

Osmium-Promoted Dipolar Cycloadditions with Pyrroles: An Efficient, Stereoselective Synthesis of 7-Azanorbornanes[§]

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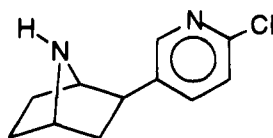
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Abstract: A series of 7-azabicyclo[2.2.1]hept-5-ene complexes are prepared from $[\text{Os}(\text{NH}_3)_5(\eta^2\text{-L})]^{2+}$ (L = pyrrole, 1-methylpyrrole, 2,5-dimethylpyrrole, 1,2,5-trimethylpyrrole, or 1-(trimethylsilyl)pyrrole) and various dipolarophiles (e.g., acrylonitrile, methyl acrylate, α -methylene- γ -butyrolactone, dimethyl fumarate, dimethyl maleate, *N*-phenyl maleimide, cyclopentene-1,2-dicarboxylic acid anhydride, and (*E*)- and (*Z*)-methyl 3-(3'-pyridyl)acrylate). The cycloaddition is promoted by coordination of the pyrrole with $[\text{Os}(\text{NH}_3)_5]^{2+}$ across C3 and C4, transforming the uncoordinated portion of the pyrrole nucleus into an azomethine ylide capable of undergoing 1,3-dipolar cycloadditions. The metal serves not only to activate the pyrrole ring but also to stabilize the resulting 7-azabicyclo[2.2.1]heptene ligands. A number of organic 7-azabicyclo[2.2.1]heptanes, including analogs of the alkaloid epibatidine, have been synthesized by this methodology. For the cases examined, the cycloaddition favors *exo* stereochemistry of the electron-withdrawing substituent when the pyrrole nitrogen is unsubstituted. Crystal structures have been determined for the complexes obtained from the reactions of pyrrole with *N*-phenylmaleimide (**8a**), 2,5-dimethylpyrrole with dimethyl maleate (**13a**), and 2,5-dimethylpyrrole with α -methylene- γ -butyrolactone (**22a**).

Introduction

Until recently, the 7-azabicyclo[2.2.1]heptane (7-azanorbornane) ring structure was thought not to exist in nature.² However, the report of a new alkaloid, epibatidine (*exo*-2-[6'-chloro-3'-pyridyl]-7-azanorbornane), found in trace amounts from skin extracts of an Ecuadoran poison frog, *Epipedobates tricolor*, has generated considerable interest in the 7-azanorbornane nucleus.³ Epibatidine is reported to be a highly potent, non-opioid analgesic and nicotinic acetylcholine receptor agonist.⁴



Epibatidine

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[§] **Abbreviations:** Os(II) = $[\text{Os}(\text{NH}_3)_5](\text{OTf})_2$; $\text{OTf}^- = \text{CF}_3\text{SO}_3^-$; CAN = ceric ammonium nitrate; DDQ = 2,3-dichloro-5,6-dicyanoquinone; DMAc = *N,N*-dimethylacetamide; DME = 1,2-dimethoxyethane; DMF = *N,N*-dimethylformamide; DMSO = dimethyl sulfoxide; 2,5-DMP = 2,5-dimethylpyrrole; DMPU = *N,N*-dimethylpropyleneurea; HFIPA = 1,1,1,3,3,3-hexafluoroisopropyl alcohol; HMDS = 1,1,1,3,3,3-hexamethyldisilazane; Hünig's base = *N,N*-diisopropylethylamine; LAH = lithium aluminum hydride; MVK = methyl vinyl ketone; NMF = *N*-methylformamide; TBAH = tetra-*n*-butylammonium hexafluorophosphate; TBSOTf = *tert*-butyldimethylsilyl triflate; TMSOTf = trimethylsilyl triflate.

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(1) Alfred P. Sloan Research Fellow 1994–1996; NSF Young Investigator 1993–1998; Camille and Henry Dreyfus Teacher–Scholar 1992–1995.

(2) For reviews on 7-azanorbornanes and related compounds, see: (a) Kricka, L. J.; Vernon, J. M. *Adv. Heterocyclic Chem.* **1974**, *16*, 87. (b) Chadwick, D. J. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W.; Cheeseman, G. W. H., Eds.; Pergamon: London, 1984; Vol. 4, pp 151, 261.

(3) Spande, T. F.; Garraffo, H. M.; Edwards, M. W.; Yeh, H. J. C.; Pannell, L.; Daly, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 3475.

(4) (a) Qian, C.; Li, T.; Shen, T. Y.; Libertine-Garahan, L.; Eckman, J.; Biftu, T.; Ip, S. *Eur. J. Pharm.* **1993**, *250*, R13. (b) Badio, B.; Daly, J. W. *Mol. Pharm.* **1994**, *45*, 563.

Most conventional approaches to the synthesis of 7-azanorbornanes include either (1) intramolecular nucleophilic ring closure of aminocyclohexane derivatives^{5,6} or (2) Diels–Alder cycloaddition of pyrroles with reactive, electron-deficient alkynes followed by hydrogenation of the resulting 7-azanorbornadienes.^{2,7,8} A retrosynthetic analysis of epibatidine suggests the substituted ring system could be generated efficiently in a single step via a Diels–Alder cycloaddition of a pyrrole with a substituted olefin. However, it is known that cycloaddition reactions of pyrroles with alkenes are limited by the inherent thermodynamic instability of the cycloadducts (with respect to either retrocycloaddition or retro-Mannich reactions and rearomatization) under typical reaction conditions.^{9,10} High pressures have been used to promote this reaction, but even in these cases the scope appears to be limited to *N*-acylated pyrroles

(5) (a) Pfister, J. R.; Wymann, W. E.; Weissberg, R. M.; Strosberg, A. M. *J. Pharm. Sci.* **1985**, *74*, 208. (b) Nelsen, S. F.; Ippoliti, J. T.; Frigo, T. B.; Petillo, P. A. *J. Am. Chem. Soc.* **1989**, *111*, 1776.

