Osmium(II)-, Rhenium(I)-, and Tungsten(0)-Promoted Dipolar Cycloaddition Reactions with Pyrroles: Exploiting the Azomethine Ylide Character of This Heterocycle

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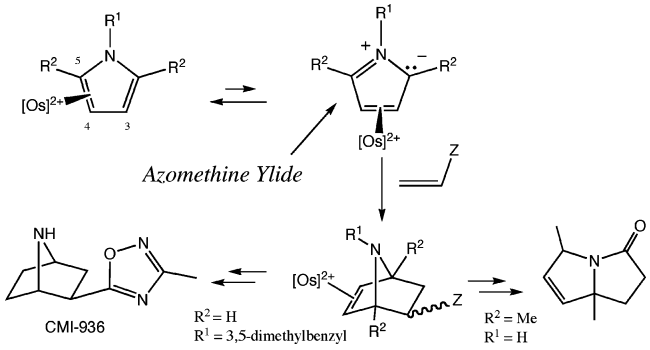
Complexes of the form TpRe(CO)(MeIm)(η^2-pyr) and TpW(NO)(PMe_3)(η^2-pyr) (where pyr = 1-methylpyrrole, 2-methylpyrrole, and 2,5-dimethylpyrrole) were prepared and combined with a range of potential dipolarophiles. In several cases a dipolar cycloaddition resulted in the formation of 7-azanorbornene complexes (one crystal structure for each metal is presented), but attempts to develop a general route to the organic bicyclic system were unsuccessful. Using the complex [$Os(NH_3)_5$(η^2-pyrrole)]$^{2+}$ an organic cycloadduct was successfully prepared with dimethyl fumarate, and this complex was elaborated into advanced synthons to several naturally occurring pyrrolizidines.

Introduction

Although uncommon in nature, the 7-azanorbornane ring system is found in a variety of acetylcholine receptor agonists that are currently of great interest to the medicinal community. In particular, epibatidine, first isolated from the skin of the poison dart frog *Epipedobates tricolor*, was initially reported by Daly et al. to be an extremely efficacious antinociceptive agent with a potency 200 times that of morphine.[1] Since then, an ever-increasing number of analogues have been reported,[2] including both nicotinic agonists such as epiboxidine[3] and muscarinic agonists such as CMI-936.[4] Since Daly's report in 1992, there have been over 50 syntheses reported for epibatidine,[5,6] and demand for this compound and its derivatives continues to grow.[7]

Our interest in the 7-azanorbornane ring system originated from work concerning the reactivity of dihapto-coordinated pyrrole complexes of osmium(II).[8] While the dearomatization agent pentaammineosmium(II) normally binds pyrroles across the C4 and C5 carbons, this species is in equilibrium with the C3−C4 isomer (Scheme 1). In the latter form, the *uncoordinated* portion of the pyrrole resembles an azomethine ylide and, as such, readily undergoes dipolar cycloadditions with a broad range of dipolarophiles to generate 7-azanorbornene complexes.[8] By this route, several novel azanorbornanes were ultimately prepared, including CMI-936.[4] In one case, a method was discovered to elaborate such an azanorbornene complex into a pyrrolizidine (see Scheme 1).[9]

Scheme 1



In recent years, we have sought alternatives to the pentaammineosmium(II) reagent that could be prepared more economically and with greater variation in coordination environment.[10] Of these, two systems, {TpReCO(MeIm)}[11] and {TpW(NO)(PMe_3)},[12] have emerged as viable alternatives, each forming stable dihapto-coordinated adducts with pyrroles. It is the intent of this study to assess the ability of these complexes to promote dipolar cycloaddition reactions for this heterocycle and to evaluate the synthetic potential of such a methodology. Both of these systems have previously been shown to promote dipolar cycloaddition reactions with furan.[13,14]

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† University of Virginia.
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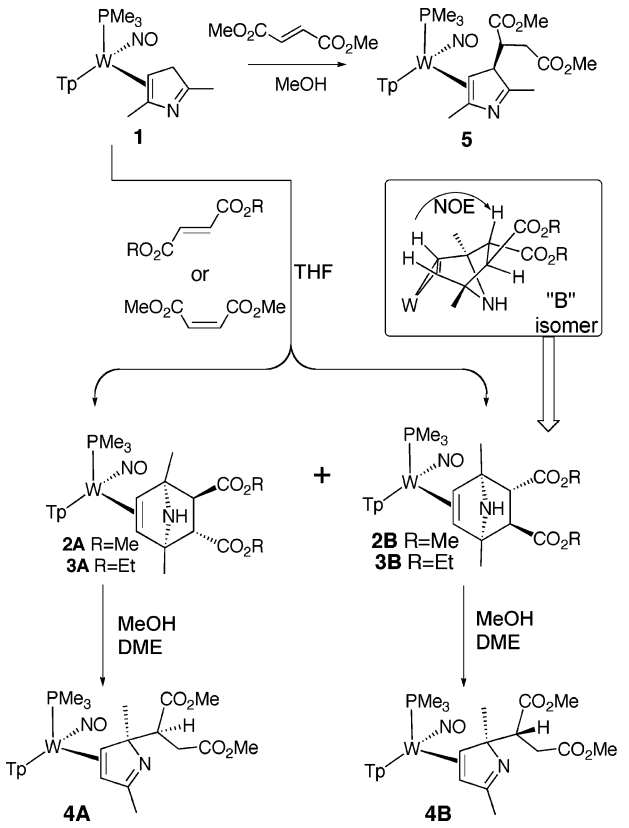
Scheme 2



Results and Discussion

2,5-Dimethylpyrrole was chosen for initial studies because the corresponding complex with osmium(II) showed the greatest reactivity with dipolarophiles.[8] Complex **1** was obtained by combining TpW(NO)(PMe_3)(η^2-benzene) (**6**) with an excess of 2,5-dimethylpyrrole as previously described.[12] In contrast to that observed for osmium, the heterocycle in **1** exists mainly as a 3*H*-pyrrole (Scheme 2). With tetrahedral geometry at the C3 carbon of **1**, the desired cycloaddition is not possible. However, the tautomerization of compound **1** back to the purported 1*H*-pyrrole followed by a linkage isomerization led to a successful reaction with either methyl or ethyl fumarate to provide the 7-azanorbornene complexes **2** and **3**. These materials were formed from a 0.6 M fumarate solution in THF and were recovered after 12 h in yields up to 85%. Cyclic voltammetry measurements of both complexes show irreversible oxidation potentials with $E_{p,a} = 700$ mV, a value that is similar to tungsten complexes of other isolated olefins.[15] Proton NMR data show that both **2** and **3** are formed initially as 1:1 mixtures of two isomers. Over time, **2B** selectively precipitates from the THF reaction solution, allowing its separation from **2A**. The ^{1}H NMR spectrum of **2A** shows two doublets of doublets at 1.50 and 2.89 ppm that include hydrogen−phosphorus coupling consistent with the metal binding the C3−C4 bond of the pyrroline ring. Quaternary bridgehead resonances in the ^{13}C NMR spectrum at 73.1 and 74.5 ppm also support the formation of an azanorbornene structure. Similarities in the spectroscopic features of **2A** and **2B** indicate their diastereomeric relationship. These complexes were ultimately determined to be the two *trans*-diester stereoisomers on the basis of coupling constants for the vicinal protons ($J_{HH} = 5.0-5.2$ Hz).[5,8] The remaining

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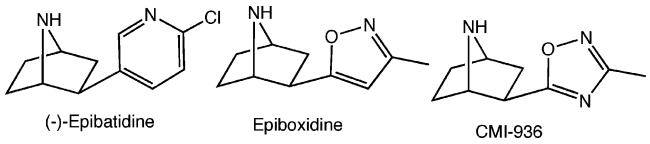


Figure 1. Several examples of acetylcholine receptor agonists containing the 7-azanorbornane ring system.

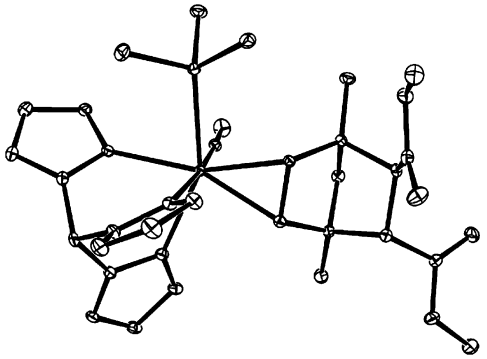


Figure 2. ORTEP diagram of the complex **2A**.

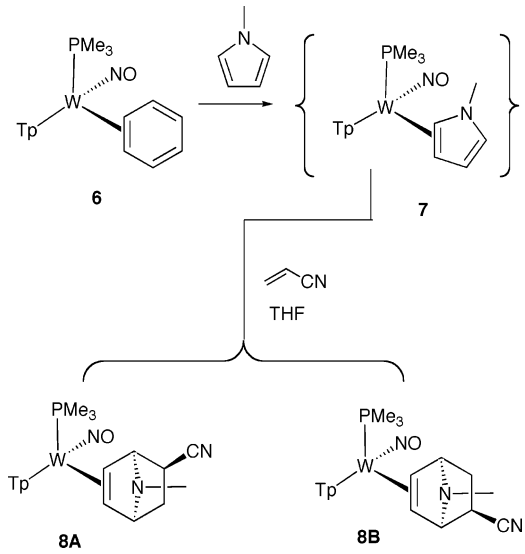
geometry of each diastereomer was determined through NOESY interactions between the endo α-proton of the ester and the corresponding olefin proton.[8] Curiously, reaction of the cis diester dimethyl maleate with **1** gives the same two azanorbornene products, **2A** and **2B**, as were identified from dimethyl fumarate, albeit in slightly lower total yield (66%). Crystals were obtained of **2A**, and the corresponding ORTEP diagram is shown in Figure 2. The metal binds in an exo geometry, consistent with the addition of the dipolarophile to the face of the pyrrole opposite that of metal coordination.

