The Synthesis of η^2-β-Vinylpyrrole Complexes and Their Conversion to Highly Substituted Indoles

L. Mark Hodges, Michael L. Spera, Marcus W. Moody, and W. Dean Harman*

Contribution from the Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901

Received April 1, 1996[⊗]

Abstract: A series of 4,5-η^2-Os(II)pentaammine-3-vinylpyrrole complexes are synthesized from the corresponding 1-methylpyrrole complex by an electrophilic addition at the β-carbon, C(3), of the pyrrole ring. Four independent synthetic routes to β-vinylpyrrole complexes are described, each introducing different functionality on the pendant double bond. The uncoordinated portion of these complexes chemically and structurally resembles an aminodiene and as such readily undergoes Diels−Alder reactions with suitably activated dienophiles to generate the 5,6,7,7a-tetrahydroindole nucleus. These tetrahydroindole complexes can be decomplexed and oxidized with DDQ to generate a series of highly functionalized indoles.

Introduction

The indole ring system, found in numerous classes of alkaloids and alkaloid derivatives, is usually synthesized by an intramolecular ring-closure of either a monosubstituted or an *ortho*-substituted benzene precursor.[1] Many classical organic syntheses of indoles such as the Fischer, Bischler, and Madelung processes fall into this category,[2] as do most organometallic methods of indole synthesis.[3,4] Using these methods, functional groups at the 2 and 3 positions are readily installed in the ring-closure sequence; however, the desired substituents at positions 4−7 must be established in the arene precursor. Less common are approaches to indoles that originate with a pyrrole and build up the carbocycle.[1,5] As a recent example of the latter approach, several tetrahydroindoles were prepared through a Diels−Alder reaction of a vinylpyrrole and an alkyne dienophile.[6] This methodology offers versatility in the substitution pattern of the carbocycle but suffers from difficulties associated with oxidation of the tetrahydroindole and the tendency of vinylpyrroles to polymerize.[6c,7]

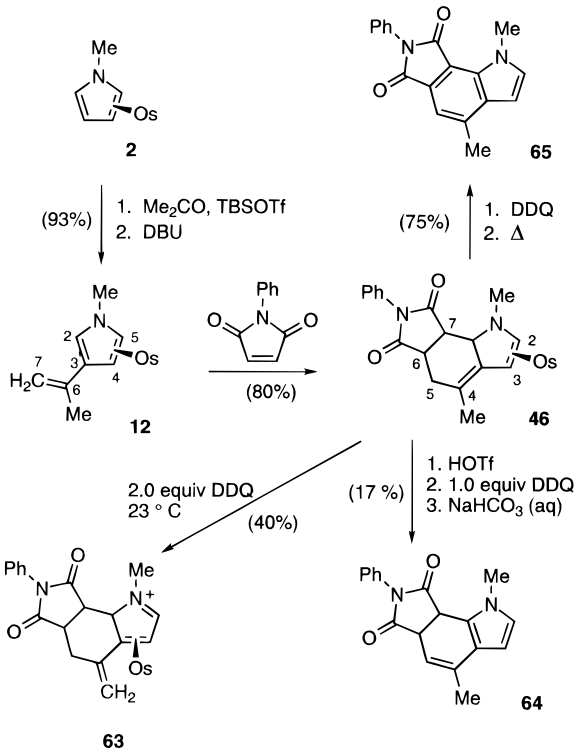


Figure 1. Synthesis of indoles from β-vinylpyrrole complexes.

In a recent communication, we showed that the dihapto-coordinated pyrrole complex 4,5-η^2-[Os$(NH_3)_5$(1-methylpyrrole)]OTf_2 (**2**) could be converted to a β-vinylpyrrole complex (**12**) in 93% yield via a Lewis-acid promoted aldol reaction with acetone (Figure 1).[8a] The vinylpyrrole complex (**12**) undergoes a facile Diels−Alder reaction with *N*-phenylmaleimide under mild conditions to generate, after decomplexation and oxidation, a highly functionalized indole (**65**) in ∼60% *overall* isolated yield (from pyrrole).[8a] In order to evaluate the potential of this osmium methodology, a full investigation into the synthesis of 3-vinylpyrrole complexes was undertaken. During the course of this study, three additional synthetic routes

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1996.

(1) Couture, A.; Deniau, E.; Gimbert, Y.; Grandclaudon, P. *J. Chem. Soc., Perkin Trans. I* **1993**, 2463, and references therein.

(2) Brown, R. K. In *Indoles Part One: The Chemistry of Heterocyclic Compounds, v. 25*; Houlihan, W. J., Ed.; John Wiley & Sons: New York, 1972; Chapter 2.

(3) For a review on indole syntheses using catalytic Pd(0) and Pd(II) salts, see: Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113.

(4) (a) Fukuyama, T.; Chen, X.; Peng, G. *J. Am. Chem. Soc.* **1994**, *116*, 3127. (b) Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215.

(5) For examples of intramolecular ring closures of a 2-substituted pyrroles, see: Ishibashi, H.; Akamatsu, S.; Iriyama, H.; Hanaoka, K.; Tabata, T.; Ikeda, M. *Chem. Pharm. Bull.* **1994**, *42*, 271. For other recent examples of this strategy, see: (a) Muratake, H.; Mikawa, A.; Seino, T.; Natsume, M. *Chem. Pharm. Bull.* **1994**, *42*, 846. (b) Muratake, H.; Mikawa, A.; Seino, T.; Natsume, M. *Chem. Pharm. Bull.* **1994**, *42*, 854. (c) Utsunomiya, I.; Muratake, H.; Natsume, M. *Chem. Pharm. Bull.* **1995**, *43*, 37.

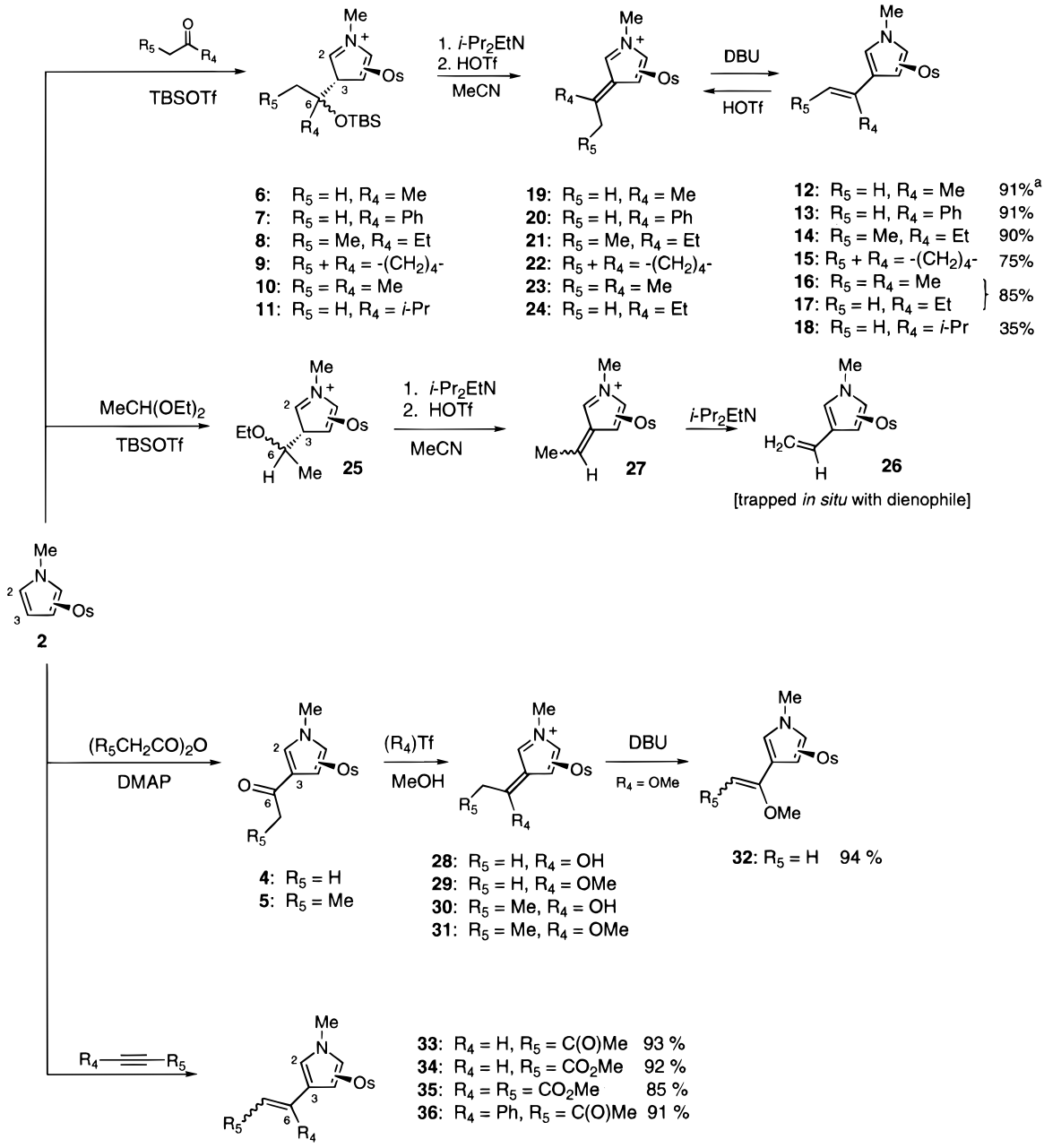
(6) For examples of Diels−Alder reactions with vinylpyrroles see: (a) Jones, R. A.; Saliente, T. A.; Arques, J. S. *J. Chem. Soc., Perkin Trans. I* **1984**, 2541. (b) Jones, R. A.; Arques, J. S. *Tetrahedron* **1981**, *37*, 1597. (c) Jones, R. A.; Marriott, M. T. P.; Rosenthal, W. P.; Arques, J. S. *J. Org. Chem.* **1980**, *45*, 4515. (d) Muchowski, J. M.; Scheller, M. E. *Tetrahedron Lett.* **1987**, *28*, 3453. For an example of a reaction between 2-vinylpyrrole and tetrachlorocyclopropene, see: Keil, J.; Massa, W.; Riedel, R.; Seitz, G.; Wocadlo, S. *Tetrahedron Lett.* **1994**, *35*, 7923.

(7) For a recent synthesis of 3-vinylpyrrole: Settambolo, R.; Lazzaroni, R.; Messeri, T.; Mazzetti, M.; Salvadori, P. *J. Org. Chem.* **1993**, *58*, 7899, and references therein.

(8) (a) Hodges, L. M.; Moody, M. W.; Harman, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 7931. (b) Hodges, L. M.; Gonzalez, J.; Koontz, J. I.; Myers, W. H.; Harman, W. D. *J. Org. Chem.* **1995**, *60*, 2125.

S0002-7863(96)01072-4 CCC: $12.00

Scheme 1



[a] All yields are overall yields from **2** and refer to isolated materials.

to β-vinylpyrrole complexes were developed, each initiated by electrophilic addition to C(3) (Scheme I). In the following account, the scope and limitations of this new approach to substituted indoles is described and compared to existing methods.