(6) A number of recent syntheses of epibatidine following this approach have been reported: (a) Broka, C. A. *Tetrahedron Lett.* **1993**, *34*, 3251. (b) Fletcher, S. R.; Baker, R.; Chambers, M. S.; Hobbs, S. C.; Mitchell, P. J. *J. Chem. Soc., Chem. Commun.* **1993**, 1216. (c) Corey, E. J.; Loh, T. P.; AchyuthaRao, S.; Daley, D. C.; Sarshar, S. *J. Org. Chem.* **1993**, *58*, 5600. (d) Fletcher, S. R.; Baker, R.; Chambers, M. S.; Herbert, R. H.; Hobbs, S. C.; Thomas, S. R.; Verrier, H. M.; Watt, A. P.; Ball, R. G. *J. Org. Chem.* **1994**, *59*, 1771. (e) Szantay, C.; Kardos-Balogh, Z.; Moldvai, I.; Szantay, C., Jr.; Temesvari-Major, E.; Blasko, G. *Tetrahedron Lett.* **1994**, *35*, 3171. (f) Senokuchi, K.; Nakai, H.; Kawamura, M.; Katsube, N.; Nonaka, S.; Sawaragi, H.; Harmanaka, N. *Synlett* **1994**, 343. (g) Sestanjk, K.; Melenski, E.; Jirkovsky, I. *Tetrahedron Lett.* **1994**, *35*, 5417. (h) Ko, S. Y.; Lerpiniere, J.; Linney, I. D.; Wrigglesworth, R. *J. Chem. Soc., Chem. Commun.* **1994**, 1775.

(7) (a) Altenbach, H. J.; Constant, D.; Martin, H. D.; Mayer, B.; Muller, M.; Vogel, E. *Chem. Ber.* **1991**, *124*, 791, and references cited therein.

(8) This approach has also been used in the synthesis of epibatidine: (a) Huang, D. F.; Shen, T. Y. *Tetrahedron Lett.* **1993**, *34*, 4477. (b) Clayton, S. C.; Regan, A. C. *Tetrahedron Lett.* **1993**, *34*, 7493. (c) Okabe, K.; Natsume, M. *Chem. Pharm. Bull.* **1994**, *42*, 1432. (d) Kotian, P. L.; Carroll, F. I. *Synth. Commun.* **1995**, *25*, 63. The ring-forming reactions in refs a and b involve *N*-alkoxycarbonylpyrroles and acetylenic sulfones. A corresponding vinyl sulfone was reported by Broka to be unreactive under similar reaction conditions (ref 6a).

(9) Alkenes generally do not react with *N*-acylated pyrroles at ambient pressures (see refs 2, 11, and Corey E. J.; Loh, T. P. *Tetrahedron Lett.* **1993**, *34*, 3979.)

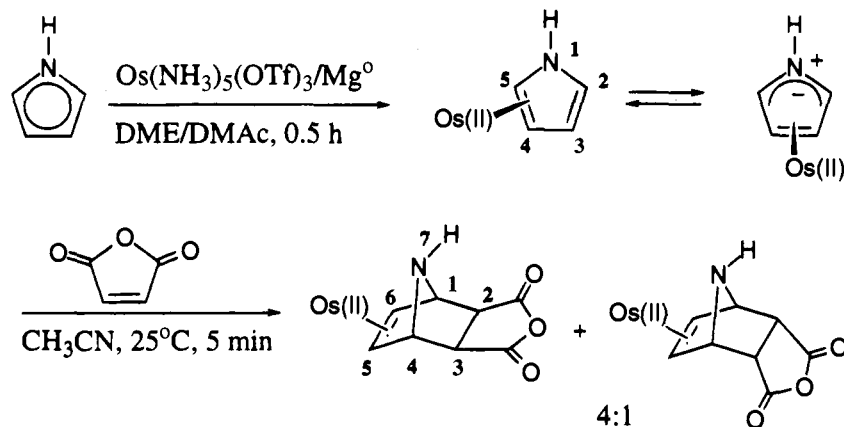


Figure 1. 1,3-Dipolar cycloaddition of the η^2 -pyrrole complex with maleic anhydride, showing numbering schemes for pyrrole and cycloadduct complexes.^{13a,14}

and highly reactive dienophiles such as *N*-alkylmaleimides (acrylates and maleates do not react).^{11,12}

Complexation of pyrrole by the π base pentaammine-osmium(II) across C3 and C4 has been shown to transform this aromatic molecule into an azomethine ylide, thereby dramatically enhancing its tendency to undergo 1,3-dipolar cycloaddition with maleic anhydride (Figure 1).^{13a} In contrast to the 7-azanorbornene ligand, which undergoes cycloreversion at ambient pressures, the resulting cycloadduct is greatly stabilized by metal coordination, allowing synthetic transformations while keeping the bicyclic framework intact. The purpose of the present study is to develop the scope of this novel cycloaddition reaction and to demonstrate its potential synthetic utility.¹³

Results

Synthesis of Cycloadduct Complexes. The pyrrole complexes (1–7) are synthesized in good yield by reducing $\text{Os}(\text{NH}_3)_5(\text{OTf})_3$ with activated Mg^0 in the presence of the pyrrole ligand in a DME/DMAc solution as reported previously (Table 1).^{13c} The pyrrole complexes will undergo substitution with acetonitrile slowly at room temperature ($t_{1/2}$ = hours) but rapidly at 50 °C ($t_{1/2}$ = minutes) to afford $[\text{Os}(\text{NH}_3)_5(\text{CH}_3\text{CN})](\text{OTf})_2$ (Table 1).

In order to establish the generality of the cycloaddition reaction, we examined this reactivity both as a function of alkyl substitution on the pyrrole ligand and of the degree of activation of the dipolarophile. The reactions of a series of alkyl-substituted pyrrole complexes with various dipolarophiles are summarized in Table 2.

The following synthesis of the cycloadduct complex **8** is typical of those described in Table 2: When an acetonitrile

(10) In an intramolecular example, the reaction was slow (>2 weeks) at temperatures required to achieve a favorable yield of cycloadduct (75% maximum conversion at 40 °C); Jung, M. E.; Rohloff, J. C. *J. Chem. Soc., Chem. Commun.* **1984**, 630.

(11) (a) Drew, M. G. B.; George, A. V.; Isaacs, N. S.; Rzepa, H. S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1277. (b) Kotsuki, H.; Mori, Y.; Nishizawa, H.; Ochi, M.; Matsuoka, K. *Heterocycles* **1982**, *19*, 1915.

(12) Introduction of an activating group at the β -position of the pyrrole ring (*N*-carbomethoxy-3-(methylthio)pyrrole) allowed reactions with methyl acrylate and phenyl vinyl sulfone under high pressure (12 Kbar) conditions: Aben, R. W. M.; Keijsers, J.; Hams, B.; Kruse, C. G.; Scheeren, H. W. *Tetrahedron Lett.* **1994**, *35*, 1299, and references cited therein.

(13) Portions of this work have been previously communicated: (a) Cordone, R.; Harman, W. D.; Taube, H. *J. Am. Chem. Soc.*, **1989**, *111*, 5969. (b) Myers, W. H.; Sabat, M.; Harman, W. D. *J. Am. Chem. Soc.* **1991**, *113*, 6682. (c) Myers, W. H.; Koontz, J. I.; Harman, W. D. *J. Am. Chem. Soc.* **1992**, *114*, 5684. (d) Hodges, L. M.; Gonzalez, J.; Koontz, J. I.; Myers, W. H.; Harman, W. D. *J. Org. Chem.* **1993**, *58*, 4788. (e) Hodges, L. M.; Gonzalez, J.; Myers, W. H.; Koontz, J. I.; Harman, W. D. *J. Org. Chem.*, in press.