In an attempt to determine the mechanism (vide infra) responsible for the formation of the same products from either fumarate or maleate esters, cycloadduct **2B** was observed over time in a methanol-d_4/acetone-d_6 solution. Instead of the anticipated deuterium exchange reaction of the protons alpha to the ester groups, a new complex was observed to form. When the experiment was repeated using protiated methanol and DME, the new compound, **4B**, was isolated after 5 days in 70% yield as a single isomer (see Scheme 2). The resulting 2*H*-pyrrole complex (**4B**) is the result of the cycloadduct complex undergoing a retro-Mannich reaction. In analogous fashion **4A** was derived from **2A**. A similar event has been observed for pentaammineosmium(II) azanorbornene complexes in aqueous solution.[8] We note that complex **4** represents a net conjugate addition of dimethyl fumarate to C2 of a 2*H*-pyrrole complex. NOESY experiments show a correlation between the methyl at C2 and the trimethylphosphine ligand, indicating a stereoselective C−N cleavage at the position furthest from the phosphine (see Scheme 2).

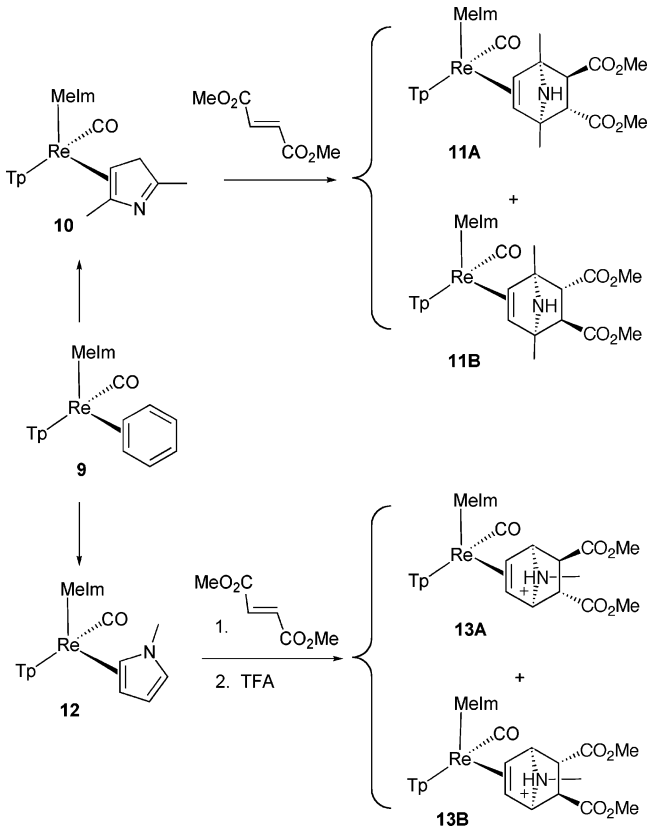
In contrast to what is observed in THF, when the 2,5-dimethyl-3*H*-pyrrole complex **1** is combined with dimethyl fumarate in methanol, the β-alkylated 3*H*-pyrrole complex **5** is formed (see Scheme 2). The proton NMR spectrum for **5** shows the presence of two β-addition products in a 4:1 ratio. The major isomer has a phosphorus-coupled doublet at 2.42 ppm, representing the proton at the metal-bound C4 position. Lack of proton−proton coupling between H3 and H4 indicates that the former proton is syn to the metal and suggests alkylation at C3. An irreversible oxidation wave at $E_{p,a} = 390$ mV is more similar to that of the 3*H*-pyrrole complex **1** than to the cycloadduct **2** or **3**.

No cycloaddition products are observed for the reaction of **1** and dimethyl fumarate in methanol. However, when DMF is

Scheme 3



Scheme 4



the solvent, a mixture of Michael addition (**5**) and cycloaddition products (**2**) is obtained.

Unfortunately the scope of dipolarophiles that react with the 3*H*-pyrrole complex **1** is limited. Treatment of **1** with more electron-deficient dipolarophiles such as *N*-methyl maleimide or maleic anhydride apparently leads to oxidation of the tungsten, as only paramagnetic materials are formed. Combining **1** with less electron-deficient, but more polarized alkenes (methyl acrylate, acrylonitrile) form only β-addition products similar to **5** (see Scheme 2).

Given the propensity of the 2,5-dimethylpyrrole complex to exist as its 3*H*-tautomer, we next considered a pyrrole in which this tautomerization was not possible. While the TpW(NO)(PMe$_3$)(η^2-1-methylpyrrole) complex **7** is too thermally unstable to be isolated, it can be synthesized in situ by dissolving the corresponding benzene complex (**6**) in 1-methylpyrrole. Addition of acrylonitrile to a solution of **7** affords the cycloaddition complex **8** as a mixture of four diastereomers. The two major species formed are the exo isomers **8A** and **8B** (2:1). Their stereochemistries were again determined from proton−proton coupling and NOE data (vide supra).[5,8] The minor isomers are believed to be the corresponding endo cycloadducts, with **8** showing an overall endo-to-exo ratio of 5:2 (Scheme 3). The scope of this reaction also proved to be narrow. Treatment of **7** with other dipolarophiles including methyl acrylate, (*E*)-methyl 3-(pyridin-3-yl)acrylate, methyl vinyl ketone, dimethyl fumarate, or fumaronitrile all resulted in the formation of paramagnetic products, consistent with oxidation of the tungsten.

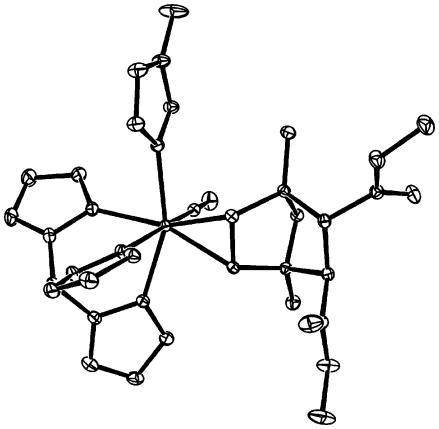


Figure 3. ORTEP (30% ellipsoids) for the complex **11B**.

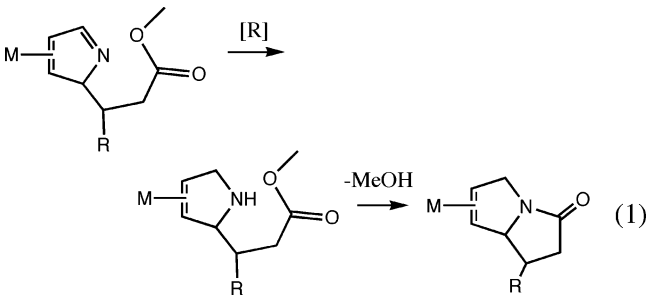
Analogous 2,5-dimethylpyrrole and 1-methylpyrrole compounds of the {TpRe(CO)(MeIm)} metal fragment can be synthesized and isolated from the rhenium η^2-benzene complex **9**.[11] Both of the resulting complexes **10** and **12** undergo cycloaddition reactions similar to those of the tungsten complex **1** when exposed to dimethyl fumarate (Scheme 4), giving **11** and **13**, respectively, each as a pair of diastereomers. The 1-methylpyrrole derivative was protonated before isolation to facilitate its separation from reactants. According to coupling and NOE data,[5,8] cycloadducts **11** and **13** also show a preservation of the trans stereochemistry of the fumarate in all the isolated diastereomers. The structure of **11B** was confirmed through X-ray crystallography, and its ORTEP diagram is shown in Figure 3.

Our attempts to form cycloadducts derived from the parent pyrrole were thwarted by our inability to obtain the corresponding pyrrole complex. For both the rhenium and tungsten systems, π coordination was pre-empted by a competing oxidative addition into the N−H bond of the pyrrole.[12] The desired complexes, TpRe(CO)(MeIm)(4,5-η^2-pyrrole) and TpW(NO)(PMe$_3$)(4,5-η^2-pyrrole), could not be prepared. The 2-methylpyrrole analogue could be generated for the rhenium system, but even after 3 days the rhenium 2-methylpyrrole complex showed no cycloadduct formation with a THF solution of dimethyl fumarate. Attempts to prepare the analogous tungsten-2-methylpyrrole complex resulted in the formation of TpW(NO)(PMe$_3$)H(1-(2-methylpyrrolyl).[12]

Previously, we have demonstrated that the organic ligand in osmium(II)-azanorbornene complexes analogous to **2**, **3**, **8**, **11**, and **13** could be removed from the metal by oxidative decomplexation. To avoid retro-cycloaddition, it was essential to first protonate the amine, then oxidize the metal, followed by hydrogenation of the previously coordinated double bond.[8] Attempts to perform this sequence with either a tungsten (**2** or

8) or rhenium cycloadduct (**11** or **13**) failed, with only intractable paramagnetic products being formed.[16]

Preparation of Pyrrolizidines. The pyrrolidine nucleus is found in numerous natural products besides azanorbornanes. Prominent examples include the pyrrolizidine, indolizidine, and tropane families of alkaloids. At the onset of our study, our hope was to develop new methods, not only for the formation of 7-azanorbornenes but also for other ring systems that could readily be derived from pyrroles. Specifically, we hoped that by utilizing 2*H*-pyrrolium complexes derived from the cycloadducts of esteric dipolarophiles (e.g., **4**), a pyrrolizidine nucleus could be obtained, according to eq 1, that could lead to the synthesis of pyrrolizidine alkaloids.



