likely multiply as the diversity of available substrates expands. The concentration and purity of DHS synthesized by AB2834 *aro*E (pKD136) is a step in this direction. At the same time, microbial syntheses of DHS warn that plasmid-directed surges of carbon flow create a set of regulatory tenets beyond those originally selected by microbial evolution. Partially rate limiting DHQ synthase influenced only the purity of the DHS synthesized by *E. coli aro*E (pKD130A). For enzyme substrates situated after the common pathway and end products of aromatic amino acid biosynthesis, genomic factors could severely dissipate plasmid-directed surges in carbon flow. Surmounting these limitations has a direct bearing on the ultimate utility of microbial syntheses of prephenic acid, L-phenylalanine, and L-tryptophan which are essential to the assembly of (respectively) antibiotic bacilysin,[10] the artificial sweetener aspartame,[11] and indigo dyes.[12]

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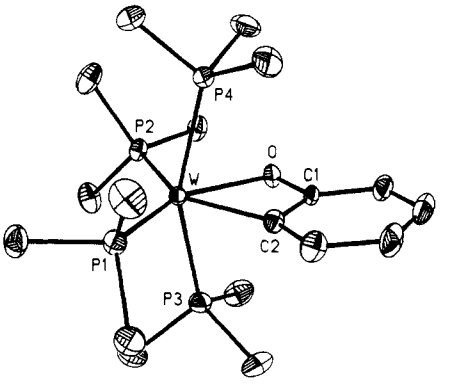


Figure 1. Molecular structure of $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$.

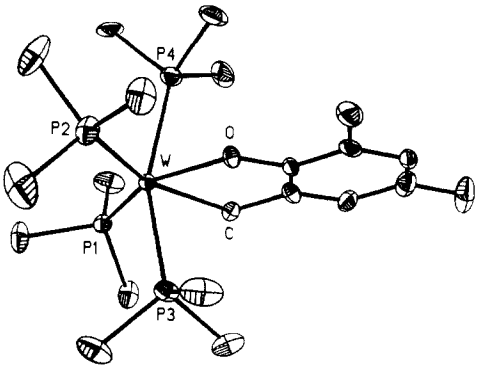
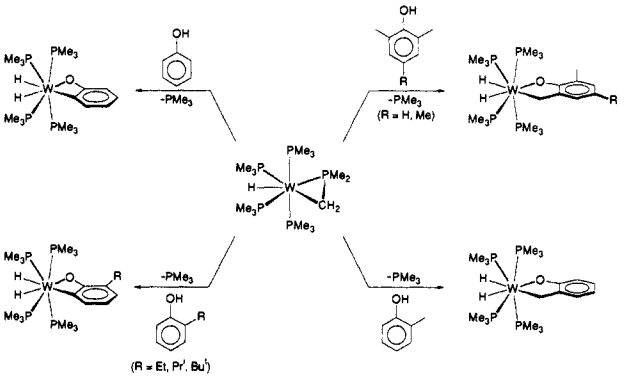


Figure 2. Molecular structure of $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_2Me_2(CH_2)\}$.

Scheme I



Competitive sp^3 and sp^2 C–H Bond Activation of Phenols by $W(PMe_3)_6$ and $W(PMe_3)_4(\eta^2\text{-}CH_2PMe_2)H$: Formation of Four- and Five-Membered Oxametallacycles

Daniel Rabinovich, Ross Zelman, and Gerard Parkin*

Department of Chemistry, Columbia University
New York, New York 10027

Received July 26, 1990

The susceptibility of the electron-rich complexes $W(PMe_3)_6$[1] and $W(PMe_3)_4(\eta^2\text{-}CH_2PMe_2)H$[2] toward oxidative addition suggests that these complexes may be candidates for selective C–H bond activation reactions.[3] Here we report that the reactions of both $W(PMe_3)_6$ and $W(PMe_3)_4(\eta^2\text{-}CH_2PMe_2)H$ with alkyl-substituted phenols result in selective C–H bond activation and formation of novel four- and five-membered oxametallacycles, in preference to the more commonly observed six-membered derivatives.