Table 1. Yields and Substitution Half-Lives for the Pyrrole complexes 1–7

compd	R ₁	R ₂	R ₃	R ₅	yield, %	$t_{1/2}^a$ (min)
	H	H	H	H	85	227
	CH ₃	H	H	H	95	153
	H	CH ₃	H	CH ₃	95	14
	CH ₃	CH ₃	H	CH ₃	94	3
	TMS	H	H	H	80	300
	H	Et	H	H	83	b
	H	H	CH ₃	H	92	220

^a The complexes were heated in CD_3CN at 50 °C. ^b Compound **6** gradually decomposed to an intractable mixture; no conversion to $[\text{Os}(\text{NH}_3)_5(\text{CH}_3\text{CN})](\text{OTf})_2$ was observed.

solution of $[\text{Os}(\text{NH}_3)_5(\eta^2\text{-pyrrole})](\text{OTf})_2$ (**1**) and 1 equiv of *N*-phenylmaleimide is allowed to stand for 2 h and then added to ether or methylene chloride, a mixture of **8a** and **8b** precipitates as an ivory-colored solid. The ¹H NMR spectrum of the *exo*-cycloadduct **8a** in CD_3CN has three sharp singlets at 3.21 (2 H), 3.22 (2 H), and 4.09 (2 H) ppm corresponding to the ring protons and ammine resonances at 3.23 (12 H) and 4.04 (3 H) ppm. In contrast, the pyrrole complex **1** has broadened ring proton resonances characteristic of fluxional behavior, and the ammine resonances appear at 2.73 (12 H) and 3.85 (3 H) ppm.^{13a} The progress of the reaction may be monitored by either ¹H NMR or cyclic voltammetry. While **1** has an irreversible oxidation wave at $E_{p,a} = 0.17$ V (NHE), the product **8a** exhibits a pseudoreversible couple at $E_{1/2} = 0.82$ V. In some cycloadditions, one of the isomers (e.g. **8a**, **10b**, **13a**, and **23a**) selectively crystallizes from the reaction mixture. In favorable cases (e.g., complexes **18** and **21**) the cycloadducts may be prepared in a one-pot reaction sequence from the pyrrole by addition of the appropriate dipolarophile to the reaction immediately following complexation. This procedure sometimes affords the cycloadducts as their DMAc solvates.

Stereochemistry of the Cycloaddition. For compounds **8**, **9**, and **12**, assignment of the stereochemistry is based on the magnitude of J_{1-2} or J_{3-4} coupling. For example, **8a** is assigned *exo* stereochemistry based on the absence of coupling between the bridgehead and *endo* ring protons.¹⁵ This stereochemistry was confirmed by X-ray crystallography; the ORTEP of the cation in **8a** is shown in Figure 2. The stereochemistry of the

(14) In this figure and throughout the paper, the pentaammineosmium(II) moiety and triflate counterions ($[\text{Os}(\text{NH}_3)_5(\text{OTf})_2]$) are abbreviated as $\text{Os}(\text{II})$.

(15) This pattern has also been observed for related 7-azanorbornenes (ref 11a).

Table 2. Cycloadduct Complexes 8–23

a (<i>exo</i>)	b (<i>endo</i>)	Cpd	R ₁	R ₂	Z	a/b ^a	Yield ^b
		8	H	H		6:1	85
		9	CH ₃	H		1:6	85
		10	H	CH ₃		5:1	89
		11	CH ₃	CH ₃		1:1	77
		12	TMS	H		<1:20	89
		13	H	CH ₃	CO ₂ CH ₃	2:1	82
		14	H	CH ₃	3-pyridyl	9:1	83
		15	H	H	CO ₂ CH ₃	-	78
		16	H	CH ₃	CO ₂ CH ₃	-	86
		17	H	CH ₃	3-pyridyl	16:1	93
		18	H	CH ₃	CO ₂ CH ₃	12:1	97
		19	H	CH ₃	CN	5:1	83
		20	CH ₃	H	CO ₂ CH ₃	1:1	84
		21	CH ₃	H	CN	1:1	98
		22	H	CH ₃		>20:1 ^c	96
		23	H	CH ₃		>10:1	84

^a The ratios of isomers were determined by ¹H NMR integrations. ^b Yields are in percent and are reported for the crude mixtures of diastereomers. ^c The *endo* isomer was not detected by ¹H NMR.

cycloadducts bearing bridgehead methyl groups is determined by NOE data. The *exo* cycloadducts have strong interactions between *endo* ring protons and the *endo* cycloadducts bearing *N*-methyl groups have interactions between the latter and *exo* ring protons (Figure 3).

The stereochemistry suggested by the NOE studies is also confirmed by crystal structures in the case of compounds **13a** and **22a** (Figures 4 and 5, respectively). Compounds bearing protons in a *syn* relationship on C2 and C3 (e.g., **14**, **18**, and **19**) have diagnostic vicinal coupling constants of <10 Hz for $J_{H2endo-H3endo}$ and >10 Hz for $J_{H2exo-H3exo}$ similar to those observed for the 7-azanorbornanes (*vide infra*).

The Effect of Pyrrole Ring Alkyl Substitution on the Reaction Rates. Solutions of the pyrrole complexes (0.06 M in CD₃CN) and a tenfold excess of *N*-phenylmaleimide were monitored by ¹H NMR at ambient temperature, and from this data the second order rate constant, *k*, was calculated by assuming pseudo-first order conditions. The rate constant of

cycloaddition (*k*) is directly related to the rate constant of tautomerization (*k'*)^{13c} for several complexes (Table 3).

The pyrrole complexes **1–5** react with most dipolarophiles in acetonitrile solution at room temperature over a period of minutes to hours. While *N*-phenylmaleimide (1 equiv) reacts quickly (< 1 h) at relatively low concentrations (~0.1 M) in acetonitrile with the pyrrole complexes **1–4**, the less reactive dipolarophiles (those having only one electron-withdrawing group) must be used in higher concentrations in order for cycloaddition to compete with solvent substitution. As a general rule, while the 2,5-dimethylpyrrole (**3**) and 1,2,5-trimethylpyrrole (**4**) complexes react rapidly at room temperature with most unhindered dipolarophiles bearing one electron-withdrawing group (0.1–0.5 M complex, 3–40 equiv dipolarophile), the pyrrole (**1**) and 1-trimethylsilylpyrrole (**5**) complexes only react with dipolarophiles bearing two electron-withdrawing groups. Compounds **6** and **7**, bearing only a C2 or a C3 substituent, respectively, are completely inert toward typical dipolarophiles.