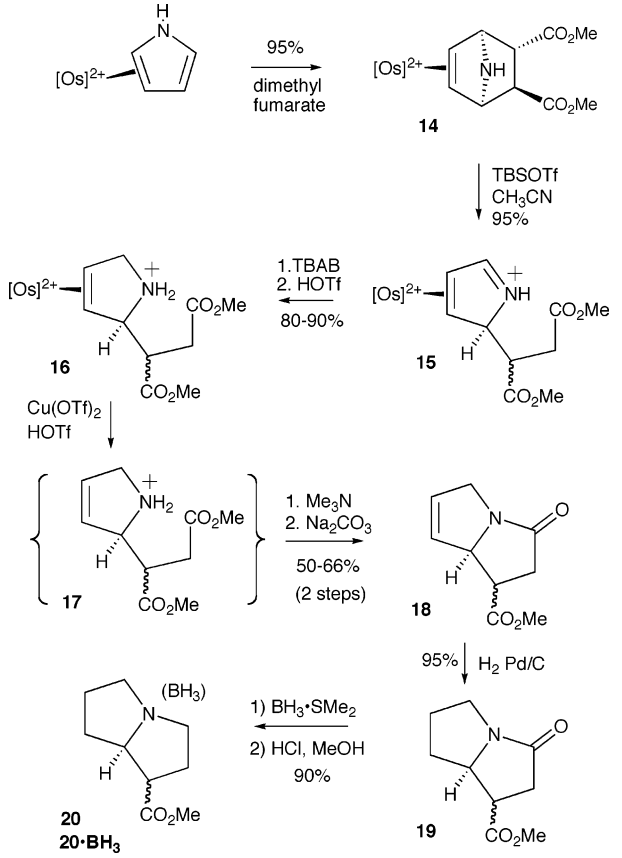
(1)

We have demonstrated this concept previously, but the resulting pyrrolizidinone had a bridgehead methyl group not found in natural products. To maintain a hydrogen at the bridgehead carbon, the prescribed cycloadduct needed to originate from pyrrole or a 2-substitued pyrrole. However, both rhenium and tungsten reagents were found to insert into the N−H bond of pyrrole.[12] Therefore, we returned to the pentaammineosmium(II) system to explore this synthetic approach.[9,17]

The pyrrole fumarate cycloadduct **14** was prepared in 95% yield according to the previously published procedure.[9] Treatment of **14** with TBSOTf or BF_3-etherate promoted a retro-Mannich ring opening of the strained 7-azanorbornene to yield the 2*H*-pyrrolium complex **15**. This complex was isolated as 1:1 mixture of diastereomers resulting from nonselective ring opening toward either the endo or exo carbomethoxy substituent (Scheme 5). The ^{1}H NMR spectrum of this complex is characterized by a downfield iminium singlet at 10.9 ppm and two methyl singlets at 3.74 and 3.75 ppm. The cyclic voltammogram features an irreversible oxidation wave $E_{p,a} = 1170$ mV, characteristic of an osmium(II)−2*H*-pyrrolium complex.[18,19] This material (**15**) was subsequently reduced with TBAB to form the pyrrolinium complex **16**. The action of $Cu(OTf)_2$ in the presence of HOTf led to a clean decomplexation of the protonated pyrroline, and subsequent workup with Me_3N followed by Na_2CO_3(aq) provided the pyrrolizinone **18** in 50−66% yield. Hydrogenation in the presence of Pd^0/C delivered **19**, a known synthon to the alkaloids labournine and isoretronecanol,[20,21] and further reduction of the amide provides **20**, an intermediate to supindine.[22]

Mechanism of Cycloaddition Reaction. Osmium(II) pyrrole complexes were first reported by Cordone et al. to undergo cycloaddition with maleic anhydride in 1989.[23] The mechanism for this reaction was subsequently investigated in considerable

Scheme 5



detail by Gonzalez et al.[8] In the latter paper, a mechanism involving a dipolar cycloaddition of an azomethine ylide intermediate was proposed on the basis of the following observations. The rate of cycloaddition depended strongly on the nature of ring substituents, with the fastest rates being observed for 2,5-dimethylpyrrole. In contrast, the 2-methylpyrrole complex has a reactivity with dipolarophiles that is dramatically lower than the parent pyrrole complex. The rationale offered for this observation was that the 2,3-η^2 and the 4,5-η^2 isomers were destabilized by the methyl substituents causing the equilibrium ratio of 3,4-η^2:(2,3-η^2 + 4,5-η^2) to increase. Also significant were the observations of only a mild solvent dependence and conservation of the stereochemistry with the two carbons originating from the C═C portion of the dipolarophile (e.g., for maleate and fumarate esters). The limited scope of cycloaddition reactions for Re and W in the present study prevents us from making such firm conclusions, but we expect this mechanism still holds. However, we note that in the cycloaddition of **1** with dimethyl maleate, the conversion of the stereochemistry to the trans configuration happens much more rapidly than was seen for osmium(II). This observation can be accounted for by considering several potential reaction pathways (Scheme 6). In path A, the cycloaddition occurs in a purely concerted fashion, preserving the cis stereochemistry, and this is followed by a retro-Mannich and Mannich sequence to form **2** or **3**. Regarding the zwitterionic intermediate, **2Z**,

(16) Oxidants tried for rhenium: CAN, $[FeCp_2]PF_6$, AgOTf with and without triflic acid added. For tungsten, AgOTf, with and without acid, with and without heating.

(17) A preliminary example of this methodology to create the hexahydro-1*H*-pyrrolizine ring system can be found in the following reference.

(18) Hodges, L. M.; Gonzalez, J.; Koontz, J. I.; Myers, W. H.; Harman, W. D. *J. Org. Chem.* **1995**, *60*, 2125.

(19) Myers, W. H.; Koontz, J. I.; Harman, W. D. *J. Am. Chem. Soc.* **1992**, *114*, 5684.

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(21) Le Coz, S.; Mann, A.; Thareau, F.; Taddei, M. *Heterocycles* **1993**, *36*, 2073.

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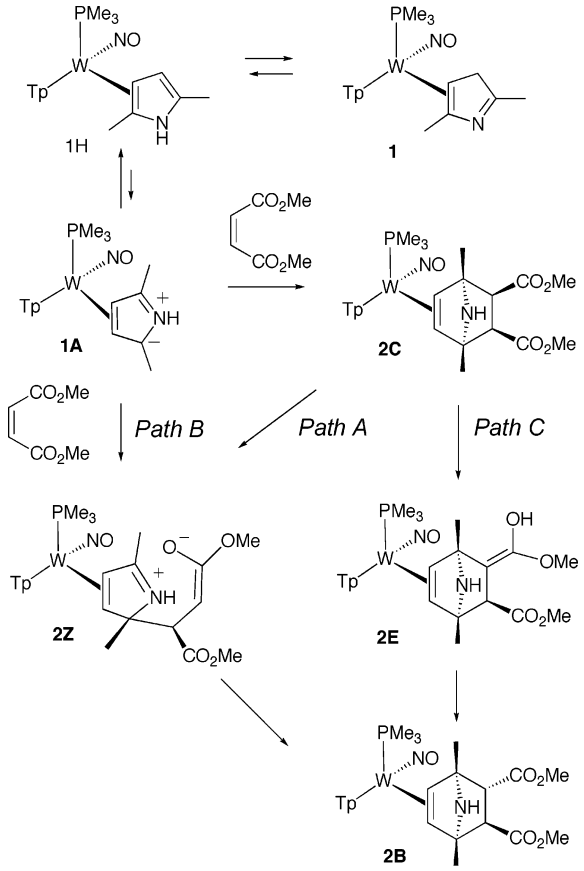
(23) Cordone, R.; Harman, W. D.; Taube, H. *J. Am. Chem. Soc.* **1989**, *111*, 5969.

Scheme 6



rotation can occur to minimize the steric interaction between the ester groups, and a subsequent ring-closure provides the observed trans stereochemistry. Pathway B represents a stepwise process involving a Michael reaction followed by a Mannich reaction. Again, rotation can occur at **2Z** before the ring-forming step. Finally, the α-epimerization of either ester group via **2E** could lead to an inversion of stereochemistry without opening up the bicyclic system (pathway C).