The reactions of $W(PMe_3)_4(\eta^2\text{-}CH_2PMe_2)H$ with phenols giving four- and five-membered oxametallacycles are summarized in Scheme I.[4] Identical products are also obtained from the analogous reactions with $W(PMe_3)_6$. The mechanism for the formation of the oxametallacycle derivatives most probably involves cyclometalation of an aryloxy–hydride intermediate (eq 1). Cyclometalation of the aryloxy ligand may occur at either

$$W(PMe_3)_4(\eta^2\text{-}CH_2PMe_2)H \xrightarrow{HArOH} [W(PMe_3)_5H(OArH)] \xrightarrow{-PMe_3} W(PMe_3)_4H_2(OAr) \quad (1)$$

the aryl ring or alkyl substituent. Thus, whereas phenol reacts to form the four-membered oxametallacycle $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$ as a result of sp^2 C–H bond activation at one of the ortho positions, the reaction with 2,6-dimethylphenol gives the five-membered oxametallacycle $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_3Me(CH_2)\}$ derived from sp^3 C–H bond activation at one of the methyl groups. Similarly, 2,4,6-trimethylphenol gives the five-membered oxametallacycle $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_2Me_2(CH_2)\}$. The presence of the four- and five-membered oxametallacycle rings in the complexes $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$[5] and $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_2Me_2(CH_2)\}$[6] has been confirmed by X-ray diffraction

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(4) All new compounds have been characterized analytically and spectroscopically.

(5) Crystal data for $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$: monoclinic, $P2_1/n$ (No. 14), a = 9.713 (2) Å, b = 16.008 (5) Å, c = 16.283 (2) Å, β = 93.51 (1)°, V = 2527.1 (9) Å^3, Z = 4, ρ_{calcd} = 1.53 g cm^{-3}, μ(Mo Kα) = 51.0 cm^{-1}, λ(Mo Kα) = 0.710 73 Å (graphite monochromator); 2364 unique reflections with $3° < 2\theta < 40°$ were collected of which 1981 with $F > 6\sigma(F)$ were used in refinement; R = 0.0262, R_w = 0.0356, GOF = 1.055.

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(Figures 1 and 2). Although the hydride ligands were not located, on the basis of steric grounds they are presumably located in the plane defined by P(3)-W-P(4), such that the overall coordination geometry is dodecahedral. Four-membered oxametallacycles,[7] which are of particular interest as potential models for olefin oxidation,[8] are rare compared with five- and six-membered derivatives.[9] Furthermore, four-membered oxametallacycles derived from ortho metalation of aryloxy ligands are surprisingly rare,[10] for which $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$ represents a structurally characterized example.

More interesting situations arise in the reactions of the monosubstituted phenols, $2\text{-}RC_6H_4OH$ (R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$), in which a variety of potential C-H bond activation reactions are now possible, leading to the formation of either four-, five-, or six-membered oxametallacycles. For example, the reaction of 2-methylphenol gives the five-membered oxametallacycle $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_3(CH_2)\}$ as a result of selective sp^3 C-H bond activation of the methyl substituent, in preference to the four-membered ortho-metalated alternative. However, in marked contrast, the corresponding reactions of the 2-ethyl-, 2-isopropyl-, and 2-*tert*-butylphenol derivatives give specifically the four-membered oxametallacycles as a result of selective sp^2 C-H bond activation at the ortho position.

The propensity for the formation of four-membered metallacycles within this system is striking, especially given the marked tendency of ortho-substituted *tert*-butyl groups in other systems to undergo facile metalation, with the resulting formation of six-membered oxametallacycles.[9] Although at present we cannot address the question whether the formation of four-membered versus six-membered oxametallacycles in this system represents a kinetic or thermodynamic preference, we note that one contributing factor may be a consequence of the 18-electron configuration of the tungsten centers in these oxametallacycles. The six-membered oxametallacycle complexes that are derived from aryloxy ligands typically possess electron-deficient metal centers. Structural studies on these oxametallacycles demonstrate that formation of the six-membered ring allows for large M-O-C bond angles, thus enabling favorable lone-pair donation from oxygen to the electron-deficient metal center.[9] Such lone-pair donation would clearly stabilize an oxametallacycle structure of an electron-deficient metal center. However, for the 18-electron complexes described here, lone-pair donation would not be expected to contribute significantly to oxametallacycle stability, and thus the preference for six-membered ring formation would be lessened.