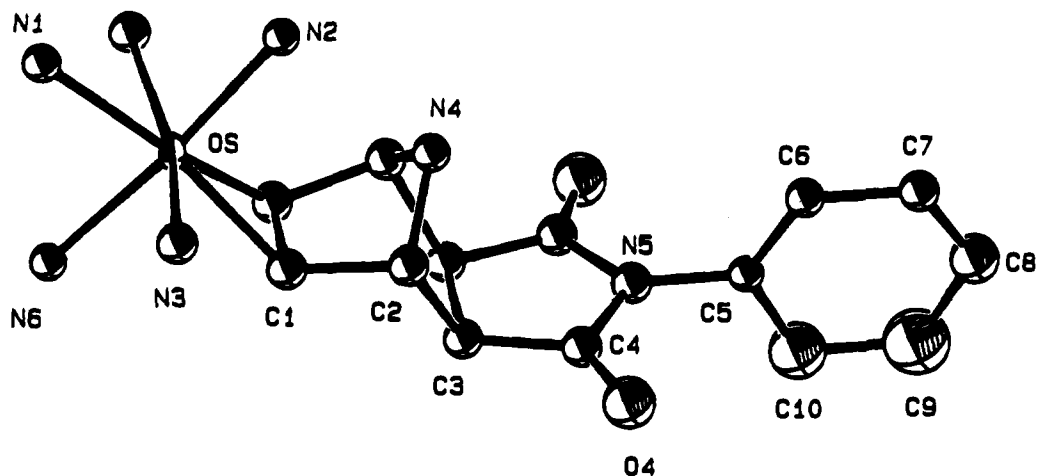


Figure 2. Structure of the cycloadduct complex **8a** from pyrrole and *N*-phenylmaleimide.

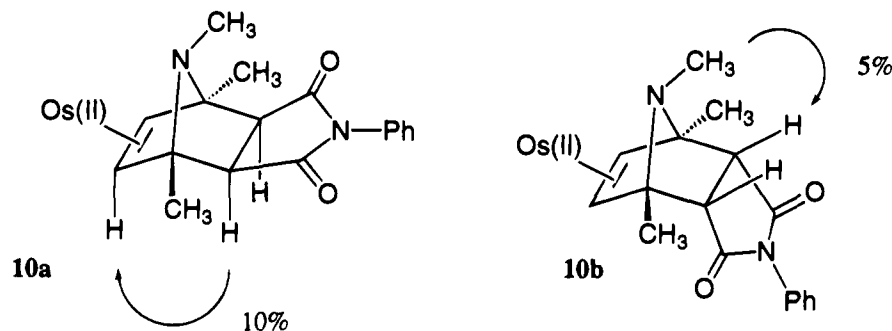


Figure 3. NOE enhancement data for cycloadduct complexes **10a** and **10b**.

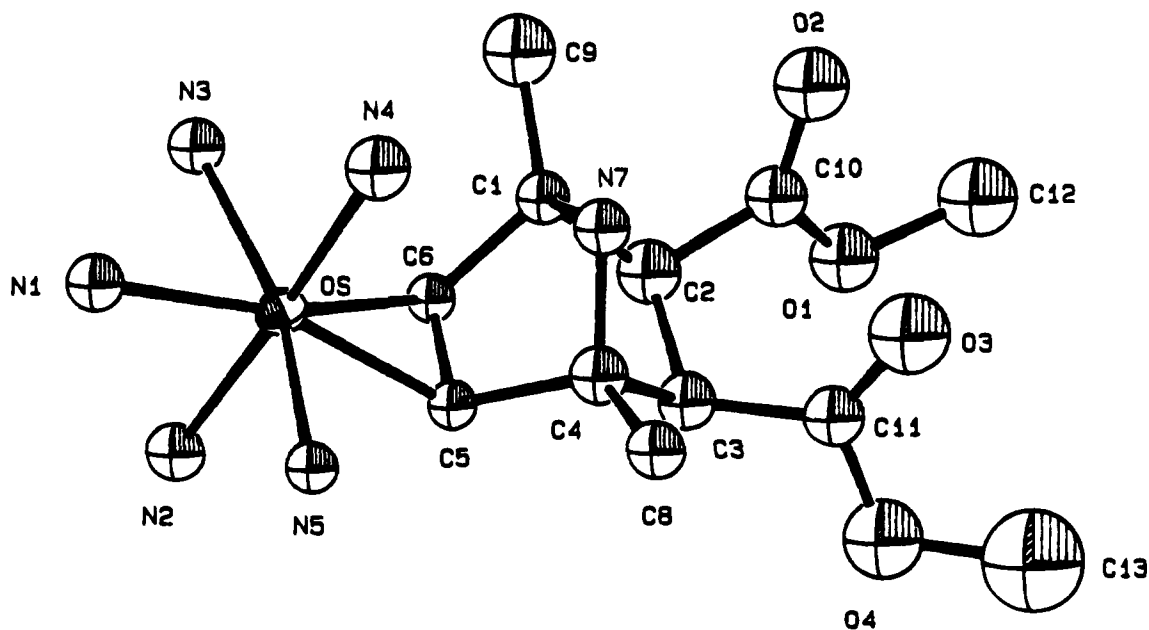


Figure 4. Structure of the cycloadduct **13a** from 2,5-dimethylpyrrole and dimethyl maleate.

When the cycloadditions are very slow, the pyrrole complexes either form intractable paramagnetic compounds or undergo substitution of the solvent for the pyrrole ligand.

Solvent Effects. The influence of the solvent on the half-lives of cycloaddition was explored in the synthesis of **15** from the parent pyrrole complex (**1**) and dimethyl fumarate by monitoring the reaction using cyclic voltammetry. Further, the influence of solvent on the stereochemistry of cycloaddition was explored for the synthesis of **18** from the 2,5-dimethylpyrrole complex (**3**) and methyl acrylate. The reaction was observed by ^1H NMR in a number of deuterated solvents (acetonitrile,

acetone, DMSO, DMF, water, and methanol), and in other cases (entries 1, 3, 7, 8, and 10 in Table 5) the product was isolated (85–95% yield) and characterized by ^1H NMR. The results, summarized in Tables 4 and 5, indicate that cycloadditions are fastest in polar aprotic solvents with high donor numbers such as DMAc or DMSO¹⁶ and that the *exo/endo* selectivity is moderately sensitive to solvent polarity.¹⁷