The ring opening of **3** in methanol to give **4** suggests that in solution the ring-opened intermediate proposed in pathway A and B is accessible. Polar protic solvents, such as methanol, not only allow for the stabilization of the zwitterionic intermediate but also provide an additional proton source for facile formation of the α-Michael adduct.

When the retro Mannich reaction for **2** is monitored by proton NMR in a methanol-d_4 solution, the final product shows an integration for the methylene group protons that is half that for other ring protons of the system. However, *no deuterium incorporation is observed for the methine group*, indicating a slow rate of epimerization of this α-ester proton in the cycloadduct (pathway C) relative to the rate of cycloadduct formation (**2**). We note, however, that the rate of epimerization for the cis and trans isomers (**2C** and **2B**) could significantly differ. It is also tempting to draw an inference between the rate of formation of **4** and the rate at which cycloadduct **2** undergoes ring-opening to form the zwitterion **2Z**, but unless protonation of **2Z** is much faster than the Mannich reaction to form **2B**, then no firm conclusions can be reached. In the earlier study with osmium(II), the maleate cycloadduct analogous to complex 2**C** could be isolated, and that product was shown to convert to the more stable trans cycloadduct in methanol-d_4 without incorporation of deuterium.[8] That the isomerization from the cis diester cycloadduct (e.g., complex **2C**) to the trans (e.g., **2B**) is faster for W(0) or Re(I) than for Os(II) is in line with the notion that the latter metal is less π-basic[15] and, thus, better able to stabilize the cationic 2*H*-pyrrolium moiety of intermediates such as complex **2Z** found in either path A or path B.

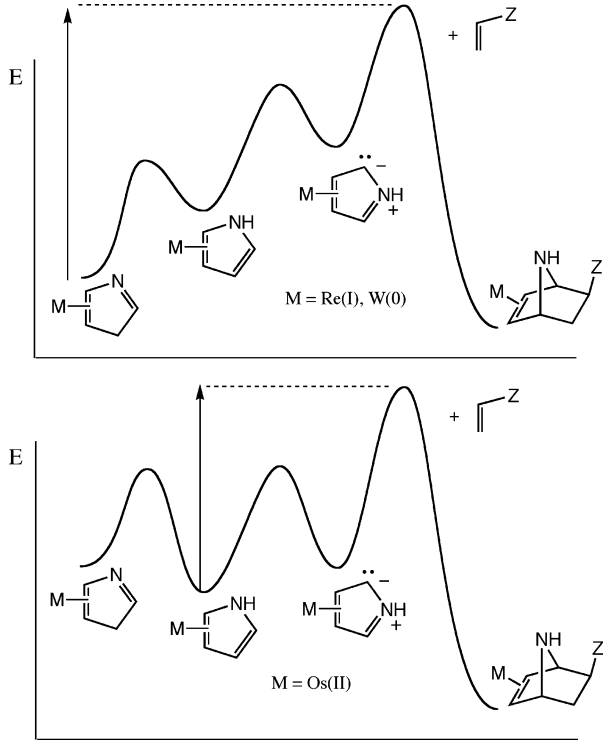


Figure 4.

Further comparing dearomatization agents, 1-methylpyrrole complexes **7** and **12** exhibit chemistry consistent with that of pentaammineosmium(II) in the presence of acrylonitrile and dimethyl fumarate, respectively. However, the scope for cycloaddition is limited by the increased vulnerability of the rhenium and tungsten to oxidation (−480 and −530 mV versus NHE for the tungsten and rhenium systems, respectively, compared to +140 mV for the complex $[Os(NH_3)_5(\eta^2\text{-}1\text{-methylpyrrole})](OTf)_2$).[19] In the case of the 2,5-dimethylpyrrole complexes **1** and **10**, the increased π donation of these metals also is responsible for altering the chemistry from that seen for osmium(II). For tungsten and rhenium, the 3*H*-tautomer becomes the dominant species, and while very stable with respect to oxidation, it is inactive with respect to the electrophile/dienophile. The observed cycloaddition reactions require a tautomerization back to the 1*H*-pyrrole, then an intrafacial linkage isomerization to the 3,4-η^2 isomer. Thus, even though the reactivity of the azomethine ylide intermediate is likely to be greater for the rhenium and tungsten systems due to the increased π donation from the metal,[15] the overall activation barrier originating from the 3*H*-pyrrole is actually higher than for osmium (Figure 4).

Conclusions

In earlier work we showed osmium(II) pyrrole complexes could be activated toward dipolar cycloaddition by utilizing the azomethine ylide character of its 3,4-η^2 isomer. The resulting 7-azanorbornene complexes can undergo retro-Mannich reactions, the products of which can be elaborated into the pyrrolizidine nucleus. In this follow-up study we used this methodology to formally prepare several naturally occurring pyrrolizidine alkaloids and explored the possibility of expanding

this methodology to group 7 and 6 transition metals. While the greater back-bonding ability of Re(I) and W(0) may indeed make the 3,4-η^2 isomer even more reactive as a 1,3-dipole, these systems were found to be more susceptible to oxidation by the dipolarophile. Also, in cases where the pyrrolic nitrogen was unsubstituted, a tautomerization to the 3*H*-tautomer occurred, which greatly reduced the effectiveness of the pyrrole complex to undergo cycloaddition reactions. Furthermore, the more negative reduction potential of the metal in these W and Re systems leads to oxidative addition of the N−H bond.

Experimental Section

General Methods. NMR spectra were obtained on a 300 or 500 MHz Varian INOVA spectrometer or a 300 or 500 MHz Bruker Avance. All chemical shifts are reported in ppm and are referenced to tetramethylsilane (TMS) using residual ^{1}H or ^{13}C signals of the deuterated solvents as internal standards. Coupling constants (*J*) are reported in hertz (Hz). Deuterated solvents were used as received from Cambridge Isotopes. Infrared spectra (IR) were recorded on a MIDAC Prospect Series (Model PRS) spectrometer as a glaze on a horizontal attenuated total reflectance (HATR) accessory (Pike Industries). Electrochemical experiments were performed under a dinitrogen atmosphere using a BAS Epsilon EC-2000 potentiostat. Cyclic voltammetric (CV) data were taken at ambient temperature at 100 mV/s in a standard three-electrode cell from +1.7 to −1.7 V with a glassy carbon working electrode, *N*,*N*-dimethylacetamide (DMA) solvent, and tetrabutylammonium hexafluorophosphate (TBAH) electrolyte (~0.5 M). All potentials are reported versus NHE (normal hydrogen electrode), the internationally accepted primary reference.[24,25] Accurate nonaqueous potentials were obtained using cobaltocenium hexafluorophosphate ($E_{1/2}$ = −780 mV) or ferrocene ($E_{1/2}$ = +550 mV) as an internal standard (in situ) and then correcting by the above-stated values. Elemental analysis (EA) was obtained from Atlantic Microlabs or with a Perkin-Elmer 2400 Series II CHNS/O analyzer. The isotopic pattern for the parent ion in mass spectra matches that calculated based on natural abundances. Unless otherwise noted, all synthetic reactions and electrochemical experiments were performed under a dry nitrogen atmosphere. THF (tetrahydrofuran), benzene, and methylene chloride were purged with nitrogen and purified by passage through a column packed with activated alumina. Other solvents and liquid reagents were purged with nitrogen prior to use. Other reagents were used as received.

Compounds **1**, **6**, **9**, **10**, **12**, **13**, and **14** have been previously reported as referenced in the main text.