Results

Synthesis of β-Vinylpyrrole Complexes. 1. Aldol Condensation. The Mukaiyama-type aldol reaction first reported for the 1-methylpyrrole complex (**2**) and acetone (Figure 1) gives satisfactory results for a number of different ketones, and the corresponding 3H-pyrrolium adducts (**6**−**11**) may be prepared in near quantitative yield for a variety of ketones (Scheme 1).[9] These compounds have been characterized by ^{1}H and ^{13}C NMR as well as by cyclic voltammetry, and the data are consistent with that of other 3*H*-pyrrolium tautomers.[8,10] In most cases (**6** and **7**), the 3*H*-pyrrolium aldol adduct is not isolated but is converted directly to the corresponding 3-vinylpyrrole complex (*vide infra*). However, adducts **8**, **9**, and **11** partially precipitate from the reaction mixture (i.e., an acetonitrile solution) and thus have been isolated and fully characterized. For an unsymmetrical ketone such as isopropyl methyl ketone, the aldol product **11** is isolated as an approximate 1:1 ratio of C(6) epimers.

Addition of a base such as *i*-Pr$_2$EtN or DBU to either an acetonitrile solution or slurry of the aldol adducts results in elimination of TBSOH and deprotonation of an α-hydrogen from one of the remaining substituents, giving the corresponding β-vinylpyrrole complex (Scheme 1).[11] This process presumably

(9) While the reaction does appear to work for pinacolone (*tert*-butyl methyl ketone) as well, the yield is compromised by significant amounts of protonation at C(3).

(10) Myers, W. H.; Koontz, J. I.; Harman, W. D. *J. Am. Chem. Soc.* **1992**, *114*, 5614.

goes through an intermediate 2-azafulvenium complex that can be generated quantitatively by protonation (HOTf, CH_3OH) of the isolated 3-vinylpyrrole complex (*vide infra*). The aldol reaction is successful for pyrrole complexes with different substitution patterns, but when the nitrogen is unsubstituted, the corresponding 3*H*-pyrrolium aldol adduct deprotonates at nitrogen yielding a 3*H*-pyrrole complex, and attempts to isomerize this species to the desired β-vinylpyrrole have failed.[8b]

When the ketone used in the aldol reaction is not symmetric, the potential exists for formation of different structural vinylpyrrole isomers. For example, when compound **10** (not isolated, Scheme 1) is combined with DBU, a 1:1 mixture of β-vinylpyrrole complexes **16** and **17** is isolated. Attempts at changing the isomer ratio to favor one or the other by repeated protonation of **16** and **17** and subsequent deprotonation of the resulting azafulvenium complexes failed. Compared to the bulkier isopropyl substituent (i.e., **11**), deprotonation of the methyl group becomes heavily favored (^{1}H NMR), however, the purity of the resulting complex (**18**) is compromised by varying amounts of metallated impurities (~30%). In the case of the vinylpyrrole complex derived from diethyl ketone (**14**), a single diasteriomer is formed with the methyl and ethyl substituents having a relative *cis*-stereochemistry (NOE).

2. Acetal Addition. Aliphatic aldehydes (e.g., acetaldehyde or isobutyraldehyde) fail to give the desired aldol product under the standard reaction conditions described above.[12] However, when acetal (acetaldehyde diethyl acetal) is combined with the 1-methylpyrrole complex (**2**) and TBSOTf, electrophilic addition readily occurs at C(3) to produce the alkoxy 3*H*-pyrrolium adduct (**25**; Scheme 1).[13] Upon addition of an amine base (*i*-Pr_2EtN), deprotonation occurs at C(3) to give the corresponding β-substituted 1H-pyrrole complex, and subsequent addition of acid (HOTf, CH_3CN) results in the elimination of ethanol to give the azafulvenium complex **27** as a 3:2 mixture of diastereomers (93%). Attempts to isolate the β-vinylpyrrole complex **26** resulting from deprotonation of azafulvenium **27** failed, but it may be trapped *in situ* with *N*-phenylmaleimide (*vide infra*).

3. Acylation and Alkylation. A third route to 3-vinylpyrrole complexes originates from 3-acylated pyrrole complexes and readily provides access to alkoxy-substituted β-vinylpyrrole complexes. Acylation of the 1-methylpyrrole complex **2** with either acetic or propionic anhydride (DMAP catalyst) gives complexes **4** and **5**, respectively (Scheme 1).[14] The carbonyl oxygen on these complexes is nucleophilic and can either be protonated (HOTf) or methylated (MeOTf) to give an alkoxy 2-azafulvenium complex. While addition of base to the hydroxy azafulvenium complex regenerates the original acylated complex, addition of DBU to the methoxy-substituted azafulvenium complex **29** results in deprotonation of the methyl group on C(6) to give the methoxy-substituted β-vinylpyrrole complex **32**. This complex is characterized by two vinyl proton resonances (4.43, 3.79 ppm, $J = 1.8-2.1$ Hz in acetone-d_6), and a methylene ^{13}C NMR resonance at 75.3 ppm. These signals are shifted significantly upfield from those of a typical alkylated vinylpyrrole complex (e.g., **12**).[15]

4. Michael Addition. β-Vinylpyrrole complexes with pendant electron withdrawing groups are easily synthesized by the Michael addition of an activated alkyne and an η^2-pyrrole complex (e.g., **2**). Reaction of either 3-butyn-2-one or DMAD with **2** produces the previously described vinylpyrrole complexes **33** and **35** (Scheme 1).[8b,16] Similarly, the reaction of methyl propiolate and 4-phenyl-3-butyn-2-one gives complexes **34** and **36**, respectively. Based on ^{1}H NMR coupling data, complexes **33** and **34** exist as *trans*-isomers, with $J \sim 15$ Hz.

The 3-vinylpyrrole complexes described above have been characterized by ^{1}H and ^{13}C NMR as well as by cyclic voltammetry (Table 1, supporting information). Present in the ^{1}H NMR spectrum (acetone-d_6) of a typical β-vinylpyrrole complex are two doublets ($J \sim 4.2$ Hz) at approximately 6.6 and 5.7 ppm for H(5) and H(4), respectively, as well as a singlet at 6.3−6.6 ppm for H(2), all of which are consistent with an η^2-pyrrole complex substituted at C(3).[8] The resonances for the protons on the terminal double bond are either broad singlets or doublets ($J \leq 2$ Hz) between 4.5 and 5.5 ppm. Present in the ^{13}C NMR spectrum is either a methylene carbon (DEPT) at ~105−115 ppm or a methine resonance at ~116 ppm for the vinyl carbon. Cyclic voltammetric data show an irreversible oxidation wave, typically at ~0.3 V (NHE).[17]

Linkage Isomerization of Vinylpyrrole Complexes. At 20 °C the β-vinylpyrrole complex **12** slowly undergoes a pyrrole-to-vinyl linkage isomerization in solution (CD_3CN, $t_{1/2} \sim 36$ h) to generate compound **42** (Figure 2).[8a] At elevated temperatures (70−80 °C), this transformation is complete in less than 1 h. The analogous transformation is also observed for the methoxy-substituted vinylpyrrole complex **32** ($t_{1/2} \sim 22$ h; 20 °C; CD_3CN), as well as for the electron-deficient vinylpyrrole complex **33** ($t_{1/2} \sim 92$ h; 20 °C; CD_3CN). ^{1}H NMR spectra for **42** show three pyrrole resonances ranging from 5.7 to 6.6 ppm and two vinyl signals (3.78, 3.23 ppm) that are shifted considerably upfield relative to the ring-bound precursor. For most of these ring-bound β-vinylpyrrole complexes, cyclic voltammetric data show an initial irreversible oxidation wave corresponding to the ring-bound isomer followed by a reversible couple. For instance, when the ring-bound β-vinylpyrrole complex **12** is oxidized by one electron ($E_{p,a} = +0.26$ V), a linkage isomerization on Os(III) rapidly occurs ($t_{1/2} < 1$ s) to give the corresponding vinyl-bound Os(III) species ($E_{1/2} = 0.48$ V) (Figure 2). Since this compound is now a better oxidant than its precursor, it quickly accepts an electron from remaining starting material to generate **42**. This phenomenon is also observed in the cyclic voltammogram of **33**, where the potential (0.84 V) of its linkage isomer (**43**) is 400 mV more positive than that of its ring-bound counterpart. This observation suggested that the linkage isomerization of both **12** and **33** could be carried out with the appropriate oxidative catalyst. When **33** is combined with 0.4 equiv of ferrocenium hexafluorophosphate ($E_{1/2} = 0.55$ V), the reaction solution turns immediately from red-orange to dark green. Precipitation of the reaction

(11) While the elimination proceeds more smoothly with a relatively strong base such as DBU (pK_a of the conjugate acid = 17.4), it can be carried out with other bases such as *i*-Pr_2EtN or Proton Sponge ($pK_a \sim 12$). Attempts to synthesize the azafulvenium complex using catalytic base fail since any azafulvenium complex that is formed is deprotonated quickly relative to the elimination of remaining starting material, thus consuming any base present.

(12) The 3*H*-pyrrolium complex (the product of C(3) protonation) is the only product isolated, possibly due to water contamination.

(13) Some protonation still takes place to give the parent 1-methyl-3*H*-pyrrolium complex as a byproduct. Protonation not observed with non-enolizable acetals (e.g., benzaldehyde dimethylacetal); see ref 8b.

(14) The acetyl complex **4** has been reported previously. See ref 8b.

(15) Complex **32** is prone to undergo either hydrolysis in wet acetone solution, or a linkage isomerization.

(16) The Michael reaction between **2** and either DMAD or 4-phenyl-3-butyn-2-one is carried out in DMSO, where the enolate anion generated ring closes at C(2) to initially give a cyclobutene-substituted 2-pyrroline complex, the synthetic equivalent to a 2 + 2 cycloaddition reaction. These intermediates are subsequently ring opened in the presence of a proton source such as methanol or phenol to give the vinyl pyrrole complexes. For characterization of the cyclobutene intermediates from the reaction with DMAD (**35**) or 3-butyn-2-one (**33**), see ref 8b.

(17) In many cases, a second *reversible* oxidation wave is observed at +0.5 V, attributed to an oxidation-promoted linkage isomerization of the osmium to the pendant double bond (see text).

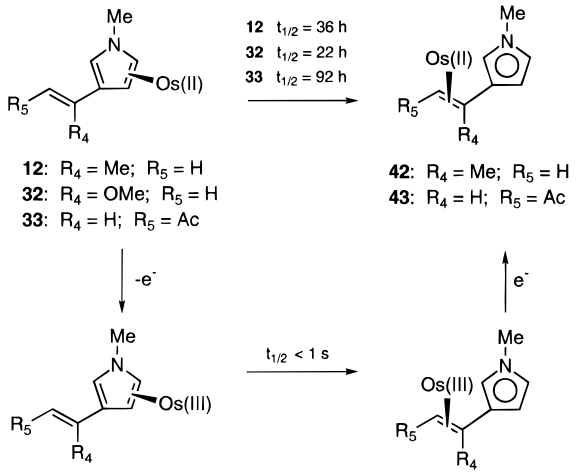


Figure 2. Linkage isomerization of β-vinylpyrrole complexes.