In cases where the cycloaddition is slow, good results are obtained using an appropriate solvent (Table 4) and an excess of the dipolarophile. For example, in the synthesis of compound **19**, when the 1-methylpyrrole complex (**2**) is treated with 15–

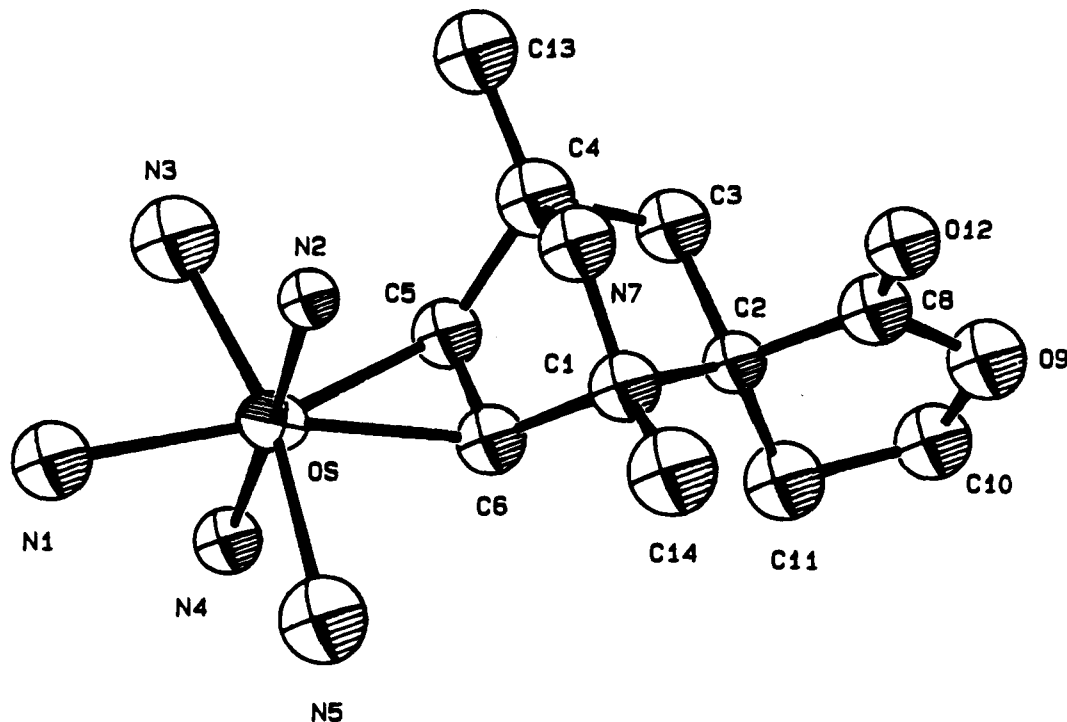


Figure 5. Structure of the cycloadduct **22a** from 2,5-dimethylpyrrole and α -methylene- γ -butyrolactone.

Table 3. Correlation between rate of Cycloaddition and Ring Slippage^{13c} for the Reactions of η^2 -Pyrrole Complexes with *N*-Phenylmaleimide

pyrrole complex	k ($s^{-1} M^{-1}$) $\times 10^{-3}$	fluxionality rate constant (s^{-1})
1-(trimethylsilyl)pyrrole (5)	2.2	$k' < 250$
pyrrole (1)	110	$k' < 70$
1-methylpyrrole (2)	1200	$80 < k' < 175$
2,5-dimethylpyrrole (3)	>2000	$300 < k'$

20 equiv of acrylonitrile containing 10 wt % DMAc (to solubilize the complex), the reaction was complete in 2–3 h. The reaction between the 2,5-dimethylpyrrole complex (**3**) (1 M in DMAc) and methyl (*Z*)-3-(3'-pyridyl)acrylate (3 equiv), one of the least reactive dipolarophiles studied, was complete in ~18 h affording compound **14**. The cycloadditions are catalyzed by lithium triflate, which affords a practical maximum rate enhancement of one order of magnitude. However, the use of stronger Lewis acids such as $BF_3 \cdot Et_2O$ results in other reactions such as β -electrophilic addition and/or ring opening, discussed below.^{13e,18}

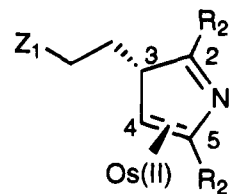
Competing β -Michael Additions and Ring-Opening Reactions. In contrast to other dipolarophiles, the reaction of MVK with compound **3** in acetonitrile affords a mixture of cycloadduct **24** and 3*H*-pyrrole tautomer **25**, resulting from a Michael addition at β -position of the pyrrole ring. Over time, compound **24** undergoes ring-opening to the 2*H*-pyrrole tautomer, **26**. A similar result is observed when water is used as the solvent in the reaction of **3** with methyl acrylate.

(16) The donor number (*DN*) is defined the negative ΔH value for the solvation of $SbCl_5$ by a donating solvent in 1,2-dichloroethane solution: Gutman, V. *The Donor-Acceptor Approach to Molecular Interactions*; Plenum Press: New York and London, 1978, Chapter 2.

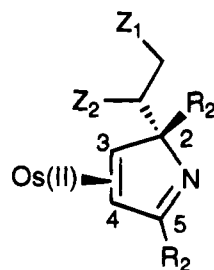
(17) The normalized empirical solvent polarity parameter, E_T^N , used in Table 5 is based on the long-wave UV/vis charge-transfer band of a pyridinium-*N*-phenoxide betaine dye (Reichardt, C. In *Solvents and Solvent Effects in Organic Chemistry*; VCH: New York, 1988; p 359). The values for entries other than 11 (D_2O) are for the corresponding hydrogen-containing solvents (water = 1.000).

(18) An exception to this involved the reaction of **5** with *N*-phenylmaleimide. This cycloaddition was moderately accelerated and afforded a cleaner product using an excess of TMSOTf.