TpW(NO)(PMe$_3$)(5,6-η^2-1,4-dimethyl-7-aza-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid dimethyl ester) [2A, 2B]. Complex **1** (462.0 mg, 0.772 mmol) was dissolved in a solution of THF (5 g) and dimethyl fumarate (550.8 mg, 3.82 mmol). After 20 h, the reaction solution was then added to stirring pentane, precipitating a white solid. The precipitate was collected via filtration and dried in vacuo to give a mixture of **2A** and **2B**. Yield of white solid: 479.0 mg (0.645 mmol, 84%). ^{1}H NMR (acetone-d_6, δ, Hz): two isomers observed in 1:1 ratio; 8.33 (1H, d, Tp), 8.30 (1H, d, Tp), 8.17 (1H, d, Tp), 8.16 (1H, d, Tp), 8.00 (2H, d, Tp), 7.99 (2H, d, Tp), 7.93 (2H, d, 2 Tp), 7.74 (2H, d, 2 Tp), 7.60 (1H, d, Tp), 7.32 (1H, d, Tp), 6.45 (H, t, Tp), 6.45 (H, t, Tp), 6.30 (H, t, Tp), 6.29 (1H, t, Tp), 6.24 (1H, t, Tp), 6.23 (1H, t, Tp), 3.72 (3H, s, ester methyl **2A**), 3.65 (3H, s, ester methyl **2B**), 3.62 (3H, s, ester methyl **2A**), 3.47 (1H, d (J = 5.2), C2H **2A**), 3.46 (3H, s, ester methyl **2B**), 3.42 (1H, d (J = 5.0), C2H or C3H **2B**), 3.28 (1H, d (J = 5.0), C2H or C3H **2B**), 3.16 (1H, d (J = 5.2), C3H **2A**), 2.89 (1H, dd (J = 12.6, 7.8), C6H **2A**), 2.75 (1H, dd (J = 13.2, 7.8), C6H **2B**), 1.77 (3H, s, bridgehead methyl **2B**), 1.63 (3H, s, bridgehead methyl **2A**), 1.55 (1H, dd (J = 7.8, 3.0), C5H **2B**), 1.51 (3H, s, bridgehead methyl **2A**), 1.50 (1H, dd (J = 7.8, 3.0), C5H **2A**), 1.36 (3H, d, bridgehead methyl **2B**), 1.03 (9H, d (J = 8.5), PMe$_3$ **2B**), 1.01 (9H, d (J = 8.4), PMe$_3$ **2A**). ^{13}C NMR (acetone-d_6, δ, Hz): two diastereomers observed; 174.5 (s, CO), 174.3 (s, 2 CO's), 174.1 (s, CO), 147.4 (s, Tp), 147.1 (s, Tp), 143.7 (d (J = 1.7), Tp), 143.6 (d (J = 1.7), Tp), 142.8 (s, Tp), 142.2 (s, Tp), 138.2 (s, Tp), 138.1 (s, Tp), 137.4 (s, 2 Tp), 136.8 (s, 2 Tp), 108.0 (s, Tp), 107.9 (s, Tp), 107.2 (s, Tp), 107.1 (s, Tp), 106.4 (s, 2 Tp), 75.0 (s, bridgehead 2b), 74.5 (s, bridgehead 2a), 74.0 (d (J = 14.4), C6 **2A**), 73.1 (s, bridgehead 2a), 72.9 (s, bridgehead 2b), 72.0 (s, C5 **2B**), 67.9 (d (J = 13.8), C6 **2B**), 65.9 (s, C5 **2A**), 61.7 (s, C3 **2B**), 60.8 (s, C3 **2A**), 60.6 (s, C2 **2A**), 60.2 (s, C2 **2B**), 51.8 (s, ester methyl **2A**), 51.6 (s, ester methyl **2B**), 51.5 (s, ester methyl **2B**), 51.4 (s, ester methyl **2A**), 23.9 (s, bridgehead methyl **2b**), 23.5 (s, bridgehead methyl **2a**), 22.1 (s, bridgehead methyl **2B**), 22.0 (s, bridgehead methyl **2A**), 13.3 (d (J = 28.7), PMe$_3$ **2A**), 13.0 (d (J = 28.7), PMe$_3$ **2B**). IR (HATR glaze): ν_{NO} = 1536 cm^{-1}; ν_{CO} = 1726 cm^{-1}. CV (DMA, TBAH, 100 mV/s, vs NHE): $E_{p,a}$ = 71 mV. Anal. Calcd for $C_{24}H_{36}BN_8O_5PW$: C, 38.84; H, 4.89; N, 15.10. Found: C, 38.65; H, 5.01; N, 14.74.

TpW(NO)(PMe$_3$)(5,6-η^2-1,4-dimethyl-7-aza-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid diethyl ester) [3A, 3B]. A solution of diethyl fumarate (176.4 mg 1.025 mmol) and DME (8.7 g) was added to complex **1** (186.3 mg, 0.3115 mmol) and allowed to react overnight (18 h). The reaction solution was then added to stirring pentane, precipitating a white solid. The precipitate was collected via filtration and dried in vacuo to give a mixture of **3A** and **3B**. Yield of white solid: 66.4 mg (0.0862 mmol, 28%). ^{1}H NMR (acetone-d_6, δ, Hz): two diastereomers observed in 1:1 ratio; 8.38 (1H, d, Tp), 8.36 (1H, d, Tp), 8.19 (2H, d, 2 Tp), 8.01 (1H, d, Tp), 8.00 (1H, d, Tp), 7.95 (1H, d, Tp), 7.94 (1H, d, Tp), 7.76 (1H, d, Tp), 7.75 (1H, d, Tp), 7.65 (1H, d, Tp), 7.35 (1H, d, Tp), 6.48 (1H, t, Tp), 6.47 (1H, t, Tp), 6.32 (2H, t, 2 Tp), 6.27 (1H, t, Tp), 6.26 (1H, t, Tp), 4.15 (6H, m, 3 ethyl methylenes), 3.94 (2H, d (J = 7.1), ethyl methylene), 3.49 (1H, d (J = 5.0), C2H or C3H), 3.44 (1H, d (J = 5.0), C2H or C3H), 3.28 (1H, d (J = 5.0), C2H or C3H), 3.17 (1H, d (J = 5.0), C2H or C3H), 2.90 (1H, dd (J = 12.7, 8.1), C6H), 2.77 (1H, dd (J = 13.1, 8.1), C6H), 1.82 (3H, s, bridgehead methyl), 1.67 (3H, s, bridgehead methyl), 1.60 (1H, dd (J = 8.1, 3.1), C5H), 1.57 (3H, s, bridgehead methyl), 1.55 (1H, buried, C5H), 1.41 (3H, s, bridgehead methyl), 1.31 (3H, d (J = 7.1), ethyl methyl), 1.28 (3H, d (J = 7.3), ethyl methyl), 1.24 (3H, d (J = 7.1), ethyl methyl), 1.07 (9H, d (J = 8.1), PMe$_3$), 1.06 (3H, buried, ethyl methyl), 1.05 (9H, d (J = 8.4), PMe$_3$). ^{13}C NMR (acetone-d_6, δ, Hz): two diastereomers observed; 174.1 (s, CO), 173.9 (s, 2 CO), 173.7 (s, CO), 147.4 (s, Tp), 147.2 (s, Tp), 143.6 (s, Tp), 142.8 (s, Tp), 142.2 (s, Tp), 138.2 (s, Tp), 138.1 (s, Tp), 137.4 (s, Tp), 137.3 (s, Tp), 136.8 (s, 2 Tp), 108.0 (s, Tp), 107.9 (s, Tp), 107.2 (s, Tp), 107.1 (s, Tp), 106.4 (s, Tp), 106.3 (s, Tp), 74.9 (s, bridgehead), 74.4 (s, 2 bridgeheads), 74.2 (s, bridgehead), 72.9 (d (J = 14.6), C6), 72.2 (s, C5), 68.2 (d (J = 13.4), C6), 66.1 (s, C5), 61.6 (s, C2 or C3), 60.9 (s, C2 or C3), 60.7 (s, CH_2), 60.6 (s, CH_2), 60.5 (s, 2 CH_2), 60.4 (s, C2 or C3), 60.0 (s, C2 or C3), 24.0 (s, CH_3), 23.6 (s, CH_3), 22.3 (s, CH_3), 22.2 (s, CH_3), 15.0 (s, CH_3), 14.9 (s, CH_3), 14.8 (s, CH_3), 14.7 (s, CH_3), 13.4 (d (J = 28.7), PMe$_3$), 13.1 (d (J = 28.7), PMe$_3$). Anal. Calcd for $C_{24}H_{36}BN_8O_5PW$: C, 40.54; H, 5.23; N, 14.55. Found: C, 40.15; H, 5.36; N, 13.98.

TpW(NO)(PMe$_3$)(3,4-η^2-(2,5-dimethyl-2*H*-pyrrol-2-yl)succinic acid dimethyl ester) [4A]. Cycloadduct **2A** (138.1 mg, 0.186 mmol) was dissolved in methanol (3 mL). After 5 days, the methanol was removed through reduced pressure. The resulting residue was dissolved in minimal methylene chloride. Addition of pentane precipitated a while solid, which was collected by filtration and dried en vacuo to give **4A**. Yield of white solid: 96.1 mg (0.132

(24) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods Fundamentals and Applications*; John Wiley & Sons: New York, 1980.

(25) To convert to the IUPAC recommended Fc^+/Fc reference, add 0.55 V to the stated NHE values.

mmol, 70%). ^{1}H NMR (acetone-d_6, δ, Hz): 8.24 (1H, d (J = 1.9), Tp), 8.11 (1H, d (J = 1.9), Tp), 8.01 (2H, t (J = 1.9), 2 Tp), 7.83 (1H, d (J = 2.3), Tp), 7.58 (1H, d (J = 2.3), Tp), 6.45 (1H, t (J = 2.1), Tp), 6.40 (1H, t (J = 2.3), Tp), 6.33 (1H, t (J = 2.3), Tp), 3.78 (1H, dd (J = 13.1, 6.9), C3H), 3.73 (3H, s, methoxy), 3.60 (3H, s, methoxy), 3.32 (1H, br m, methylene), 3.14 (1H, br m, methylene), 2.93 (1H, dd (J = 5.4, 2.7), methine), 2.39 (1H, dd (J = 7.3, 1.9), C4H), 1.42 (3H, s, C2 methyl), 1.06 (9H, d (J = 8.5), PMe_3), Note: the C5 methyl group was not observed due to rapid deuterium exchange with NMR solvent. IR (HATR glaze): ν_{NO} = 1557 cm^{-1}; ν_{CO} = 1729 cm^{-1}. CV (DMA, TBAH, 100 mV/s, vs NHE): $E_{p,a}$ = 0.73 V.