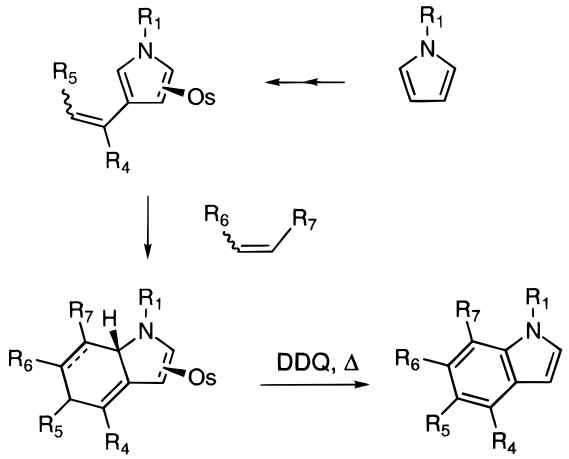
mixture yields a product whose cyclic voltammogram and ^{1}H NMR spectrum show complete conversion to the linkage isomer (**43**, $E_{1/2}$ = 0.84 V).[18]

2-Azafulvenium Complexes. η^2-2-Azafulvenium complexes are readily generated from the corresponding β-vinylpyrrole by protonation with methanolic triflic acid (**19**−**31**; Scheme 1). The color of these complexes ranges from emerald green to turquoise to purple-brown depending on substituents due to low energy absorptions (ϵ = 400−900 L·M^{-1} cm^{-1}) in the range of 525−600 nm. These complexes have been characterized by ^{1}H and ^{13}C NMR, UV/vis, and cyclic voltammetric data (supporting material). The resonances for H(5) and H(4) appear at 6.9−7.4 ppm (acetone-d_6) and 6.1−6.6 ppm, respectively, considerably downfield from those of unconjugated 3*H*-pyrrolium complexes.[8,9] The iminium H(2) resonance appears at 8.6−9.1 ppm, and the C(2) iminium resonance appears at ∼156 ppm, values shifted upfield from those of unconjugated 3H-pyrrolium complexes due to extended conjugation. Electrochemical data show an irreversible Os(II/III) oxidation wave at ∼1.25 V for alkyl azafulvenium complexes (e.g., **19**) and at 1.0−1.1 V for the alkoxy azafulvenium derivatives. Scanning the potential negatively results in an irreversible ligand-centered reduction wave at ∼ −0.6 to −1.1 V. Since these complexes may be handled in air and are stable in both CD_3CN and D_2O for several hours at 80 °C (indefinitely at room temperature), they serve as convenient precursors to a wide variety of β-vinylpyrrole complexes.

In cases where the two substituents on the exocyclic double bond differ significantly either sterically or electronically from each other, a high stereoselectivity (>90% de) is generally observed.[19] In general, bulky substituents tend to favor a position *trans* to the organometallic substituent but donor groups (i.e. hydroxy or methoxy) appear to favor a *cis*-orientation.

Diels−Alder Reactions. Synthesis of Tetrahydroindole Complexes. The uncoordinated portion of the β-vinylpyrrole complexes described above resembles an electron-rich diene and, as such, reacts under mild conditions with electron-deficient alkenes and alkynes in a Diels−Alder fashion (Table 1, Scheme 2). When the vinylpyrrole complex **12** is combined with *N*-phenylmaleimide in acetonitrile, the cycloaddition is complete within 15 min producing the 5,6,7,7a-tetrahydroindole complex **46** in 80% yield.[8a] This reaction is general for all of the

Scheme 2



vinylpyrrole complexes described and has been carried out with a broad array of dienophiles including 4-cyclopentene-1,3-dione, *N*-phenyl maleimide, DMAD, dimethyl fumarate, and methyl acrylate. A summary of reaction conditions and yields are given in Table 1. As expected, the stereochemistry and rate of this reaction are sensitive to the electronic and steric nature of the reactants. For example, the reaction between the phenyl-substituted vinylpyrrole complex **13** and 1 equiv of dimethyl fumarate is complete within 1 h in acetonitrile. When methyl acrylate is used, the reaction is considerably more sluggish, and the use of a Lewis acid (e.g., BF_3·Et_2O) or a large excess of dienophile is required for a satisfactory yield (e.g., **50** and **54**; Table 1).[20] When the vinylpyrrole complex contains an electron withdrawing group (e.g., **33**), the vinylpyrrole is deactivated and only highly electron-deficient dienophiles such as maleimides react at a sufficient rate that linkage isomerization is avoided (*vide supra*).

These complexed tetrahydroindoles are characterized primarily by ^{1}H, ^{13}C NMR, and combustion analysis data. Proton resonances (CD_3CN) for a typical cycloadduct include two doublets (J = 4.5 Hz) between 4 and 6 ppm for H(2) and H(3), *cis*- and *trans*-ammine resonances at ∼3 and 4 ppm, respectively, and a singlet between 2.5 and 3.0 ppm for the *N*-methyl group. Resonances in the ^{13}C NMR spectrum include peaks at ∼85 and 40 ppm for C(2) and C(3), and a peak at 60−65 ppm for C(7a). Cyclic voltammetry shows a broad irreversible oxidation wave ($E_{p,a}$ = 0.2−0.4 V) followed by a broad reduction wave ($E_{p,c}$ ∼ −0.15 V) on the return scan.

Stereochemistry. In most cases, the tetrahydroindole complexes described above are isolated as single diastereoisomers (de ≥ 80%), even though up to four chiral centers have been created. For two of these complexes, a thorough spectroscopic analysis using 2D NOESY and COSY data was performed.[21] With respect to the metal, both **46** and **48** possess *anti* stereochemistry at C(7a), which is consistent with the electrophile attacking the ring face opposite that of metal coordination, as has been observed without exception for other electrophilic addition reactions.[22] In the case of **46**, the imide moiety was found to be *anti* with respect to metal coordination, the product of an *endo* cycloaddition (Figure 3). For the case of the

(18) When this reaction was attempted using <10 mol% of oxidant at a similar concentration, only 20% conversion occurred after a 30 min reaction time. The dark green appearance of the product is probably due to an impurity.

(19) Stereochemistry assigned through NOE data, which are reported in the experimental section.

(20) This reaction is cleaner using the latter procedure. Use of both polar aprotic solvents and/or salts such as LiOTf have been shown to enhance the reactivity of similar electrophiles in the dipolar cycloaddition reaction of these pyrrole complexes. Gonzalez, J.; Koontz, J. I.; Hodges, L. M.; Nilsson, K. R.; Neely, L. K.; Myers, W. H.; Sabat, M.; Harman, W. D. *J. Am. Chem. Soc.* **1995**, *117*, 3405.

(21) For a more detailed explanation of the determination of the stereochemistry, see the experimental and supporting information.

Table 1. Experimental Details for the Synthesis of Tetrahydroindole Complexes **46**−**86**

starting material	R_1	R_4	R_5	R_6	R_7	dienophile[a,b]	pdt	yld[c]
12	Me	Me	H	−C(O)N(Ph)C(O)−		NPM	**46**	77
13	Me	Ph	H	−C(O)N(Ph)C(O)−		NPM	**47**	82
12	Me	Me	H	CO_2Me	CO_2Me	DMFum	**48**	79
13	Me	Ph	H	CO_2Me	CO_2Me	DMFum	**49**	84
13	Me	Ph	H	H	CO_2Me	MeAcr	**50**[d]	79
26	Me	H	H	−C(O)N(Ph)C(O)−		NPM	**51**	78
12	Me	Me	H	CO_2Me	CO_2Me	DMAD[e]	**52**	81
32	Me	OMe	H	−C(O)N(Ph)C(O)−		NPM	**53**	77
32	Me	OMe	H	H	CO_2Me	MeAcr	**54**	76
33	Me	H	Ac	−C(O)N(Ph)C(O)−		NPM	**55**	84
34	Me	H	CO_2Me	−C(O)N(Ph)C(O)−		NPM	**56**	82
35	Me	CO_2Me	CO_2Me	−C(O)N(Ph)C(O)−		NPM	**57**	75
36	Me	Ph	Ac	−C(O)N(Ph)C(O)−		NPM	**58**	82
37	H	H	Ac	−C(O)N(Ph)C(O)−		NPM	**59**	78
12	Me	Me	H	−C(O)CH_2C(O)−		CPD	**60**	44
14	Me	Et	Me	−C(O)CH_2C(O)−		CPD	**61**	65
15	Me	*f*	*f*	−C(O)N(Ph)C(O)−		NPM	**62**	84
3	Ar[g]	Me	H	−C(O)N(Ph)C(O)−		NPM	**83**[h]	72
85	Ar	H	Ac	−C(O)N(Ph)C(O)−		NPM	**86**	81

[a] Abbreviations for dienophiles: NPM = *N*-phenylmaleimide; DMFum = dimethylfumarate; MeAcr = methyl acrylate; DMAD = dimethylacetylenedicarboxylate; CPD = 4-cyclopentene-1,3-dione. [b] Cycloadditions performed in acetonitrile except for **50** and **54** in which DMAc was used. [c] Yield calculated from 1-methylpyrrole. [d] This compound can also be prepared in slightly lower yield using $BF_3{\cdot}Et_2O$ at −50 °C. [e] Reaction preformed at −50 °C in 2:1 MeCN/EtCN. [f] $R_4 = R_5 = -(CH_2)_4-$. [g] Ar = 3,5-dimethylbenzyl. [h] Synthesized in a one-pot procedure from **3**.

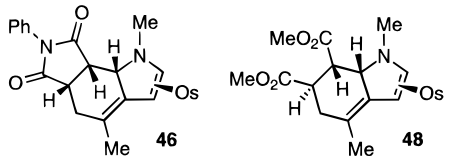


Figure 3. Stereochemistry of 5,6,7,7a-tetrahydroindole complexes.

fumarate adduct **48**, only one isomer is observed initially; however, over several days in acetonitrile solution, the initial product epimerizes to eventually give a 1:1 equilibrium ratio of a new isomer along with the original product. With respect to the osmium, the initial isomer was identified as the 6-*syn*, 7-*anti* isomer as shown in Figure 3 (i.e., the carbomethoxy group at C(7) is in an *endo* orientation). Due to overlapping of resonances for both isomers, no stereochemical data could be obtained for the new isomer.

Synthesis of Indoles. Treating the tetrahydroindole complexes with 2 equiv of DDQ followed by moderate heating results in formation of the corresponding indole (Scheme 2).[8a,23] The oxidant in this reaction serves two functions: (1) to liberate the ligand from the metal and (2) to oxidize the tetrahydroindole ligand to the indole. Optimization of this reaction with respect to equivalents of DDQ, solvent, temperature, and acidic or basic conditions has been carried out in several cases. In general, treatment of the tetrahydroindole complexes with 2 equiv DDQ in either DMAc or CH_3CN followed by heating (120−200 °C) without the addition of external acid or base affords the highest yields of indole (Table 2).[24] The yield of the decomplexation/oxidation process varies considerably (5−74%) depending on the tetrahydroindole, but performing the reaction in DMAc at 160−165 °C appears to give the best results.[25] In general, we find that addition of acid dramatically reduces the yield, and addition of base to the reaction does not significantly improve the yield except for the case of indole **65** where addition of 3 equiv of Hünig's base improved the yield from 64 to 74%.

While most of the indoles described in this paper were prepared directly from the corresponding tetrahydroindole complexes synthesized in an inert atmosphere drybox, a one-pot procedure for synthesizing some of the reported indoles has been developed to be carried out on the bench starting with the air stable complex $[Os(NH_3)_5OTf]OTf_2$. This complex is reduced (Zn/Hg) under argon in the presence of excess 1-methylpyrrole in Aldolmethanol followed by addition of a methanolic solution of triflic acid to give the air-stable β-protonated 1-methylpyrrole complex (**88**).[26,27] This complex may be isolated and subsequently converted on-the-bench to a variety of indoles in a one-pot reaction sequence.