The reactivity of **3** toward MVK is sensitive to both solvent and temperature, resulting in enhanced β -selectivity at low temperatures or in protic solvents.¹⁹ In the absence of Lewis acids or protic solvents, β -Michael additions are observed only for MVK, acrolein, and acetylenic electrophiles.²⁰ In the presence of the Lewis acid TBSOTf, however, β -electrophilic addition is the dominant reaction for most dipolarophiles, resulting in the formation of 3*H*-pyrrolium species analogous to the protonated form of **25** in the case of $Z_1 = CN$ or CO_2CH_3 .¹⁹



25, $R_2 = CH_3$, $Z_1 = COCH_3$



26, $R_2 = CH_3$, $Z_1 = COCH_3$, $Z_2 = H$

27, $R_2 = H$, $Z_1, Z_2 = CON(Ph)CO$

28, $R_2 = CH_3$, $Z_1 = CO_2CH_3$, $Z_2 = H$

29, $R_2 = CH_3$, $Z_1 = CO_2CH_3$, $Z_2 = 3$ -Pyridyl

The spontaneous ring-opening observed in acetonitrile in the transformation of **24** to **26** also occurs for other cycloadducts, although at considerably slower rates. In contrast to the MVK adduct **24**, the methyl acrylate-derived analog **18** is resistant to

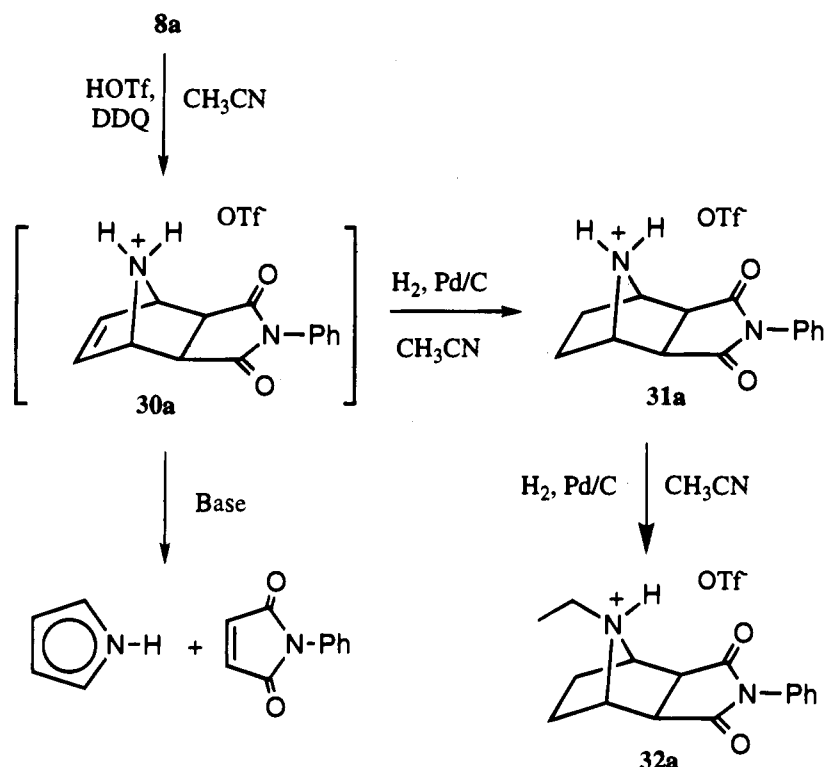


Figure 6. Decomplexation of the cycloadduct **8a**.

Table 4. Empirical Reaction Half-Lives as a Function of Solvent in the Synthesis of **15** from **1** ($0.10 \pm 0.01\text{M}$) and Dimethyl Fumarate ($0.30 \pm 0.03\text{M}$)

	solvent	$t_{1/2}$ (min)	DN (kcal mol ⁻¹) ¹⁶
(1)	acetonitrile	185	14.1
(2)	acetone	111	17.0
(3)	2 M LiOTf (DME)	25	
(4)	methanol	22	19.0
(5)	DMF	15	26.6
(6)	DMAc	9	27.8
(7)	NMF	6	
(8)	DMSO	5	29.8
(9)	DMPU	5	
(10)	5 M LiOTf (DME)	5	

ring opening in either its basic or protonated form.²¹ However, treatment of the cycloadduct complexes with 1 equiv of TBSOTf followed by water results in their facile ring-opening to 2*H*-pyrrolium complexes (e.g., *N*-protonated **28**).^{13d,e} Although cycloadducts other than **24** are relatively stable in polar aprotic solvents such as acetonitrile or DMAc, some undergo facile ring opening to 2*H*-pyrroles in water. Upon attempted purification by ion-exchange chromatography (Sephadex CM C-25, 0.35 M NaCl), compounds **12**, **18**, and the *exo*-pyridyl cycloadduct **14a** convert to the 2*H*-pyrrole complexes **27**, **28**, and **29**, respectively.²² In contrast, both isomers of the acrylonitrile adduct **19** and the *endo*-pyridyl isomer **17a** are stable under these conditions and can be stored as tetraphenylborate monohydrate salts.

(19) Both the cycloaddition and β -Michael addition reactions proceed in methanol at a rate that is ~ 10 fold faster than that observed in acetonitrile. A more detailed study of the solvent dependence of this reaction is described in ref 13e.

(20) Acetylenic dienophiles react with pyrrole and *N*-methylpyrrole complexes, affording [2 + 2] cycloadducts in DMSO. These compounds undergo subsequent ring-opening to 3-vinylpyrrole complexes in protic solvents (ref 13e).

(21) Under forcing conditions (HOTf in acetonitrile; 3 h at 75 °C) the retro-Mannich reaction takes place, but the yield of ring-opened material is low due to the competing formation of paramagnetic products.

(22) A number of complexes undergo decomposition to intractable mixtures under these conditions.

The maleate cycloadduct **13a** undergoes a quantitative isomerization to the fumarate complex **16** that is complete in <5 min in water and in several days in methanol. This *exo* to *endo* epimerization, which is observed *only* for **13a**, does not incorporate deuterium when it takes place in deuterated solvents.

Decomplexation of Organic Ligands: General Synthesis of 7-Azanorbornanes. Treatment of the cycloadduct complex **8a** with CAN (1 equiv) results in the recovery of pyrrole and *N*-phenylmaleimide. However, when a solution of **8a** is treated with excess of triflic acid (3 equiv) in CD₃CN followed by CAN (1 equiv) or DDQ (0.5 equiv), the ¹H NMR spectrum reveals the formation of the protonated 7-azanorbornene (**30a**), liberated upon oxidation of the metal (Figure 6).²³ The diagnostic olefinic ring protons of the free ligand appear at ~ 6.5 ppm, considerably downfield from those of the corresponding complex resonances at ~ 3.1 ppm. This decomplexation reaction is general for most cycloadduct complexes when acetonitrile is used as the solvent under highly acidic conditions (~ 3 equiv triflic acid). Intractable mixtures, cycloreversion, or low yields result when methanol is used as the solvent. When DDQ is used as the oxidant, the major products of the reaction other than **30a** included the osmium(III) acetonitrile complex and the hydroquinone from DDQ.²⁴ When base is added to the reaction mixture containing the 7-azanorbornene **30a**, a fast (complete in <5 min at 25 °C) cycloreversion occurs, forming pyrrole and *N*-phenylmaleimide. A similar result is obtained for the 2,5-dimethylpyrrole/methyl acrylate cycloadduct **18**.