TpW(NO)(PMe_3)(3,4-η^2-(2,5-dimethyl-2*H*-pyrrol-2-yl)succinic acid dimethyl ester) [4B]. Cycloadduct **2B** (94.0 mg, 0.127 mmol) was dissolved in DME (2.5 mL). Methanol (233 mg) was added. After 5 days, the solution was added to stirring pentane, precipitating a white solid, which was collected by filtration to give **4B**. Yield of white solid: 57.7 mg (0.077 mmol, 61%). ^{1}H NMR ($CDCl_3$, δ, Hz): 8.24 (1H, d (J = 2.2), Tp), 8.04 (1H, d (J = 2.2), Tp), 7.71 (1H, d (J = 2.2), Tp), 7.70 (1H, d (J = 2.2), Tp), 7.57 (1H, d (J = 2.2), Tp), 7.41 (1H, d (J = 2.2), Tp), 6.29 (1H, t (J = 2.2), Tp), 6.23 (1H, t (J = 2.2), Tp), 6.19 (1H, t (J = 2.2), Tp), 3.74 (3H, s, methoxy), 3.66 (1H, dd (J = 12.9, 7.0), C3H), 3.62 (3H, s, methoxy), 3.45 (1H, dd (J = 11.5, 3.5), methine), 2.98 (1H, dd (J = 17.3, 11.5), methylene), 2.54 (1H, dd (J = 17.3, 3.5), methylene), 2.49 (1H, dd (J = 7.0, 2.3), C4H), 2.23 (3H, s, C5 methyl), 1.56 (3H, s, C2 methyl), 0.96 (9H, d (J = 8.0), PMe_3). ^{13}C NMR ($CDCl_3$, δ, Hz): 179.9 (from HMBC, imine), 175.5 (s, carbonyl), 173.8 (s, carbonyl), 145.4 (s, Tp), 143.1 (s, Tp), 140.9 (s, Tp), 136.8 (s, Tp), 136.3 (s, Tp), 135.7 (s, Tp), 106.9 (s, Tp), 106.3 (s, Tp), 105.7 (s, Tp), 90.0 (s, C2), 69.2 (d (J = 13.8), C3), 67.3 (s, C4), 54.3 (s, methine carbon), 51.7 (s, methoxy), 51.5 (s, methoxy), 32.6 (s, methylene carbon), 28.3 (s, C2 methyl), 20.6 (s, C5 methyl), 13.9 (d (J = 27.6), PMe_3). IR (HATR glaze): ν_{NO} = 1563 cm^{-1}; ν_{CO} = 1731 cm^{-1}. CV (DMA, TBAH, 100 mV/s, vs NHE): $E_{p,a}$ = 0.70 V.

TpW(NO)(PMe_3)(4,5-η^2-2-(2,5-dimethyl-3*H*-pyrrol-3-yl)succinic acid dimethyl ester) [5]. A mixture of dimethyl fumarate (450.8 mg, 3.13 mmol) in methanol (3.24 g) was added to complex **1** (305.4 mg, 0.520 mmol). After 72 h, methanol was removed through reduced pressure and nitrogen stream. The resulting residue was dissolved in minimal THF and added to stirring pentane. The resulting precipitate was collected via vacuum filtration and dried in vacuo to give two diastereomers of **5**. Yield of white solid: 184.4 mg (0.248 mmol, 48%). ^{1}H NMR (acetone-d_6, δ, Hz): two diastereomers obsevered in a 4:1 ratio; 8.72 (1H, d, Tp major), 8.64 (1H, d, Tp minor), 8.01 (1H, d, Tp minor), 7.99 (1H, d, Tp minor), 7.97 (1H, d, Tp major), 7.94 (2H, d, Tp major and minor), 7.92 (1H, d, Tp major), 7.90 (1H, d, Tp minor), 7.80 (1H, d, Tp major), 7.70 (1H, d, Tp minor), 7.58 (1H, d, Tp major), 6.38 (1H, t, Tp minor), 6.36 (1H, t, Tp major), 6.33 (1H, t, Tp minor), 6.32 (1H, t, Tp major), 6.30 (1H, t, Tp major), 6.28 (1H, t, Tp minor), 4.03 (1H, t (J = 2.3), C3H minor), 4.00 (1H, t (J = 2.3), C3H major), 3.79 (3H, s, methoxy major), 3.75 (3H, s, methoxy minor), 3.64 (3H, s, methoxy minor), 3.62 (3H, s, methoxy major), 3.41 (1H, buried, CH minor), 3.38 (1H, dd (J = 11.5, 3.1), CH major), 2.95 (1H, dd (J = 17.3, 11.5), CH2 major), 2.56 (1H, dd (J = 13.4, 10.4), CH2 minor), 2.50 (1H, d (J = 11.1), C4H minor), 2.42 (1H, d (J = 11.1), C4H major), 2.22 (3H, s, C2 methyl major), 2.06 (3H, s, C2 methyl minor), 2.06 (1H, buried, CH_2 minor), 2.05 (1H, dd (J = 17.3, 3.1), CH_2 major), 1.37 (9H, d (J = 8.1), PMe_3 minor), 1.22 (9H, d (J = 8.5), PMe3 major), 1.11 (3H, d (J = 1.2), C5 methyl major), 1.08 (3H, d (J = 1.2), C5 methyl minor). IR (HATR glaze): ν_{NO} = 1559 cm^{-1}; ν_{CO} = 1729 cm^{-1}. CV (DMA, TBAH, 100 mV/s, vs NHE): $E_{p,a}$ = 0.39 V.

TpW(NO)(PMe_3)(5,6-η^2-7-methyl-7-aza-bicyclo[2.2.1]hept-5-ene-2-carbonitrile) [8A, 8B]. 1-Methylpyrrole (4.75 g) was added to a solution of **6** (235.6 mg, 0.4055 mmol), and the resulting solution was allowed to stand for 5 h. Acrylonitrile (146.2 mg, 2.755 mmol) was then added to the reaction mixture. The resulting solution was allowed to stand for 1 h. The reaction solution was then added to stirring pentane, precipitating a light brown solid. The precipitate was collected via filtration and dried in vacuo to give a mixture of **8A** and **8B**. Yield of light brown solid: 60.9 mg (0.0956 mmol, 24%). ^{1}H NMR (acetone-d_6, δ, Hz): four isomers observed; major two isomers fully assigned; major: 8.17 (1H, d, Tp), 8.15 (1H, d, Tp), 7.93 (1H, d, Tp), 7.87 (1H, d, Tp), 7.73 (1H, d, Tp), 7.38 (1H, d, Tp), 6.39 (1H, t, Tp), 6.27 (1H, t, Tp), 6.25 (1H, t, Tp), 3.77 (1H, d (J = 3.5), C1H), 3.65 (1H, d (J = 3.3), C4H), 3.12 (1H, m, C2H), 2.70 (1H, dd (J = 11.9, 8.6), C6H), 2.48 (1H, m, C3H endo), 2.16 (3H, s, *N*-methyl), 1.60 (1H, dd (J = 11.3, 4.2), C3H exo), 1.36 (9H, d (J = 8.5), PMe_3), 1.13 (1H, dd (J = 8.6, 2.9), C5H); secondary: 8.13 (1H, d, Tp), 7.93 (1H, d, Tp), 7.84 (2H, d, 2 Tp), 7.51 (1H, d, Tp), 7.47 (1H, d, Tp), 6.41 (1H, t, Tp), 6.22 (1H, t, Tp), 6.20 (1H, t, Tp), 3.85 (1H, d (J = 3.2), C4H), 3.56 (1H, d (J = 3.6), C1H), 3.10 (1H, m, C3H), 2.86 (1H, dd (J = 8.7, 5.2), C5H), 2.52 (1H, m, C2H endo), 2.42 (3H, s, N-Me), 1.88 (1H, dd (J = 8.9, 11.6), C6H), 1.79 (1H, dd (J = 11.9, 4.5), C2H exo), 1.35 (9H, d (J = 8.5), PMe_3). ^{13}C NMR (acetone-d_6, δ, Hz): major isomer only. 144.8 (s, 2 Tp), 141.9 (s, Tp), 137.7 (s, Tp), 136.9 (s, Tp), 135.7 (s, Tp), 106.9 (s, Tp), 106.6 (s, 2 Tp), 71.8 (s, C1), 68.8 (s, C4), 31.1 (s, C2), 60.4 (d (J = 16.1), C6), 34.5 (s, *N*-methyl), 37.8 (s, C3), 64.4 (s, C5), 14.4 (d (J = 28.2), PMe_3). IR (HATR glaze): ν_{NO} = 1555 cm^{-1}. CV (DMA, TBAH, 100 mV/s, vs NHE): $E_{p,a}$ = 0.76 V.