For example, indole **66** was prepared in 40% isolated, chromatographed yield from **88** using this procedure (propionitrile solvent; 37% overall yield from 1-methylpyrrole). The indoles described in this paper have been characterized by ^1H and ^{13}C NMR data (supporting information) and UV−visible (supporting information).[28]

Synthesis of the Benz[*e*]indole and Herbindole Systems. When the 4-(1-cyclohexenyl)-1-methylpyrrole complex **15** undergoes cycloaddition with a dienophile such as *N*-phenylmaleimide, the resulting tetrahydroindole complex (**62**) contains a fused six-membered ring at C(4)−C(5) (Figure 4), and thus may be considered an octahydrobenz[*e*]indole derivative. In principle, the use of an additional 2 equiv of DDQ during the decomplexation step would result in isolation of the fully aromatic benz[*e*]indole. When the decomplexation of **62** is carried out with 4−5 equiv of DDQ, the major product is the 6,7,8,9-tetrahydro-3*H*-benzindole, **79**. However, when these compounds are isolated from the osmium and quinone decomplexation byproducts and then treated with additional DDQ, oxidation to the fully aromatized derivative (**82**) proceeds smoothly.[29]

Recently, two new structurally similar classes of biologically active indoles were isolated from marine sponges collected off

(22) By convention, the osmium is drawn to coordinate the top face of the pyrrole ring. Note that since all of the complexes are racemic mixtures, this designation is done only to illustrate *relative* stereochemistry of the molecule.

(23) DDQ has been used successfully to decomplex the metal from several classes of dihapto-Os(II) complexes including both 2- and 3-pyrrolines, 7-azanorbornenes, furans, anilines, phenols, anisoles, dienes, and olefins. See ref 8b and references therein.

(24) The only significant impurities observed are dihydroindoles, which are easily removed by chromatography. While increasing the DDQ to three equivalents tends to prevent the observation of dihydroindoles, it fails to increase the yield and, in some cases, results in slightly lower yields of the indole.

(25) Increasing the temperature beyond 165 °C does not increase the yield and, in some cases, causes decomposition of the indole.

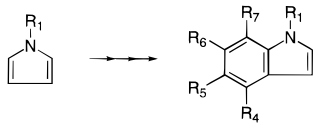
(26) This air stable adduct is synthesized directly from the 1-methylpyrrole complex (**2**) by protonation with triflic acid in methanol in an overall yield of 91% from 1-methylpyrrole. See refs 8b and 9. For details of the bench procedure, see the Experimental Section.

(27) The air stability of **88** in *solution* is highly dependent on the solvent; **88** is least stable in DMAc solution outside of the box due to facile deprotonation by the solvent and subsequent rapid oxidation of the resulting 1-methylpyrrole complex. Solutions of **88** are stable in acetonitrile for 1−2 days, and in acidic acetonitrile, several days to a week.

(28) Many of these indoles, particularly those prepared from *N*-phenylmaleimide, are highly fluorescent under long wave ultraviolet light (366 nm).

(29) Attempts were made to synthesize the dibenzindole nucleus by combining **15** with 2-cyclohexene-1-one; however, the Diels−Alder reaction with this dienophile failed, even in the presence of the Lewis acid $BF_3{\cdot}Et_2O$.

Table 2. Overall Isolated Yields Based on Complexed Pyrrole for Indoles **65**−**87**



compd	pre-cursor	R_1	R_4	R_5	R_6	R_7	overall yield[a]
65	**46**	Me	Me	H	−C(O)N(Ph)C(O)−		58(74)
66	**47**	Me	Ph	H	−C(O)N(Ph)C(O)−		48(60)
67	**48**	Me	Me	H	CO_2Me	CO_2Me	35(42)
68	**49**	Me	Ph	H	CO_2Me	CO_2Me	48(55)
69	**50**	Me	Ph	H	H	CO_2Me	39(49)
70	**50**	Me	H	H	−C(O)N(Ph)C(O)−		7(12)
71	**53**	Me	OMe	H	−C(O)N(Ph)C(O)−		29(37)
72	**54**	Me	OMe	H	H	CO_2Me	12(17)
73	**55**	Me	H	Ac	−C(O)N(Ph)C(O)−		46(52)
74	**56**	Me	H	CO_2Me	−C(O)N(Ph)C(O)−		14(17)
75	**57**	Me	CO_2Me	CO_2Me	−C(O)N(Ph)C(O)−		49(66)
76	**58**	Me	Ph	Ac	−C(O)N(Ph)C(O)−		22(27)
77	**59**	H	H	Ac	−C(O)N(Ph)C(O)−		4(5)
78	**61**	Me	Et	Me	$-C(O)CH_2C(O)-$		9(14)
79	**62**	Me	$-(CH_2)_4-$		−C(O)N(Ph)C(O)−		38(45)
80	**81**	Me	OMe	Me	CO_2Me	CO_2Me	5(6)
82	**79**	Me	$-(CH{=}CH)_2-$		−C(O)N(Ph)C(O)−		16(40)
84	**83**	Ar[b]	Me	H	−C(O)N(Ph)C(O)−		49(69)
87	**86**	Ar[b]	H	Ac	−C(O)N(Ph)C(O)−		50(67)
66[c]	**88**	Me	Ph	H	−C(O)N(Ph)C(O)−		37(40)
67[c]	**88**	Me	Me	H	CO_2Me	CO_2Me	40(42)

[a] Values represent the overall isolated yield of purified indole starting from pyrrole. Value in parentheses is yield for decomplexation/oxidation step alone. [b] Ar = 3,5-dimethylbenzyl. [c] Prepared outside of glovebox from air-stable 3*H*-pyrrolium **88**.

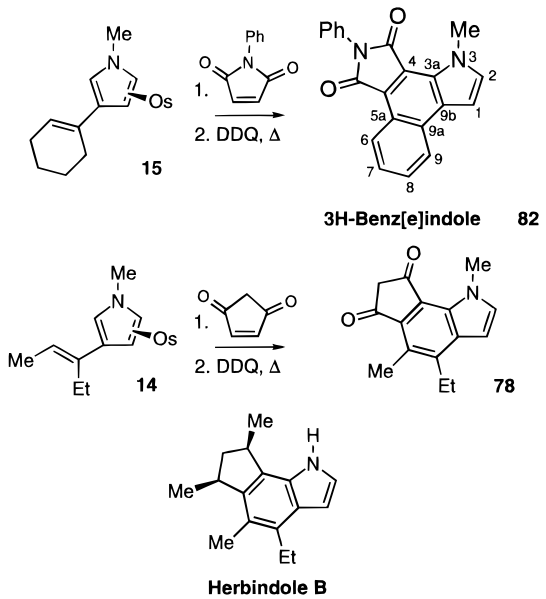


Figure 4. 3*H*-Benz[*e*]indole and herbindole B skeletons.

of the coast of Australia: the trikentrins and the herbindoles.[30] Both classes of indoles are characterized by a fused alkylated five membered ring at C(6) and C(7) and a lack of substitution at C(3) as well as varying alkyl substitution at C(4) and C(5). The structure of Herbindole B is given in Figure 4. By combining the β-vinylpyrrole complex **14** with a five-membered carbocycle dienophile we hoped it would be possible to synthesize the carbon skeleton of these indoles. When **14** is combined with 4-cyclopentene-1,3-dione in acetonitrile solution, the tetrahydroindole complex **61** is quickly formed and precipitates from solution (77%). This complex, which is formed as only one isomer, has been characterized by both ^{1}H and ^{13}C NMR spectroscopy, which indicate that the carbonyl closest to the pyrrole nitrogen exists as its enol form. This is supported by a singlet at 4.67 ppm integrating to one proton in the ^{1}H NMR as well as a methine resonance at 103 ppm (^{13}C NMR, DEPT). Unfortunately, decomplexation/oxidation of **61** has afforded the corresponding indole **78**, in low overall yields (14%) as its diketo isomer.[31]

Synthesis of *N*-Benzyl Derivatives. In an attempt to prepare indoles with an unsubstituted nitrogen, pyrroles with several common *N*-protecting groups were investigated. While both the 1-methoxymethyl- and 1-methoxyethoxymethylpyrrole complexes fail to undergo either a TBSOTf-promoted Aldol condensation with acetone or a Michael addition with 3-butyn-2-one, the 1-(3,5-dimethylbenzyl)pyrrole complex (**3**) readily undergoes both reactions.[32] Starting from the 1-(3,5-dimethylbenzyl)pyrrole complex (**3**), two different *N*-benzylated indoles were prepared using above-described methods in good overall yields. While in principle *N*-benzyl protecting groups may be removed from amines by hydrogenation or dissolving metal reduction, we are unaware of such a reaction for indoles and in agreement with this observation, attempts to debenzylate the *N*-(3,5-dimethylbenzyl)indoles described herein failed. Hydrogenation of **87** with either Pd/C or PtO_2 afforded a mixture of benzyl-containing indoles and perhydroindoles. Addition of ammonium formate did not improve the reaction. Attempts to reduce either **84** or **87** to the corresponding indolines (HBF_4 (aq)/PtO_2/20 °C)[33] were also unsuccessful. Murakami et al.[34] report that *N*-benzylindoles undergo debenzylation in the presence of either LDA or methyllithium. In our hands, **84** failed to debenzylate under such conditions. The use of other removable substituents for the pyrrole nitrogen were explored (e.g., *tert*-butyl[35], trimethylsilyl), but these failed, either due to lack of reactivity toward Michael acceptors (e.g., 1-methoxymethylpyrrole), incompatibility with Lewis acids (e.g., 1-trimethylsilylpyrrole and 1-methoxymethylpyrrole), or failure to eliminate (*tert*-butyl).

Observation of a Dihydroindole Intermediate. When **46** and 2.0 equiv of DDQ are combined in CD_3CN, a 40% NMR yield of a protonated metallated indole derivative is observed (**63**). ^{1}H and ^{13}C NMR (CD_3CN) for this compound show a resonance for an iminium proton at 9.16 ppm, three singlets (6.04, 5.09, 4.53 ppm) consistent with vinyl protons, a singlet for an *N*-methyl group at 3.68, and *cis*- and *trans*-ammine resonances at 3.87 and 5.26 ppm. In addition, two methylene carbons are observed at 113.40 and 36.24 ppm along with a methine resonance at 191.90 ppm (DEPT). Cyclic voltammetry of isolated **63** in CH_3CN/DMAc solution shows a broad irreversible oxidation wave at ~ +1.5 V (NHE) along with a

(30) (a) Capon, R. J.; MacLeod, J. K.; Scammells, P. J. *Tetrahedron* **1986**, *42*, 6545. (b) Herb, R.; Carroll, A. R.; Yoshida, W. Y.; Scheuer, P. J.; Paul, V. J. *Tetrahedron* **1990**, *46*, 3089.

(31) The 1,4-dimethyl analog was similarly prepared from vinylpyrrole complex **12**. ^{1}H NMR ($CDCl_3$) δ 7.47 (s, 1H), 7.29 (d, J = 3.3 Hz, 1H), 6.67 (d, J = 3.0 Hz, 1H), 4.37 (s, 3H), 3.26 (s, 2H), 2.66 (s, 3H).