Although the 7-azanorbornene salts such as **30a** are unstable and difficult to isolate, they are readily hydrogenated to stable 7-azanorbornanes while preserving the stereochemistry at C2 and C3. Thus, when the reaction mixture containing **30a** is

(23) DDQ gave consistently higher yields and more reproducible results than CAN.

(24) This is based on electrochemical and ¹³C NMR data, respectively. The reaction mixture also contains ammonium ion (usually ~ 10 – 15% by ¹H NMR) and other paramagnetic species (observed using cyclic voltammetry) that are presumably formed via fragmentation of the pentaammine-osmium moiety. Attempts to recover the osmium from this precipitate are currently in progress.

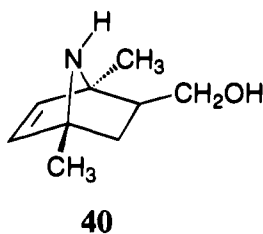
Table 5. Stereochemistry as a Function of Solvent for the Synthesis of **18** from **3** and Methyl Acrylate^a

	solvent	exo/endo ^b	E_T^{N17}
(1)	acetone- d_6	92:8	0.355
(2)	1:1:1 DMAc/2,5-DMP/methyl acrylate ^c	92:8	
(3)	methyl acrylate (neat) ^d	92:8	0.426
(4)	DMF- d_7	91:9	0.404
(5)	DMSO- d_6	91:9	0.444
(6)	acetonitrile- d_3	90:10	0.460
(7)	HFIPA/methyl acrylate	90:10	
(8)	5 M LiOTf/DME	87:13	
(9)	methanol- d_4	84:16	0.762
(10)	formamide	82:18	0.799
(11)	D ₂ O ^e	67:33	0.991

^a Conditions for entries other than 3: 0.1 M complex and 4 equiv methyl acrylate at 20 °C. ^b Based on ¹H NMR integration of bridgehead methyl resonances. ^c Methyl acrylate was added to the reaction mixture following the synthesis of **3**. ^d The reaction was heterogeneous. ^e Other product were formed using this solvent (discussed in text under competing reactions).

subjected to 1 atm H₂ over 10% Pd/C (20 mol %), reduction to compound **31a** is complete in 1 h (Figure 6).²⁵ The reaction sequence of protonation, oxidation, and hydrogenation has been applied to the synthesis of a number of organic 7-azanorbornanes (Table 6). No significant change in the ratio of diastereomers is observed in the transformation of the cycloadduct complexes to the organic products.

In an alternative approach, chemical modification of the electron-withdrawing substituents on the ring allows isolation of 7-azanorbornanes. For example, the carboxylate group on **18** may be reduced to the primary alcohol with 2 equiv of lithium 9-BBNH in THF. When an acetonitrile solution of the reduced complex **39** is treated with an excess of HOTf (~5 equiv) followed by 1 equiv of CAN, the intact organic ligand **40** is obtained after an aqueous/organic workup.^{13d,26}



Characterization of 7-Azanorbornanes. The stereochemistry of these compounds is easily determined by the magnitude of ¹H NMR coupling constants, as illustrated in the case of compounds **33**²⁷ and **35** (Figure 7). The coupling constants of ~0 Hz for H_{bridgehead}–H_{endo} and ~3.5–5 Hz for H_{bridgehead}–H_{exo} are diagnostic for *exo* and *endo* substitution, respectively.²⁸ Likewise, the H₂–H₃ vicinal coupling constants observed in compounds **34**–**37** are smaller in *exo* isomers (6 < ³J_{Hendo,Hendo}

(25) Exposure of **31a** to long reaction times (18–24 h) in acetonitrile resulted in the unexpected formation of the *N*-ethyl derivative, **32**, that was not formed when methanol was used as the hydrogenation solvent. Presumably, **32** is formed via acylation of the bridging nitrogen by acetonitrilium triflate (protonated acetonitrile), followed by reduction of the intermediate.

(26) Failure to treat the complex with acid prior to oxidation resulted in a greatly reduced yield, presumably as a result of olefin-to-amine linkage isomerization on osmium(III), a reaction that has been reported for osmium(III)–aniline complexes: Harman, W. D.; Taube, H. *J. Am. Chem. Soc.* **1988**, *110*, 5403.

(27) This compound has been synthesized by an independent route: (Rohloff, J. C., Ph.D. Dissertation, UCLA, 1985, and ref 10). The ¹H and ¹³C NMR spectra of **33** matched perfectly with those reported by Rohloff and Jung, with the exception of the long range coupling between H_{3β} and H_{5β} which was not reported by these authors.

(28) This has also been observed in related systems: see ref 2a, p. 95.

< 10 Hz) than in *endo* isomers (10 < ³J_{Hexo,Hexo} < 12 Hz).²⁹ In addition, the presence of long-range W-coupling between *exo* ring protons is useful in cases where the bridgehead positions are substituted (e.g., compounds **37** and **38**).³⁰ In order to assign H₂ and H₃ in compound **38**, the carboxylate group was reduced with LAH to afford the corresponding *exo*-hydroxymethyl compound **41** (H₃ changed in chemical shift and multiplicity).³¹

Discussion

The aromatic character of pyrrole severely limits its reactivity toward cycloaddition reactions. While cyclopentadiene or furan undergo facile Diels–Alder cycloadditions with maleic anhydride under ambient conditions, pyrrole reacts only with extensive heating, and Michael addition at C₂, rather than cycloaddition, dominates.³² Strategies used to improve the facility and yield of pyrrole cycloadditions include the use of electron-withdrawing groups on nitrogen in combination with either Lewis acids or high pressures, but most examples are limited to either highly reactive or acetylenic dienophiles.^{2a,7,11,33}

A transition metal bound across C₃ and C₄ activates the pyrrole ring by a mechanism complementary to that in which electron-withdrawing groups on nitrogen are employed. In the latter approach, interaction of an electrophilic substituent with the nitrogen π-electrons disrupts the aromaticity of the ring, thereby enhancing the dienelike nature of the pyrrole. Metal coordination at C₃ and C₄ also localizes the π-electron density of the ring, but here the uncoordinated portion of the ring resembles an azomethine ylide as shown in Figure 8.^{13a} Although the osmium(II) moiety used in this study is cationic, the presence of ammine ligands and the strong π-interaction with the pyrrole appears to render the metal overall electron-donating.^{13b}

It has been demonstrated that donating substituents on azomethine ylides enhance reactivity toward electron deficient dipolarophiles, presumably by raising the energy of the HOMO for the 1,3-dipole.³⁴ Since the pentaammineosmium moiety acts as an electron donor, the reactivity of the 1,3-dipole fragment in Figure 8 should correlate with electron density at the metal center. Solvents that are good electron-pair donors should increase electron density on the metal center via a hydrogen-bonding interaction with the ammine ligands, which may explain the inverse correlation of cycloaddition half-lives with solvent donor number (Table 4).³⁵

Although it is the 3,4-η² tautomer of the pyrrole complex that is active toward cycloaddition, the dominant tautomer in solution for these species is one in which the metal occupies the 4,5- or the 2,3-η² position, even in cases where the α carbons

(29) This observation appears to be general for 7-azanorbornanes, based on the data reported in refs 6d, 6e, 8b, 12, and 39a.