Studies indicate that the four- and five-membered oxametallacycles are also highly reactive. For example, $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$ is hydrogenated rapidly by H_2 at room temperature to give $W(PMe_3)_4H_3(OC_6H_5)$.[11] Deuterium labeling demonstrates that this reaction proceeds via initial reductive elimination of the metallacycle-hydride unit (eq 2).

$$W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4) \rightarrow [W(PMe_3)_4H(OC_6H_5)] \xrightarrow{D_2} W(PMe_3)_4HD_2(OC_6H_5) \quad (2)$$

In conclusion, these studies have demonstrated the selectivity with which electron-rich tungsten complexes may form four- and five-membered oxametallacycle complexes, in contrast to the more commonly observed six-membered derivatives that are obtained for electron-deficient metal complexes.

Supplementary Material Available: Tables of spectroscopic data for all new compounds, crystal and intensity collection data, atomic coordinates, bond distances and angles, and anisotropic displacement parameters and ORTEP drawings (21 pages); tables of observed and calculated structure factors for $W(PMe_3)_4H_2(\eta^2\text{-}OC_6H_4)$ and $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_2Me_2(CH_2)\}$ (28 pages). Ordering information is given on any current masthead page.

(6) Crystal data for $W(PMe_3)_4H_2\{\eta^2\text{-}OC_6H_2Me_2(CH_2)\}$: monoclinic, $P2_1/n$ (No. 14), a = 9.898 (3) Å, b = 28.065 (9) Å, c = 10.663 (3) Å, β = 104.33 (2)°, V = 2870 (1) Å^3, Z = 4, ρ_{calcd} = 1.45 g cm^{-3}, μ(Mo Kα) = 44.9 cm^{-1}, λ(Mo Kα) = 0.710 73 Å (graphite monochromator); 4474 unique reflections with $3° < 2\theta < 48°$ were collected of which 2556 reflections with $F > 6\sigma(F)$ were used in refinement; R = 0.0455, R_w = 0.0451, GOF = 1.274.

(7) Examples of four-membered oxametallacycles include $(AsPh_3)_2Pt\{OC(CN)_2C(CN)_2\}$,[7a,b] $(PPh_3)_2Pt(CH_2OCH_2)$,[7c] $(\eta^5\text{-}C_5Me_5)(PMe_3)Ir(OCMe_2CH_2)$,[7d] $(\eta^5\text{-}C_5H_5)_2Ti\{OC(CH_2)CH_2\}$,[7e] $(\eta^5\text{-}C_5H_5)_2[Zr(OC_6H_8)]_2$,[7f] and $(\eta^5\text{-}C_5Me_5)_2Zr(OCPh{=}CPh)$.[7g] (a) Schlodder, R.; Ibers, J. A.; Lenarda, M.; Graziani, M. *J. Am. Chem. Soc.* **1974**, *96*, 6893-6900. (b) Lenarda, M.; Ros, R.; Traverso, O.; Pitts, W. D.; Baddley, W. H.; Graziani, M. *Inorg. Chem.* **1977**, *16*, 3178-3182. (c) Hoover, J. F.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 6466-6468. (d) Klein, D. P.; Hayes, J. C.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 3704-3706. (e) Ho, S. C.; Hentges, S.; Grubbs, R. H. *Organometallics* **1988**, *7*, 780-782. (f) Vaughan, G. A.; Hillhouse, G. L.; Lum, R. T.; Buchwald, S. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1988**, *110*, 7215-7217. (g) Vaughan, G. A.; Hillhouse, G. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 7994-8001.

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Peptide Architecture. Design of Stable α-Helical Metallopeptides via a Novel Exchange-Inert Ru^{III} Complex

M. Reza Ghadiri* and A. Katharina Fernholz

Departments of Chemistry and Molecular Biology
Research Institute of Scripps Clinic
La Jolla, California 92037

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There is considerable interest in the design of linear polypeptides that can adopt stable and well-defined solution conformations. Such systems can serve as models for the study of the early events in protein folding[1] as well as possess substantial utility in the design of peptide-based therapeutic agents.[2] However, in spite of a few encouraging results, design of short monomeric peptides with stable secondary structure conformations in water has not been forthcoming.[3] Here we report for the first time the utility of an exchange-inert metal complex[4,5] in the formation of remarkably stable α-helical peptides. Formation of a macrocyclic *cis*-$[Ru(NH_3)_4L_2]^{3+}$ complex, where L_2 are the side chains of two histidines in positions i and $i + 4$ of a peptide, is shown to be a simple and effective method for constraining the intervening chain in an α-helical conformation and effecting helix nucleation. A 17-residue polypeptide functionalized in this way has a melting

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