(32) This alkyl-substituted benzyl protecting group was required to ensure that arene coordination did not occur during the complexation step.

(33) Smith, A.; Utley, J. H. P. *J. Chem. Soc., Chem. Commun*. **1965**, 427.

(34) Suzuki, H.; Tsukuda, A.; Kondo, M.; Aizawa, M.; Senoo, Y.; Megumi, N.; Wantanabe, T.; Yokoyama, Y.; Murakami, Y. *Tetrahedron Lett.* **1995**, *36*, 1671.

(35) The *tert*-butyl group was found to unexpectedly eliminate to afford an N−H indole upon heating a 1-*tert*-butylindole. See ref 6c. In our hands *N*-phenyl (4-methyl-1-*tert*-butylindole)-6,7-dicarboximide failed to eliminate at 140 °C and decomposed to several unidentifiable products at higher reaction temperatures. Characterization of *N*-phenyl (4-methyl-1-*tert*-butylindole)-6,7-dicarboximide ^{1}H NMR ($CDCl_3$) δ 7.47−7.25 (m, 6H), 6.91 (d, J = 3.3 Hz, 1H), 6.16 (d, J = 3.3 Hz, 1H), 1.98 (s, 3H), 1.72 (s, 9H).

reversible oxidation wave ($E_{1/2}$ = 0.73 V) consistent with that observed for a reduced form of DDQ, presumably present as the counterion for the metal complex.[36] From this data, **63** is assigned to be a 3,3a-η^2-[7a*H*-(6,7-dihydroindolium)] complex (Figure 1), formally the product of hydride abstraction from the C(4) methyl.[37] Heating a solution of **63** (DMAc, 3.0 equiv of *i*-Pr_2EtN) results in the anticipated indole **65** in 74% isolated yield. Of note, compound **63** is not observed when either 1 or 3 equiv of DDQ is used even though only 1 equiv of DDQ is required in principle. ^{1}H NMR data fail to show any diamagnetic organometallic species (i.e., Os(II)) present in solution upon addition of 1 equiv of oxidant and suggests that the initial reaction is simply oxidation of the metal to osmium(III). A dihydroindole complex is not observed when the analogous fumarate cycloadduct (**48**) is treated with 2.0 equiv of DDQ.

Discussion

Described in this paper are several independent methods for preparing osmium(II)-stabilized 2-azafulvenium and 3-vinylpyrrole complexes. The latter readily undergo cycloaddition with suitable dienophiles, and the resulting tetrahydroindole products may be elaborated efficiently into functionalized indoles. This sequence of steps constitutes a new synthetic methodology for indoles complementary to existing organic and organometallic methods. Although metals such as Pd(0), Pd(II), and Ti are seeing increased use in the synthesis of indoles, they have predominately been used either in ring closure of the heterocycle or in the functionalization of an intact indole ring system.

Vinylpyrroles have been extensively studied in the context of polymerization and synthesis of natural products.[6,7,38] In particular, vinylpyrroles have been used successfully to prepare indoles via a Diels−Alder cycloaddition with activated alkynes.[6] However, the use of vinylpyrroles in this context has been limited essentially to the 2-vinylpyrroles, owing to the lack, until recently,[7] of a suitable preparative method for the 3-vinyl derivatives.[39] In pioneering studies of Jones et al.,[6a−c] 2- and 3-vinylpyrroles were observed to react with various alkenes and alkynes to form tetrahydro- and dihydroindoles, respectively. Focusing mainly on 2-vinylpyrroles,[40] these studies demonstrated the potential of such an approach to indoles[41] but also revealed important limitations. Specifically, when substituents such as acetyl, carbomethoxy, or phenyl were present on the terminal double bond, cycloaddition was not observed; rather Michael reactions at C(5) became the dominant reaction. Furthermore, when olefins were used as the dienophile, the initial product, a 5,6,7,7a-tetrahydroindole, rapidly isomerized to its aromatic isomer (a 4,5,6,7-tetrahydroindole), a species that resists dehydrogenation by DDQ or Pd/C.[6c]

The ability of the pentaammineosmium(II) moiety to dearomatize and activate the pyrrole ring toward electrophilic addition at the β-carbon and to stabilize pyrrolium intermediates through a strong metal-ligand π-backbonding interaction has been well documented.[8] These features are exploited in the present work in several ways. Each of the four methods for preparation of β-vinylpyrroles have as their key step the selective electrophilic addition at the β-carbon away from osmium coordination. Specifically, addition of ketones, acetals, Michael acceptors, and acyl groups readily occur at C(3) without complication from addition at C(2), multiple alkylation or polymerization. With the exception of the Michael addition of alkynes, elaboration into β-vinylpyrroles depends on the ability of the metal to stabilize the 2-azafulvenium intermediates resulting from either elimination or alkylation (Scheme 1). Once formed, the β-vinylpyrrole complexes show significantly greater reactivity toward dienophiles than do their uncomplexed counterparts due to the π-electron donating properties of the metal and the localization of π-electron density between C(2) and C(3). Finally, as a result of being coordinated to the osmium moiety, the cycloaddition product, a 5,6,7,7a-tetrahydroindole, does not rearomatize; as a consequence treatment with DDQ is capable of oxidizing the tetrahydroindole to its fully aromatic form.

This approach offers considerable flexibility in the choice of substituents at C(4)−C(7), positions that are often difficult to functionalize by more conventional methods. Substitution at C(4) and C(5) are established by the appropriate choice of ketone, alkyne, acetal, or anhydride (Scheme 1) leading to the corresponding β-vinylpyrrole. The choice of dienophile controls the placement of substituents at C(6) and C(7). The versatility of this procedure is illustrated by the synthesis of indole **78** (albeit in poor overall yield), a compound with the carbon skeleton of the trikentrins and Herbindoles. In this case, the unusual substitution at the 4- and 5-positions match that of the natural product Herbindole B.[42] Alternatively, a benz[*e*]indole (**82**) was readily prepared via the preparation of a cyclohexenone-derived β-vinylpyrrole. While coordination of the metal prevents direct functionalization of C(3) prior to decomplexation, uncomplexed indoles undergo facile electrophilic addition primarily at this position.[43,44]

Tetrahydroindole Stereochemistry. For essentially all of the tetrahydroindole complexes isolated, the products of cyclo-

(36) When isolated **63** is treated with excess triflic acid in methanol followed by precipitation with Et_2O, the reversible wave at 0.71 V is no longer observed. This observation is consistent with the [DDQH]$^-$ anion being exchanged for triflate.

(37) Note the presence of a 2*H*-pyrrolium fragment in the structure of **63**. Partial characterization of **63**: ^{1}H NMR (CD_3CN, 5% DMSO-d_6) δ 9.16 (s, 1H), 7.45−7.10 (m, 5H), 6.04 (s, 1H), 5.26 (br s, 3H), 5.09 (s, 1H), 4.53 (s, 1H), 4.24 (dd, J = 8.7, 6.6 Hz, 1H), 3.87 (br s, 12H), 3.68 (s, 3H), 3.52 (dd, J = 7.2, 7.2 Hz, 1H), 2.78 (m, 1H) (two proton resonances not assigned); ^{13}C NMR and partial DEPT (45° and 135° pulses) (CD_3CN) δ 191.90 (CH), 178.27 (CO), 175.25 (CO), 143.41 (C), 130.22 (CH), 130.03 (CH), 127.77 (CH), 113.40 (CH_2), 73.36 (CH), 49.21 (CH), 40.76 (CH), 38.52 (CH_3), 35.95 (CH), 36.24 (CH_2). Not all quaternary carbons are assigned.

(38) For a review of vinylpyrroles, see: Trofimov, B. A. In *Pyrroles Part Two: The Chemistry of Heterocyclic Compounds, v. 48*; R. A. Jones, Ed.; John Wiley & Sons: 1992; Chapter 2, and references therein.

(39) A common method for the synthesis of vinylpyrroles is formylation of the pyrrole ring followed by a Wittig reaction to introduce the double bond.

(40) The only example in the literature to date of a cycloaddition with a 3-vinylpyrrole is for the case of 1-*tert*-butyl-3-vinylpyrrole. See ref 6c.

(41) In related studies by Noland et al. substituted tetrahydrocarbazoles have been synthesized by Diels−Alder reactions with vinylindoles, which were prepared directly by electrophilic addition to the starting indole. Oxidation of the tetrahydrocarbazoles with two equivalents of DDQ gave the final carbazoles in high yield. See: (a) Noland, W. E.; Walhstrom, M. J.; Konkel, M. J.; Brigham, M. E.; Trowbridge, A. G.; Konkel, L. M. C.; Gourneau, R. P.; Scholten, C. A.; Lee, N. H.; Condoluci, J. J.; Gac, T. S.; Pour, M. M.; Radford, P. M. *J. Heterocycl. Chem.* **1993**, *30*, 81, and references therein. (b) Noland, W. E.; Konkel, M. J.; Tempesta, M. S.; Cink, R. D.; Powers, D. M.; Schlemper, E. O.; Barnes, C. L. *J. Heterocycl. Chem.* **1993**, *30*, 183, and references therein.

(42) Although the use of methyl ethyl ketone results in a 1:1 ratio of structurally different vinylpyrroles, it has been demonstrated that both isomers convert cleanly to tetrahydroindoles with *N*-phenylmaleimide. Reaction of the mixture of vinylpyrrole complexes with 4-cyclopentene-1,3-dione followed by decomplexation would give a mixture of isomeric indoles, which in principle, could be separated. One of these isomers is the 4,5-dimethyl analog, which matches the substitution pattern for herbindole A. The other possesses a 4-ethyl substituent with a hydrogen at C(5), which matches the substitution pattern for trikentrin A.

(43) Remers, W. A. In *Indoles Part One: The Chemistry of Heterocyclic Compounds, v. 25*; Houlihan, W. J., Ed.; John Wiley & Sons: New York, 1972; Chapter 1.

(44) Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1994**, *35*, 2405, and references therein. For considerations on the synthesis and reactivity of 3-haloindoles, see: Powers, J. C., in *Indoles Part Two: The Chemistry of Heterocyclic Compounds, v. 25*; Houlihan, W. J. Ed.; John Wiley & Sons: New York, 1972; Chapter 5.

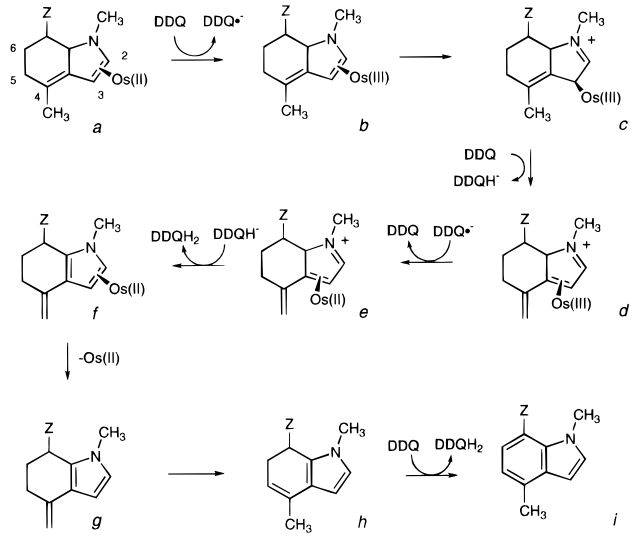


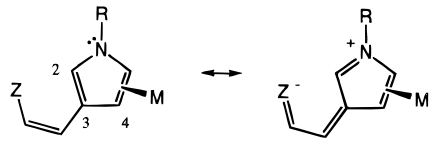
Figure 5. Proposed mechanism of decomplexation of 5,6,7,7a-tetrahydroindole complexes.

addition are formed as single diastereomers (>10:1). While the occurrence of overlapping proton resonances has prevented spectroscopic stereochemical elucidation in many cases, two compounds (**46** and **48**) have been fully characterized (Figure 3). NOE studies establish that H(7a) is *syn* with respect to the metal in both complexes, indicative of dienophile addition to the ring face opposite metal coordination. Inspection of molecular models indicates that addition of the dienophile to the osmium-bound face can be in general ruled out on the grounds of steric interactions. The stereochemistry at C(6) and C(7) for **46** is consistent with the Alder rule where an *endo* attack of the dienophile is observed.

