. Proton NMR data indicate that **13** is formed as a single diastereomer, as was originally reported by Talley.[13] ^1H NMR data exactly match those reported for the isomer shown above.



Although the reactions reported herein do not occur with optimal efficiency, they represent a novel approach to the manipulation of QMs in which a transition metal promotes the formation and protects the QM for later use. Related to our findings, Milstein et al. have reported a palladium complex of an η^2-bound *p*-QM (derived from BHT) that sheds the free *p*-QM upon exposure to an electron-deficient alkene.[7] Given the exceptionally mild reaction conditions required for the π-base-promoted aldol condensation of a phenol and aldehyde and the ability to release the QM using a one-electron oxidant, η^2-coordinated QM complexes may prove to be useful tools for synthetic chemistry and biochemistry.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. This work was also supported by the NSF (Grant Nos. CHE0111558 and 9974875) and the NIH (NIGMS: Grant No. R01-GM49236).

Supporting Information Available: Text giving experimental preparations for **3**−**13** and an ORTEP diagram for $[Os(NH_3)_5(OPh)](OTf)_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

OM0305317

---

(12) Amantini, D.; Fringuelli, F.; Pizzo, F. *J. Org. Chem.* **2002**, *67*, 7238.

(13) Talley, J. J. *J. Org. Chem.* **1985**, *50*, 1695.