TpRe(CO)(1-methylimidazole)(5,6-η^2-1,4-dimethyl-7-azabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid dimethyl ester) [11A, 11B]. Dimethyl fumerate (110.2 mg, 0.765 mmol) and **10** (43.0 mg, 0.0711 mmol) were dissolved in DME (1.018 g). The reaction solution was stirred overnight (20 h). The solution was then added to stirring hexanes. The resulting precipitate was collected by vacuum filtration and dried in vacuo to give a mixture of **11A** and **11B**. Yield of white solid: 20.6 mg (0.0275 mmol, 39%). ^{1}H NMR (acetone-d_6, δ, Hz): two diastereomers observed in 4:1 rati; major (**11A**): 8.38 (1H, d, Tp), 8.18 (1H, s, Im), 8.06 (1H, d, Tp), 8.02 (1H, d, Tp), 7.93 (1H, d, Tp), 7.89 (1H, d, Tp), 7.85 (1H, d, Tp), 7.21 (1H, t, Im), 7.08 (1H, t, Im), 6.55 (1H, t, Tp), 6.35 (1H, t, Tp), 6.29 (1H, t, Tp), 3.96 (3H, s, Im methyl), 3.83 (3H, s, C2, carbomethoxy), 3.80 (3H, s, C3, carbomethoxy), 3.52 (1H, d (J = 5.2), C2H), 3.20 (1H, d (J = 6.1), C6H), 3.19 (1H, d (J = 5.2), C3H), 2.63 (1H, d (J = 6.1), C5H), 1.68 (3H, s, C4 methyl), 1.19 (3H, s, C1 methyl); minor (**11B**): 8.32 (1H, d, Tp), 8.22 (1H, d, Tp), 8.20 (1H, s, Im), 8.06 (1H, d, Tp), 7.98 (1H, d, Tp), 7.88 (1H, d, Tp), 7.85 (1H, d, Tp), 7.26 (1H, t, Im), 7.24 (1H, t, Im), 6.56 (1H, t, Tp), 6.34 (1H, t, Tp), 6.29 (1H, t, Tp), 3.99 (3H, s, Im methyl), 3.77 (3H, s, methoxy), 3.63 (3H, s, methoxy), 3.50 (1H, d (J = 5.2), C2H), 3.29 (1H, d (J = 5.2), C3H), 3.23 (1H, d (J = 6.3), C6H), 2.53 (1H, d (J = 6.3), C5H), 1.90 (3H, s, C4 methyl), 0.96 (3H, s, C1 methyl). ^{13}C NMR (acetone-d_6, δ, Hz): major isomer only observed; major (**11A**): 200.2 (s, CO), 173.5 (s, ester carbonyl), 173.2 (s, ester carbonyl), 148.4 (s, Tp), 142.8 (s, Tp), 142.3 (s, Im), 139.5 (s, Tp), 136.2 (s, Tp), 135.1 (s, Tp), 134.3 (s, Tp), 131.2 (s, Im), 121.3 (s, Im), 105.7 (s, Tp), 105.6 (s, Tp), 105.5 (s, Tp), 73.3 (s, C1), 73.0 (s, C6), 71.7 (s, C5), 71.3 (s, C4), 59.0 (s, C2), 58.5 (s, C3), 50.6 (s, ester methyl), 50.4 (s, ester methyl), 33.5 (s, Im methyl), 19.9 (s, C4 methyl), 17.6 (s, C1 methyl). CV (DMA, TBAH, 100 mV/s, vs NHE): $E_{p,a}$ = 0.41 V.

[Os(NH_3)$_5$(2-(3,4-η^2-2*H*-pyrrolium-2-yl)dimethyl succinate]-(OTf_2) [15]. Two solutions, one of **14** (4.96 g, 6.32 mmol) in acetonitrile (10 g) and a second of TBS−OTf (3.34 g, 12.65 mmol) in acetonitrile (2 g), were prepared and chilled to −40 °C. The solutions were combined, and an immediate color change from yellow to reddish-purple ensued. The solution was removed from

the cold bath and allowed to slowly warm to room temperature. After 6 h, the solution was again cooled to −40 °C and cold (−40 °C) methanol/water (∼1 mL, 50 mg, respectively) was added. The solution was again allowed to warm to room temperature and subsequently stand for 30 min before being added into stirring Et_2O. The light purple precipitate was collected on a fine frit, washed with Et_2O (2 × 10 mL), and dried in vacuo to yield the product as a light purple solid (5.37 g, ∼90%). This product is isolated as a 1:1 mixture of diastereomers. Partial NMR characterization is reported owing to the presence of impurities that could not be removed from the sample through precipitation. ^{1}H NMR (CD_3CN, δ, Hz): 10.94 (2H, bs, NH), 9.42 (2H, bs, H5 **A** and **B**), 4.79 (6H, bs, trans-NH_3), 3.75 (3H, s, OMe), 3.74 (3H, s, OMe), 3.68 (3H, s, OMe), 3.67 (3H, s, OMe), 3.48 (24H, bs, cis-NH_3 **A** and **B**), 2.9−2.5 (4H, H3′). ^{13}C NMR (CD_3CN, δ): 191.83 (CH, C5), 191.53 (CH, C5), 172.7 (C, CO), 172.4 (C, C═O), 171.5 (C, C═O), 170.8 (C, C═O), 121.6 (CF_3, J_{CF} = 320 Hz, OTf), 72.04 (CH, C3), 71.79 (CH, C3), 58.07 (CH, C4), 58.00 (CH, C4), 53.43 (CH_3, OMe), 53.34 (CH_3, OMe), 52.78 (CH_3, OMe), 50.90 (CH_3, OMe), 42.11 (CH, C2), 41.80 (CH, C2), 32.20 (CH, C2′), 32.11 (CH, C2′), 26.36 (CH_2, C3′), 26.03 (CH2, C3′); IR (HATR, glaze): $\nu_{C=O}$ = 1727 cm^{-1}. CV: $E_{p,a}$ = 1170 mV.

[Os(NH$_3$)$_5$(3,4-η^2-(2-(1,2-bis(methoxycarbonyl)ethyl)-2,5-dihydro-1*H*-pyrrolium)] [16]. Three solutions, one of pyrrolium complex **15** (1.04 g, 1.1 mmol) in CH_3CN (3 g), the second of $NaBH_4$ (47 mg, 1.24 mmol) in MeOH/CH_3CN (1:3, 3 mL), and the third of HOTf (82 mg, 0.5 mmol) in MeOH (1 mL), were prepared. The solutions of Os complex and HOTf were chilled to −40 °C, then combined. The borohydride solution was added slowly as H_2 is evolved. When the addition was complete, the reaction mixture was removed from the cold bath and allowed to stand an additional 60 min. The solution was once again chilled to −40 °C, and a cold (−40 °C) solution of HOTf (165 mg, 1.1 mmol) in MeOH (∼ 1 mL) was added. The golden solution was added dropwise to stirring Et_2O. The resulting precipitate was collected on a fine frit, washed with Et_2O (10 mL × 3), and dried in vacuo to yield **16** as an ivory solid, which was contaminated with NaOTf. Estimated purity > 80%, calculated on the basis of ^{1}H NMR signals for the product versus durene as an internal standard. This product was a mixture of diastereomers. Partial NMR characterization is reported: ^{1}H NMR (CD_3CN, δ, Hz) 7.9 (bs, 4H, NH_2 × 2), 4.37 (m, 2H, H2 × 2), 4.27 (bs, 6H, trans-NH_3 × 2), 4.22 (m, 4H, H5 × 4), 3.95 (2H, bd, J = 6.9 Hz, H3 × 2), 3.83 (2H, bd, J = 7.7 Hz, H4 × 2), 3.77 (bs, 6H, OMe × 2), 3.72 (s, 3H, OMe), 3.71 (s, 3H, OMe), 3.15 (bs, 24H, cis-NH_3 × 2). ^{13}C NMR (CD_3CN): δ 173.8 (C, C═O), 173.6 (C, C═O), 173.1 (C, C═O), 172.8 (C, C═O), 65.8 (CH, C2 A), 65.5 (CH, C2 B), 53.6 (CH_3, OMe), 53.5 (CH_3, OMe), 53.3 (CH_3, OMe), 53.2 (CH_3, OMe), 52.4 (CH_2, C5), 52.2 (CH_2, C5), 51.4 (CH, bound), 51.0 (CH, bound), 50.4 (CH × 2, bound), 45.6 (CH, C2′), 45.2 (CH, C2′), 33.9 (CH_2, C3′), 32.9 (CH_2, C3′). CV: $E_{p,a}$ = 1160 mV.