On the Mechanism of Decomplexation. The tetrahydroindole complexes can be decomplexed and oxidized by DDQ in one step to generate the corresponding indoles. While this process could in principle require up to 3 equiv of oxidant, two for the organic oxidation and one for the metal,[45] 2 equiv have consistently given the best results. Since yields for the decomplexation/oxidation step have reached as high as 74%, the oxidation of osmium does not appear to be required. Given that uncomplexed 5,6,7,7a-tetrahydroindoles easily rearomatize and resist further oxidation by DDQ,[6c] the osmium is likely to remain bound to the indole ring system until dehydrogenation has commenced. In one case, an isolated intermediate in the oxidation/decomplexation process offers some insight into this mechanism (Figure 5). When the tetrahydroindole **46** is treated with 2 equiv of DDQ at 20 °C, the intermediate **63** can be isolated (40%; Figure 1). In contrast, repeating the same experiment with exactly 1 equiv of DDQ results in complete loss of all diamagnetic organometallic species.[46] Finally, cyclic voltammetric data indicate that oxidation of **46** is *chemically irreversible* (even in the absence of DDQ). A plausible mechanism consistent with the above observations might involve the following: The initial one-electron oxidation of the tetrahydroindole (***a*** → ***b***) followed by a linkage isomerization could generate an intermediate such as ***c*** in Figure 5. This could be followed by a hydride abstraction from a carbon *adjacent* to C(4) to give a species ***d***. In earlier studies,[8b,10] we have shown that 2*H*-pyrrolium complexes of pentaammineosmium(III) such as ***d*** are potent one-electron oxidants ($E_{1/2} \sim 1.5$ V), that under the stated reaction conditions should easily be reduced to ***e***, a species similar to **63**. Osmium(II)−2*H*-pyrrolium complexes[8b,10] such as ***e*** are known to rapidly convert to 1*H*-pyrrole complexes (i.e., ***f***) in the presence of base, and indeed this is the experimental outcome for **63** as well. Upon loss of metal[47] (***f*** → ***g***) and double bond isomerization (***g*** → ***h***), the 6,7-dihydroindole (e.g., **64**) should rapidly undergo dehydrogenation by DDQ to yield the indole product (***i***). Conversions from ***e*** → ***f***, ***e*** → ***h***, and ***e*** → ***i*** have been independently verified in our laboratories for the indole system **65** starting with the tetrahydroindole complex **46**. Finally, in cases where C(4) is unsubstituted, a direct hydride extraction at C(5) is hypothesized.

Synthesis of Indoles Lacking Nitrogen Substituents. A limitation of the osmium methodology is that indoles without substitution on the nitrogen have, at present, been synthesized only in low yield. As mentioned previously, both deprotonation and acylation occur at the nitrogen in preference to the β-position when the nitrogen is unsubstituted, preventing the formation of the desired vinylpyrrole complex. While a 5-acetyltetrahydroindole complex (**59**) originating from pyrrole and an electron-deficient alkyne can be readily synthesized, its decomplexation under the optimized reaction conditions fails to produce an appreciable yield of the indole (**77**, 4% overall yield). A further disadvantage to this approach is that the electron-withdrawing groups that promote the Michael addition used to prepare vinylpyrrole complexes such as **59** also deactivate the resulting vinylpyrrole complexes toward Diels−Alder reactions. Our search for a removable nitrogen protecting group led us to prepare an *N*-benzylpyrrole derivative **3**, yet all attempts at debenzylating both **84** and **87** using transfer hydrogenation, metal reduction, or lithium bases failed.

Linkage Isomerizations. β-Vinylpyrrole complexes of pentaammineosmium(II) undergo a linkage isomerization in which the osmium moves to the pendant vinyl double bond. The rate at which this isomerization takes place is dependent on the electronic nature of the pendant vinyl group. Withdrawing substituents on the uncomplexed β carbon (C3) have an enhanced interaction with the "enamine-like" uncoordinated portion of the pyrrole ring.[48]



In order for the osmium to migrate from its starting position to the vinyl group it must pass through a 3,4-η^2 intermediate and such coordination would interrupt this donor−acceptor interaction. Accordingly, the slowest isomerization is observed for the electron deficient Michael adduct **33** ($t_{1/2} \sim 92$ h, CD_3CN), while conversely, the fastest linkage isomerization is observed for the methoxy vinylpyrrole complex **32** ($t_{1/2} \sim 22$ h, CD_3CN). Although the vinyl-bound isomers are heavily favored thermodynamically over their heterocyclic linkage isomers, this isomerization is sufficiently slow that cycloadditions may be carried out at ambient temperatures with a variety

(45) Olefins and arenes are typically decomplexed from pentaammineosmium(II) by treatment of the metal with a one-electron oxidant such as DDQ or AgOTf.

(46) This conclusion is based upon a completely silent ^{1}H NMR spectrum and is an expected result in consideration of the known one-electron oxidation potential for **46** (0.29 V) and the reduction potential for DDQ (0.75 V).

(47) This process is described in Hodges, L. M., Ph. D. Dissertation, University of Virginia, May 1995.

(48) The ring-bound 3-acetylpyrrole complex does not undergo a linkage isomerization to the carbonyl and is stable to solvent substitution in CD_3CN at 80 °C. In contrast, the 2-acetylpyrrole complex, isolated as a 3:1 mixture of carbonyl-bound and ring-bound isomers, will undergo a linkage isomerization to the carbonyl followed by substitution by solvent at room temperature.

of dienophiles. However, when the metal center is oxidized by one electron to Os(III), essentially all backbonding character of the metal is lost, and the metal quickly isomerizes to the thermodynamically favored vinyl-bound isomer ($t_{1/2}$ < 1 s).

2-Azafulvenium Complexes. Although azafulvene and azafulvenium derivatives have been identified as important reaction intermediates,[49] relatively few reports of transition metal azafulvenes and azafulvenium complexes exist in the literature. An *N*-bound tungsten azafulvene was recently reported,[50] and a second report described a tin-metalated azafulvene dimer.[51] Uncoordinated 1- and 2-azafulvenium salts are highly reactive toward deprotonation or nucleophilic attack. In essentially all cases in which the azafulvenium salt can be isolated, strongly electron releasing groups are present on the exocyclic double bond.[52,53] As observed with 2*H*- and 3*H*-pyrrolium complexes, the pentaammineosmium(II) metal center stabilizes these electron-deficient ligands through backbonding such that they can be isolated and further derivatized. Remarkably, the 2-azafulvenium complex **19** is stable at 80 °C in CD_3CN solution for several hours with no isomerization and does not undergo decomposition or hydrolysis in water, even at elevated temperatures.

Conclusions. Four independent methods for the synthesis of β-vinylpyrrole complexes have been developed, each exploiting a different regioselective β-electrophilic addition for a dihapto-coordinated pyrrole. These compounds have been successfully elaborated into a series of 3-vinylpyrrole derivatives where the osmium is dihapto-coordinated to the *pyrrole*. Although these compounds are thermodynamically unstable with respect to their vinyl-bound linkage isomers, the isomerization is sufficiently slow that Diels−Alder cycloaddition reactions may be carried out with appropriate electron-deficient olefins, and the resulting tetrahydroindoles may be readily converted to the corresponding indoles. In addition to these findings, a series of novel metal-stabilized 2-azafulvenium complexes have been isolated and characterized, which serve as stable precursors to the corresponding 3-vinylpyrrole derivatives.

Experimental Section[54]

Synthesis of Complexes. The synthesis and characterization of the starting pyrrole complexes $[Os(NH_3)_5(L)]$ $(OTf)_2$ [L = pyrrole (**1**), 1-methylpyrrole (**2**), 3-acetyl-1-methylpyrrole (**4**), and 3-propionyl-1-methylpyrrole (**5**)] have been previously described, as have the 3*H*-pyrrolium aldol adduct **6**, vinylpyrrole complexes **12**, **33**, **35**, **37**, 2-azafulvenium complex **19**, and tetrahydroindole complex **46**.[8,10] The 1-(3,5-dimethylbenzyl)pyrrole complex (**3**) has been synthesized previously.[55] The characterization of these complexes is not given here but may be found in the supporting information. Representative procedures are given for several classes of compounds; full experimental data for all compounds are given in supporting information. Modifications to the general procedures are detailed in the Experimental Section when warranted.

Synthesis of 3H-Pyrrolium Complexes. {4*β*,5*β*-η^2-[Os(NH$_3$)$_5$]-3α-[3-(*tert*-Butyldimethylsiloxy)-3-pentyl]-1-methyl-3*H*-pyrrolium} (OTf)$_3$ [8]. In a 25 mL Erlenmeyer flask, a solution of **2** (1.027 g, 1.569 mmol) and diethyl ketone (201 mg, 2.33 mmol) in 3.9 g of acetonitrile was prepared with stirring. A solution of TBSOTf (452 mg, 1.71 mmol) in 1.0 g of acetonitrile was added with stirring, giving a red-orange precipitate within 30 s. The slurry was transferred to a 30 mL medium porosity frit with 5 mL of a 2:1 Et_2O/CH_3CN solution. The slurry was filtered, washed with 2:1 Et_2O/CH_3CN, Et_2O, and then dried *in vacuo* to afford the title compound as an orange-red powder. Yield: 1.304 g (1.30 mmol, 83%). ^{1}H NMR (CD_3CN, 5% DMSO-d_6) δ 8.73 (s, 1H), 6.26 (d, J = 4.2 Hz, 1H), 4.71 (d, J = 4.8 Hz, 1H), 4.67 (br s, 3H), 3.76 (s, 3H), 3.39 (br s, 12H), 2.84 (s, 1H), 1.88 (m, 4H), 0.99 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H), 0.86 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (CD_3CN, 5% DMSO-d_6) δ 174.16 (CH), 81.11 (C), 75.50 (CH), 64.12 (CH), 45.97 (CH), 42.38 (CH_3), 32.39 (CH_2), 30.24 (CH_2), 26.35 (C(CH_3)), 19.05 (C), 9.19 (CH_3), 9.00 (CH_3), −1.22 (CH_3), −1.50 (CH_3). Anal. Calcd for $C_{19}H_{47}N_6O_{10}S_3F_9SiOs\cdot 0.5CH_3CN$: C, 23.42; H, 4.77; N, 8.88. Found: C, 23.50; H, 4.52; N, 9.05.

One-Pot Synthesis of *β*-Vinylpyrrole Complexes via Aldol Condensation. {*E*-4,5-η^2-[Os(NH$_3$)$_5$]-3-(1-Ethyl-1-propenyl)-1-methylpyrrole} (OTf)$_2$ [14].[56] A solution of 1-methylpyrrole complex **2** (500 mg, 0.764 mmol) and diethyl ketone (103 mg, 1.20 mmol) in acetonitrile (2.1 g) was prepared. A solution of TBSOTf (243 mg, 0.920 mmol) in 0.5 g acetonitrile was then added, giving a red solution. After a few minutes, an orange-red precipitate (**8**) formed. After 10 min, a solution of DBU (152 mg, 1.00 mmol) in acetonitrile (0.5 g) was added to the slurry, giving a light brown solution. The reaction mixture was added to 90 mL stirred CH_2Cl_2, giving a tan precipitate, which was filtered, washed with CH_2Cl_2 and Et_2O, and dried *in vacuo*. Yield of light tan powder: 498 mg (0.688 mmol, 90%). ^{1}H NMR (acetone-d_6) δ 6.59 (s, 1H), 6.48 (d, J = 4.5 Hz, 1H), 5.78 (q, J = 7.2 Hz, 1H), 5.63 (d, J = 3.9 Hz, 1H), 4.43 (br s, 3H), 3.56 (s, 3H), 3.42 (br s, 12H), 2.27 (m, 2H), 1.69 (d, J = 6.9 Hz, 3H), 1.03 (t, J = 7.8 Hz, 3H); ^{13}C NMR (acetone-d_6) δ 139.39 (C), 125.66 (CH), 123.95 (C), 113.07 (CH), 80.37 (CH), 52.09 (CH), 36.57 (CH_3), 21.76 (CH_2), 14.07 (CH_3), 12.49 (CH_3). Anal. Calcd for $C_{12}H_{30}N_6O_6S_2F_6Os$: C, 19.94; H, 4.18; N, 11.63. Found: C, 19.28; H, 4.18; N, 11.64.

Stereochemistry assigned through NOE data: Irradiation of the C(7)-methyl group gives a 3.4% NOE with the CH_2 group on the C(6)-ethyl group. Irradiation of the methylene protons on the ethyl group gives a 4.0% NOE for the C(7)-methyl group and no enhancement for the C(7)-proton.

Synthesis of 2-Azafulvenium Complexes. {*Z*-3,4-η^2-[Os(NH$_3$)$_5$]-2,6-Dimethyl-6-phenyl-2-azafulvenium} (OTf)$_3$ [20]. A solution of **13** (117 mg, 0.155 mmol) was prepared in methanol (475 mg) which was then added to a solution of HOTf (35 mg, 0.23 mmol) in methanol (200 mg) to give an emerald green solution. After 10 min, the reaction mixture was added to 40 mL of stirred Et_2O, giving an emerald green precipitate which was filtered, washed with Et_2O, and dried *in vacuo* affording the title compound as an emerald green powder. Yield: 127 mg (0.140 mmol, 93%). ^{1}H NMR (acetone-d_6) δ 8.65 (s, 1H), 7.55 (d, 2H), 7.43 (m, 3H), 7.36 (d, J = 3.9 Hz, 1H), 6.60 (d, J = 4.2 Hz, 1H), 5.28 (br s, 3H), 4.16 (br s, 12H), 4.12 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (acetone-d_6) δ 157.98 (CH), 157.44 (C), 143.51 (C), 141.55 (C), 129.83 (CH), 129.11 (CH), 128.53 (CH), 73.84 (CH), 42.33 (CH), 40.66 (CH_3), 24.72 (CH_3).

(49) Barcock, R. A.; Moorcroft, N. A.; Storr, R. C.; Young, J. H.; Fuller, L. S. *Tetrahedron Lett.* **1993**, *34*, 1187, and references therein.

(50) Aumann, R.; Kuckert, E.; Krüger, C.; Angermund, K. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 563.

(51) Veith, M.; Zimmer, M.; Huch, V.; Denat, F.; Gaspard-Iloughmane, H.; Dubac, J. *Organometallics* **1993**, *12*, 1012.

(52) In many cases, these groups are capable of supporting a positive charge as well as the pyrrole nitrogen, making the azafulvenium salts represent one resonance structure where a pyrrole possessing a positively charged substituent is the other. Examples of stabilizing groups include dialkylamino, cyclopentenyl, phenyl, and various sulfur-containing ring systems.

(53) Sammes, M. P. In *Pyrroles Part One: The Chemistry of Heterocyclic Compounds, v. 48*; Jones, R. A., Ed.; John Wiley & Sons: 1990; Chapter 4, and references therein.

(54) For a detailed explanation of general experimental methods, reagent preparation, and solvent purification, see supporting information.

(55) Gonzalez, J.; Spera, M. L.; Nilsson, K. R.; Liu, R.; Chen, H.; Myers, W. H.; Harman, W. D. Manuscript in preparation.

(56) The intermediate 3*H*-pyrrolium aldol adduct (**8**) has been isolated and characterized.

(57) The presence of a light green color arises from formation of a small amount of the azafulvenium complex **20** during the reaction due to trace acid in the reaction mixture. This impurity is avoided by preparing the complex using excess methyl acrylate in DMAc solution (procedure 2).

(58) When DMAc is used as the solvent for the reaction, filtration through silica gel facilitates the filtration of the tacky metal precipiate. Final column chromatography removes the last traces of DMAc.

(59) Alternatively, purification can be accomplished using preparatory TLC using 6:1 $CHCl_3$/ethyl acetate as the mobile phase, especially if acetonitrile is the reaction solvent.

Stereochemistry assigned through NOE data: Irradiation of the C(6) methyl group gives a 10% enhancement for H(4) and no enhancement for the iminium proton. Compare to NOE data obtained for **29**.

Synthesis of β-Vinylpyrrole Complexes via Activated Alkynes. {4,5-η²-[Os(NH₃)₅]-3-(1-Carbomethoxy-1-ethenyl)-1-methylpyrrole} OTf₂ [34]. To a solution of **2** (148 mg, 0.226 mmol) in methanol (877 mg) is added 963 mg (11.46 mmol) of freshly distilled methyl propriolate. After 1.5 h, the deep red solution is added to 50 mL of stirring diethyl ether. The resulting orange-red precipitate is filtered, washed with diethyl ether, and dried *in vacuo* affording compound **34** as 141 mg (85%) of an orange-red powder. ^{1}H NMR (acetone-d_6) δ 7.66 (d, J = 15.3 Hz, 1H), 7.09 (s, 1H), 6.61 (d, J = 4.3 Hz, 1H), 6.03 (d, J = 15.3 Hz, 1H), 5.78 (d, J = 4.3 Hz, 1H), 4.65 (br s, 3H), 3.65 (s, 3H), 3.60 (s, 3H), 3.58 (br s, 12H); ^{13}C NMR (acetone-d_6) δ 169.06 (C), 142.51 (CH), 139.09 (CH), 120.21 (C), 105.22 (CH), 78.39 (CH), 51.23 (CH), 50.72 (CH_3), 37.05 (CH_3).

Synthesis of Tetrahydroindole Complexes. For most of the tetrahydroindole complexes described herein, the experimental procedures are similar; the synthesis of complex **47**, given below, is representative. For complexes **50**, **51**, and **61**, the procedures are somewhat unique; therefore the details for their preparation are provided.

{*N*-Phenyl(2,3-η²-[Os(NH₃)₅]-1-methyl-4-phenyl-5,6,7,7a-tetrahydroindole)-6,7-dicarboximide} (OTf)₂ [47]. A solution of **13** (180 mg, 0.237 mmol) and *N*-phenylmaleimide (49 mg, 0.28 mmol) in acetonitrile (0.8 g) was prepared, giving a golden yellow solution. After 40 min, the reaction mixture was added to 40 mL of stirred Et_2O, giving a yellow precipitate, which was filtered, washed with Et_2O, and dried *in vacuo*. Yield of yellow powder: 199 mg (0.214 mmol, 90%). ^{1}H NMR (CD_3CN) δ 7.50−7.13 (m, 10H, Ph), 5.87 (d, J = 4.5 Hz, 1H), 4.81 (d, J = 4.5 Hz, 1H), 3.89 (br s, 3H), 3.66 (dd, J = 6.9, 7.2 Hz, 1H), 3.18 (ddd, J = 1.8, 7.2, 7.2 Hz, 1H), 3.08 (s, 3H), 2.99 (d, J = 1.8 Hz, 1H), 2.93 (br s, 12H), 2.47 (dd, J = 6.3, 14.7 Hz, 1H) (other H(5) buried); ^{13}C NMR (CD_3CN) δ 179.54 (C), 176.22 (C), 147.74 (C), 142.11 (C), 133.75 (C), 126.36 (C), 87.63 (CH), 65.43 (CH), 41.86 (CH), 38.37 (CH), 37.38 (CH), 36.01 (CH_3), 32.03 (CH_2). CV: $E_{p,a}$ = 0.29 V.

{(2,3-η²-[Os(NH₃)₅])-7-carbomethoxy-1-methyl-4-phenyl-5,6,7,7a-tetrahydroindole)} (OTf)₂ [50]. Procedure 1. A sample of **13** (249 mg, 0.329 mmol) was dissolved in 1.5 g of a 1:1 mixture of acetonitrile and propionitrile. Methyl acrylate (35 mg, 0.41 mmol) was added, and the solution cooled to −55 °C. A solution of BF_3·Et_2O was prepared in acetonitrile/propionitrile (0.5 g, 1:1), and also cooled to −55 °C. The solutions were combined, giving a green solution, which was allowed to react for 10 min at −55 °C. After 10 min, the solution was added to 75 mL of stirred Et_2O, giving a green precipitate, which was filtered, washed with Et_2O, and dried *in vacuo*. Yield of light green powder:[57] 245 mg (0.291 mmol, 88%).

Procedure 2. A slurry of **13** (636 mg, 0.840 mmol) in methyl acrylate (3.31 g, 38.4 mmol, ∼46 equiv) was prepared. DMAc (0.7 g) was added with stirring, giving a homogenous solution. The reaction mixture was allowed to stand for 11 h and then added to 100 mL stirred Et_2O, giving a tacky precipitate. The precipitate was isolated, redissolved in acetone (∼10 mL), and added to 75 mL stirred Et_2O, giving a tan precipitate. The precipitate was filtered, washed with Et_2O, and dried *in vacuo*. Yield of tan powder: 613 mg (0.727 mmol, 87%). ^{1}H NMR (acetone-d_6) δ 7.37 (m, 5H), 5.85 (d, J = 4.5 Hz, 1H), 4.37 (br s, 3H), 4.29 (d, J = 4.5 Hz, 1H), 3.63 (s, 3H), 3.57 (br s, 12H), 3.17 (m, 1H), 2.99 (m, 1H), 2.86 (s, 3H), 2.36 (m, 2H), 1.98 (m, 2H); ^{13}C NMR (acetone-d_6) δ 173.04 (C), 142.97 (C), 140.57 (C), 130.0−127.0 (overlap, 3 × CH (Ph), (C)), 80.01 (CH), 64.14 (CH), 50.89 (CH_3), 42.93 (CH), 38.38 (CH), 36.09 (CH_3), 29.48 (CH_2), 22.71 (CH_2). CV: $E_{p,a}$ = 0.36 V.