Methyl 3-oxo-2,3,5,7a-tetrahydro-1*H*-pyrrolizine-1-carboxylate [18-endo] and Methyl 3-oxo-2,3,5,7a-tetrahydro-1*H*-pyrrolizine-1-carboxylate [18-exo]. The following procedure was performed outside of the glovebox and may be scaled for 4 g of complex. Two solutions were prepared: (1) A 25 mL round-bottom flask with stir bar was charged with complex **16** (265 mg, 0.2 mmol) and acetonitrile (2 mL). (2) In a test tube, $Cu(OTf)_2$ (110 mg, 0.5 mmol) was dissolved in acetonitrile (2 mL). Both solutions were warmed to 55 °C in an oil bath for 10 min, then combined. The mixture was stirred for 30 min, then removed from the oil bath, and the solvent was removed under reduced pressure to yield a dark brown residue. This residue was dissolved in Me_3N (∼20% aqueous). Brine (20 mL) was added, and the solution was stirred for 30 min. Aqueous, saturated Na_2CO_3 (10 mL) was added, then the volatiles were removed under reduced pressure. The resulting aqueous solution was diluted with water (50 mL), then extracted with $CHCl_3$ (3 × 50 mL). The combined organic extract was dried over Na_2SO_4, then concentrated to afford a thick oil containing the crude product. Chromatography (silica gel, EtOAc/hexanes, 1:1) afforded the separate diastereomers in approximately 1:1 ratio. Typical yields range from 50 to 66%. **18-endo** (less polar isomer, TLC, EtOAc, R_f 0.5): ^{1}H NMR ($CDCl_3$) δ 6.2−5.8 (2H, m, H6 and H7), 4.77 (1H, m, H7a), 4.42 (1H, dddd, J = 1.9, 2.1, 3.9, 15.8 Hz, H5α), 3.77 (3H, s, OMe), 3.70 (1H, m, H5β), 3.2−2.8 (2H, m, H1 and H2α), 2.60 (1H, m, H2β). ^{13}C NMR ($CDCl_3$): δ 175.44 (C, C3), 171.99 (C, CO), 129.26 (CH), 129.20 (CH), 69.15 (CH, C7a), 52.38 (CH, C5), 50.14 (CH_3, OMe), 47.67 (CH, C1), 36.97 (CH_2, C2). Data for the β-carbomethoxy **18-exo** (more polar isomer, TLC, EtOAc, R_f 0.2): ^{1}H NMR ($CDCl_3$) δ 5.94 (1H, m, H6), 5.82 (1H, m, H7), 4.95 (1H, m, H7a), 4.40 (1H, dddd, J = 15.3, 2.1, 2.2, 4.4, H5α), 3.70 (1H, dddd, J = 15.6, 2.1, 2.2, 4.5 Hz, H5β), 3.48 (1H, dd, J = 8.4, 7.1 Hz, H1), 2.87 (1H, dd, J = 17.3, 7.4 Hz, H2β), 2.63 (1H, d, J = 17.2 Hz, H2α). ^{13}C NMR ($CDCl_3$): δ 176.5 (C, C═O), 171.83 (C, C═O), 130.02 (CH, C7), 126.57 (CH, C6), 68.94 (CH, C7a), 51.8 (CH_2, C5), 50.33 (CH_3, OMe), 45.11 (CH, C1), 36.73 (CH_2, C2). IR (HATR, glaze): $\nu_{C=O}$ =1703 cm^{-1}; ν_{CO} = 1733 cm^{-1}. Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.68. Found: C, 59.62; H, 6.36; N, 7.68.

Methyl 3-oxohexahydro-1*H*-pyrrolizine-1-carboxylate [19-exo]. The synthesis and characterization of this compound have been previously reported.[20,21] Pyrrolizine product **18-exo** (15.6 mg, 0.09 mmol) was dissolved in THF/MeOH (∼10:1, 2 mL). Pd−C (10%) was added and the mixture stirred under H_2 (1 atm) for 3 h. The mixture was filtered through Celite to remove the catalyst and the filtrate concentrated to yield the product as a colorless oil. No further purification was performed. Yield: 14.3 mg, 90%. ^{1}H NMR ($CDCl_3$, δ, Hz): 3.95−4.10 (1H, m, 7a), 3.73 (3H, s, OMe), 3.45−3.61 (1H, m, H5), 2.9−3.15 (3H, overlapping m, H5, H1, H2α), 2.6−2.75 (1H, m, H2β), 1.80−2.25 (3H, overlapping, H7α, H6α, H6β), 1.30−1.55 (1H, m, H7α). ^{13}C NMR ($CDCl_3$, δ): 172.4 (C), 172.0 (C), 63.7 (CH, C7a), 52.3 (CH3, OMe), 45.8 (CH2, C5), 41.2 (CH, C1), 38.4 (CH2, C2), 31.6 (CH2, C7), 26.7 (CH2, C6). IR (HATR glaze): ν = 1733, 1690 cm^{-1}.

Methyl hexahydro-1*H*-pyrrolizine-1-carboxylate·BH$_3$ [20·BH$_3$-exo]. To a solution of **19-exo** (15 mg, 0.082 mmol) in THF (∼1 mL) was added BH_3−SMe_2 complex (200 μL of a 2 M solution in THF). The reaction was stirred overnight. MeOH (∼5 mL) was added, and then the mixture was stirred 30 min, then concentrated under reduced pressure to afford the crude product as a pale yellow oil. This product was purified by chromatography on silica (25% EtOAc/hexanes, R_f = 0.3). ^{1}H NMR ($CDCl_3$, δ, Hz): 3.88 (1H, m, H7a), 3.70 (3H, s, OMe), 3.41 (2H, H1, H5 overlapping), 3.22 (1H, ddd, J = 11.8, 10.0, 7.2 Hz, H3), 3.05 (1H, ddd, J = 11.9, 7.3, 3.9 Hz, H3′), 2.89 (1H, m, H5′), 2.31−1.79 (5H, H2 × 2, H7, H6 × 2), 1.66−1.0 (4H, H7 and BH_3 overlapping). ^{13}C NMR ($CDCl_3$,δ) 171.9 (C, C═O), 73.6 (CH, C7a), 64.1 (CH_2, C5), 62.0 (CH_2, C3), 52.0 (CH_3, OMe), 46.0 (CH, C1), 28.9 (CH_2, C7), 26.1 (CH_2, C2), 24.4 (CH_2, C6). IR (HATR, glaze): ν_{BH} = 2381 cm^{-1}; $\nu_{C=O}$ = 1735 cm^{-1}; ν_{BN} = 1167 cm^{-1}. Anal. Calcd for $C_9H_{18}BNO_2$: C, 63.88; H, 8.93; N, 8.27. Found: C, 63.90; H, 8.91; N, 8.27.

Methyl hexahydro-1*H*-pyrrolizine-1-carboxylate·BH$_3$ [20·BH$_3$-endo]. This product was prepared using the same procedure as **19-exo**. ^{1}H NMR ($CDCl_3$): δ 3.88 (1H, ddd, J = 8.24, 3.4, 3.4, H7a), 3.72 (3H, s, OMe), 3.45 (1H, m, H3), 3.21 (1H, m, H5), 3.0−2.8 (2H, H5′, H3′),2.67 (1H, m, H1), 2.43 (1H, m, H2), 2.24 (1H, m, H7), 2.14 (1H, m, H2′), 2.05 (1H, m, H6), 1.90 (1H, m, H6′), 1.82 (1H, m, H7′). ^{13}C NMR ($CDCl_3$) δ 171.98 (C, C═O), 75.31 (CH_2, C7a), 63.84 (CH_2, C5), 63.10 (CH_2, C3), 52.30 (CH_3, OMe), 50.52 (CH, C1), 31.28 (CH_2, C2), 28.04 (CH_2, C6), 24.17 (CH_2, C7). IR: ν_{BH} = 2385 cm^{-1}; $\nu_{C=O}$ = 1737 cm^{-1}; ν_{BN} = 1167 cm^{-1}. Anal. Calcd for $C_9H_{18}BNO_2$: C, 59.05; H, 9.91; N, 7.46. Found: C, 58.98; H, 9.80; N, 7.46.

Methyl hexahydro-1*H*-pyrrolizine-1-carboxylate (20-exo). The synthesis and characterization of this compound have been previously reported.[22] To a solution of the pyrrolizine−borane adduct **19a-exo** (14.6 mg, 0.08 mmol) in MeOH (10 mL) was added concentrated HCl (∼20 mg) in MeOH (2 mL), and the solution was refluxed 2 h. The solvent was removed under reduced pressure, and the resulting residue was dissolved in saturated Na_2CO_3 (1 mL) and extracted with $CHCl_3$ (3 × 3 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The product was chromatographed on alumina (preparative TLC, $R_f = 0.7$ EtOAc). Yield: 12 mg, 0.07 mmol, 88% two steps. ^{1}H NMR ($CDCl_3$, δ, Hz): 3.68 (3H, s, OMe), 3.60 (1H, ddd, J = 7.4, 5.3, 5.1 Hz, H7a), 3.17 (1H, ddd, J = 10, 5.0, 5.1 Hz, H3), 2.95 (1H, ddd, J = 10, 6.0, 6.0, H5), 2.59 (1H, m, H3), 2.57−2.45 (2H, H1 and H5), 2.17−2.05 (2H, H6 and H6′), 1.99 (1H, m, H7), 1.88−1.69 (2H, H2 and H2′), 1.62 (1H, m, H7′). ^{13}C NMR ($CDCl_3$): δ 174.7 (C, C═O), 68.13 (CH, C7a), 54.90 (CH_2, C5), 54.48 (CH_2, C3), 51.75 (CH_3, OMe), 50.11 (CH, C1), 31.44 (CH_2, C7), 30.58 (CH_2, C6), 25.59 (CH_2, C2).

Methyl hexahydro-1*H*-pyrrolizine-1-carboxylate [20-endo]. The synthesis and characterization of this compound has been previously reported.[9,19,20] Yield: 90%, two steps. ^{1}H NMR ($CDCl_3$): δ 3.70 (3H, s, OMe), 3.55−3.65 (1H, ddd, J = 8.0, 11.0, 8.0 Hz, H3), 3.35−3.45 (1H, ddd, J = 8.0, 8.0, 8.3 Hz, H5), 2.98−3.10 (1H, ddd, J = 3.6, 8.0, 11.0 Hz, H3), 2.80−2.85 (2H, m, H5 and H1), 1.60−2.55 (6H, m).

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Supporting Information Available: Spectra for selected compounds and crystallographic details for compounds **2A** and **11B**. This material is available free of charge via the Internet at http://pubs.acs.org

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