{2,3-η²-[Os(NH₃)₅]-1-methyl-N-phenyl-5,6,7,7a-tetrahydro-6,7-indoledicarboximide} OTf₂ [51]. A sample of **27** (222 mg, 0.267 mmol) and *N*-phenyl maleimide (465 mg, 2.67 mmol) are dissolved in 2.1 g of a 2:1 cosolvent mixture of acetonitrile and propionitrile and cooled to −50 °C. A solution of iPr_2EtN (69 mg, 0.534 mmol) is dissolved in 102 mg of propionitrile and cooled to −50 °C. The solutions were combined, giving a brown solution, which was allowed to react for 18 h at −55 °C. After 10 min, the solution was added to 150 mL of stirred CH_2Cl_2, giving a brown-violet precipitate, which was filtered, washed with CH_2Cl_2 and Et_2O, and dried *in vacuo*. Yield of brown-violet powder: 177 mg (0.207 mmol, 78%).

{2,3-η²-[Os(NH₃)₅]-(1,5-Dimethyl-4-ethyl-8-hydroxy-1,5,5a,6,8a,8b-hexahydro-cyclopent[g]indole)-6-one (OTf)₂ [61]. A solution of **14** (1.200 g, 1.660 mmol) was prepared in acetonitrile (5.75 g) and subsequently added to a stirred slurry of 4-cyclopentene-1,3-dione (189 mg, 1.97 mmol) in acetonitrile (1.5 g). After 5 min, the formation of a dark tan precipitate was observed in the reaction flask. After 40 min, the slurry was transferred to a frit using ∼10 mL of a 1:1 mixture of acetonitrile/Et_2O, and the precipitate filtered. The filter cake was washed with acetonitrile (1 mL) and Et_2O (30 mL) and then dried *in vacuo*. Yield of light brown powder: 1.072 g (1.277 mmol, 77%). ^{1}H NMR (CD_3CN, 5% DMSO-d_6) δ 5.49 (d, J = 4.5 Hz, 1H), 4.79 (s, 1H), 4.64 (d, J = 4.8 Hz, 1H), 4.39 (br s, 3H), 3.35 (br s, 12H), 3.10 (dd, J = 6.6, 6.3 Hz, 1H), 2.87 (d, J = 6.0 Hz, 1H), 2.66 (s, 3H), 2.40−2.30 (m, 3H), 2.09 (m, 1H), 1.35 (d, J = 6.6 Hz, 3H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CD_3CN, 5% DMSO-d_6) δ 205.21 (C), 197.43 (C), 136.65 (C), 135.68 (C), 107.43 (C), 74.42 (CH), 66.42 (CH), 45.91 (CH), 45.79 (CH), 39.99 (CH), 37.10 (CH_3), 36.89 (CH), 23.04 (CH_2), 15.69 (CH_3), 14.16 (CH_3). CV: $E_{p,a}$ = 0.33 V (DMAc solution). Anal. Calcd for $C_{17}H_{34}N_6O_8S_2F_6Os$·0.5$CH_3CN$: C, 25.76; H, 4.26; N, 10.85. Found: C, 25.86; H, 4.43; N, 11.20.

Synthesis of Indoles from Tetrahydroindole Complexes. The following optimized procedure for the decomplexation of η²-tetrahydroindole complexes is representative; details are provided for the conversion of **46** to **65**.

A slurry of the tetrahydroindole complex **42** (303 mg, 0.341 mmol) in DMAc (2.8 g) was prepared and added to an Ace pressure tube. A solution of DDQ (165 mg, 0.727 mmol, 2.1 equiv) in 3 g of DMAc was then added, giving a dark orange reaction mixture. After ∼5 min, a solution of *i*-Pr_2EtN (135 mg, 1.05 mmol, 3.1 equiv) in 1.3 g of DMAc was then added, giving a dark solution with a slightly yellowish hue. The reaction was then heated to ∼160 °C for a 3 h reaction period.

Workup A. The reaction mixture was allowed to cool to room temperature and then added to 150 mL of stirred CH_2Cl_2, giving a black precipitate. The pressure tube was washed with several small (∼5−10 mL) aliquots of both acetonitrile and CH_2Cl_2, which were added to the bulk slurry. The slurry was filtered through a pad of silica gel in a fine porosity frit,[58] giving a yellow filtrate, which was evaporated to give a dark yellow oil. The crude indole was chromatographed on silica gel (2:1 petroleum ether/ethyl acetate)[59] to give a light yellow solid. Yield: 73 mg (0.25 mmol, 74% last step; 58% overall from 1-methylpyrrole). Crystallization of the final product affords analytically pure material for elemental analysis.

Workup B. Alternatively, the crude reaction mixture after the heating step can be evaporated under vacuum and the resulting solid or oil partitioned between CH_2Cl_2 and saturated $NaHCO_3$ (aqueous). The layers are then separated, and organic phase washed twice with saturated $NaHCO_3$ (aqueous), dried (K_2CO_3), and then evaporated to give the crude indole, which can be chromatographed as described above.

A listing of the fully characterized indoles reported with their respective ^{1}H and ^{13}C NMR data as well as UV−visible data may be found in the Supplemental Section.

***N*-Phenyl (1,4-dimethylindole)-6,7-dicarboximide [65]:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (t, 2H), 7.5 (s, overlap, 1H), 7.46 (d, 2H), 7.39 (t, 1H), 7.23 (d, J = 3.0 Hz, 1H), 6.65 (d, J = 3.0 Hz, 1H), 4.30 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.70 (C), 167.63 (C), 137.83 (C), 135.42 (C), 133.94 (CH), 132.16 (C), 131.09 (C), 128.92 (CH), 127.60 (CH), 127.27 (C), 126.76 (CH), 114.52 (CH), 112.82 (C), 101.85 (CH), 37.69 (NCH_3), 19.26 (CH_3). Mp = 193.5−195 °C. Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.06; H, 4.58; N, 9.37.

Synthesis of Benzindoles. The benzindoles described below were synthesized by combining the isolated crude mixture of tetrahydro- and dihydrobenzindole derivatives with DDQ in acetonitrile solution and then heating the mixture at ∼ 100 °C for 1 h. The reaction mixture was then cooled to room temperature and evaporated to dryness. The residue was then chromatographed on silica gel (2:1 petroleum ether/EtOAc mobile phase) to afford the pure benzindole.

***N*-Phenyl (3-methyl-3*H*-benz[*e*]indole)-4,5-dicarboximide [82]:** isolated in 16% overall yield from 1-methylpyrrole; ^{1}H NMR ($CDCl_3$)

δ 9.12 (d, J = 7.5 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.69−7.40 (m, 7H), 7.33 (d, J = 3.0 Hz, 1H), 7.12 (d, J = 3.0 Hz, 1H), 4.38 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.04 (C), 167.37 (C), 133.37 (CH), 131.96 (C), 131.55 (C), 130.62 (C), 128.97 (CH), 128.20 (CH), 127.66 (CH), 126.79 (CH), 126.29 (C), 126.15 (CH), 125.65 (CH), 123.34 (C), 123.01 (CH), 121.10 (C), 118.73 (C), 101.92 (CH), 38.47 (CH_3). Mp = 207−208 °C. Anal. Calcd for $C_{21}H_{14}N_2O_2$: C, 77.29; H, 4.32; N, 8.58. Found: C, 77.51; H, 4.01; N, 8.70.

Bench Procedure for the Synthesis of Indoles. While the syntheses of the indoles described above were carried out in a drybox out of convenience as well as to allow thorough characterization of intermediates (the vinylpyrrole and tetrahydroindole complexes are both air sensitive), a procedure was developed to prepare a select number of indoles in a one-pot procedure starting from the pyrrole and Os(III)-$(NH_3)_5$(OTf) $(OTf)_2$. A representative synthesis is given for **66**.

Synthesis of the 1-Methyl-3*H*-pyrrolium Complex (88). A 25-mL, three-necked round-bottomed flask was fitted with a stir bar and two rubber septa. Solid $Os(NH_3)_5OTf_3$ (1.00 g, 1.39 mmol) and zinc amalgam (6.00 g) were added, followed by an argon inlet. The system was connected to a bubbler and flushed with argon for 20 min. Degassed 1-methylpyrrole (1.50 g, 18.34 mmol) was added via syringe, followed by 4.33 g of degassed methanol. The reaction mixture is stirred for 30 min. A solution of HOTf (0.317 g, 2.11 mmol) in degassed methanol (2.1 g) was added via syringe forming a red slurry, which was stirred for an additional 5 min. The slurry was then added to ~200 mL of stirring Et_2O. The residual zinc amalgam was washed with several small portions of methanol, and the washings were transferred to the stirring ether. The resulting red precipitate was filtered through a 30 mL fine porosity fritted glass funnel, washed with ether, and dried *in vacuo*, affording 1.06 g (95%) of a pink-orange powder whose ^{1}H and ^{13}C NMR were indistinguishable from those of a sample of **88** prepared in a glovebox.

Benchtop Synthesis of Indole 66. A 25-mL, two-necked, round-bottomed flask fitted with a small magnetic stir bar and Claisen adapter was assembled. An argon inlet was added, and the system was connected to a bubbler. The flask flushed with argon for 15 min. The flask was charged with solid **88** (351 mg, 0.436 mmol), and the flask was flushed with argon for an additional 15−20 min. A solution of degassed *i*-PrEt_2N (64 mg, 0.50 mmol) and acetophenone (64 mg, 0.53 mmol) in 1.25 g of propionitrile was added via syringe with stirring, giving a golden brown solution of **2**. After 5 min, a solution of TBSOTf (138 mg, 0.522 mmol) in 0.75 g of propionitrile was added, giving a red solution. After 20 min, a solution of Proton Sponge (122 mg, 0.570 mmol) and *N*-phenylmaleimide (91 mg, 0.53 mmol) in 1.0 g of propionitrile was added, giving a golden brown solution. After 50 min, a solution of DDQ (197 mg, 0.868 mmol, 2.0 equiv) in 2.0 g of propionitrile was added, giving a dark solution. An additional 2 g of degassed solvent was used to wash the sides of the flask. The reaction mixture was heated to reflux (bp of propionitrile = 97 °C) with an oil bath for 1.5 h.

The reaction mixture was allowed to cool to room temperature and then added to 75 mL stirred CH_2Cl_2. The flask was washed with several aliquots of acetonitrile, and the washings were added to the slurry. The slurry was filtered through a silica gel pad in a 60 mL fine porosity frit, giving a yellow filtrate, which was evaporated to dryness. The resulting oily solid was chromatographed (2:1 petroleum ether/ethyl acetate) on silica gel to give an orange solid, consisting of indole **66** and unreacted *N*-phenylmaleimide. The mixture was separated by preparatory TLC (6:1 $CHCl_3$/ethyl acetate mobile phase), giving pure **66**. Yield: 62 mg (0.18 mmol, 40%). Overall yield from 1-methylpyrrole: 37%.

Acknowledgment is made to the National Institutes of Health (RO1-GM49236), the Camille and Henry Dreyfus Foundation, and Alfred P. Sloan Foundation, the National Science Foundation (NYI program), and Colonial Metals Inc. (Elkton, MD; OsO_4) for their generous support of this work.

Supporting Information Available: Additional information on the synthesis and characterization of compounds (52 pages). See any current masthead page for ordering and Internet instructions.

JA961072M