(30) The magnitude of this 4J coupling in 7-azanorbornanes can be as large as 3 Hz; see refs 6d and 6e.

(31) Partial characterization of **41** (1,4-dimethyl-2α-(3'-pyridyl)-3β-(hydroxymethyl)-7-azabicyclo[2.2.1]heptane): ¹H NMR (CDCl₃) δ 8.43 (m, 2H), 7.51 (d, J = 7.8 Hz, 1H), 7.24 (dd, J = 7.8, 4.8 Hz, 1H), 3.78 (dd, J = 10.6, 2.8 Hz, 1H), 3.47 (dd, J = 10.6, 3.0 Hz, 1H), 3.07 (dd, J = 5.0, 1.9 Hz, 1H, H₂), 1.94 (m, 1H, H₂), 1.8–1.5 (m, s overlap, 5H), 1.43 (s, 3H, CH₃), 1.22 (s, m overlap, 4H); ¹³C NMR (CDCl₃) δ 150.2 (CH), 147.7 (CH), 135.9 (CH), 135.5 (C), 123.1 (CH), 67.0 (C), 65.6 (C), 62.9 (CH₂), 54.4 (CH), 52.3 (CH), 40.4 (CH₂), 33.1 (CH₂), 20.3 (CH₃), 18.9 (CH₃).

(32) (a) Jones, R. A.; Bean, G. P. *The Chemistry of Pyrroles*; Academic Press: New York, 1977. (b) Jones, R. A. in *The Chemistry of Heterocyclic Compounds*, v.48 *Pyrroles*; Wiley & Sons: New York, 1990; p 405.

(33) (a) Ahmed, M.; Vernon, J. M. *J. Chem. Soc., Chem. Commun.* **1976**, 462. (b) Kreher, R.; Pawelczyk, Z. *Naturforsch., Teil. B* **1976**, *31*, 599.

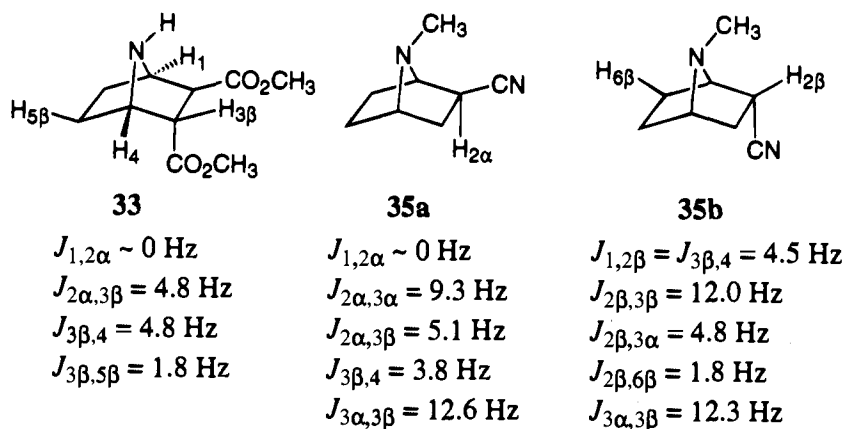
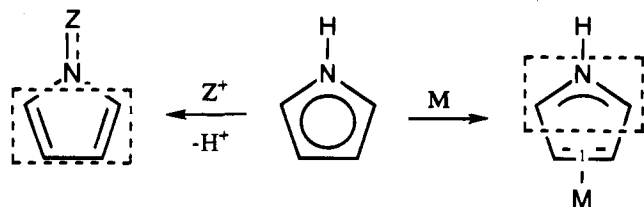
(34) Padwa, A.; Schoffstall, A. M. *Adv. Cycloaddition* **1990**, *2*, 50.

(35) The redox potentials of the osmium complexes are sensitive to solvent effects. For the hexaammineosmium species, the more donating solvents such as DMF shift the reduction potentials *negative* by ~0.2 V relative to the less donating solvents such as acetone or acetonitrile (Harman, W. D. Doctoral Thesis, Stanford, 1987; p 201).

Table 6. Synthesis of 7-Azanorbornanes from the Corresponding Cycloadduct Complexes

Organic Product ^a	Z	Compound	Yield(%)
	(<i>exo</i>)	31a	39 ^c
	(<i>endo</i>)	31b	41 ^c
		33	42 ^c
	CO ₂ CH ₃	34	65 ^b
	CN	35	67 ^b
		36a	60 ^b
	(<i>exo</i>)	37a	46 ^b
	(<i>endo</i>)	38a	69 ^b

^a Compounds **31a** and **31b** were prepared from crude **8a** and **8b**, respectively. Compounds **37a** and **37b** were prepared from crude **14a** and **17a**, respectively. ^b This represents the isolated yield of *both* isomers, either as a mixture or separated, following chromatography. ^c The low overall yield of compounds derived from **1** is due, in part, to the formation of paramagnetic impurity in the synthesis of **1**.

**Figure 7.** Diagnostic H–H coupling constants in 7-azanorbornanes.**Figure 8.** Localization of pyrrole π electrons by electron withdrawing groups on nitrogen (left) and by 3,4- η^2 metal coordination (right).

are substituted.^{13b} Methyl substituents either on C1 or on C2 and C5 of the pyrrole destabilize the 4,5- η^2 tautomer, thereby increasing both the rate of tautomerization and the relative population of the active 3,4- η^2 tautomer.^{13c} Thus, the rate of

tautomerization, at least for the symmetrical pyrroles investigated, correlates with the rate of cycloaddition, provided that the α carbons and the nitrogen are not too hindered (Table 3). For the 2,5-dimethylpyrrole complex (**3**), cycloadducts are obtained in 30 min at 20 °C with dipolarophiles as mild as methyl acrylate (i.e., **18**) and as hindered as cyclopentene-1,2-dicarboxylic anhydride. In the latter reaction, four quaternary centers are formed in a single step (i.e., **23**). By contrast, the substituents on the unsymmetrically substituted pyrrole complexes **6** and **7** destabilize the 3,4- η^2 tautomer relative to the 4,5- η^2 form, thus rendering these complexes unreactive toward cycloaddition.

The pentaammineosmium(II) moiety acts as a protecting group for the 7-azanorbornene nucleus, presumably by reducing

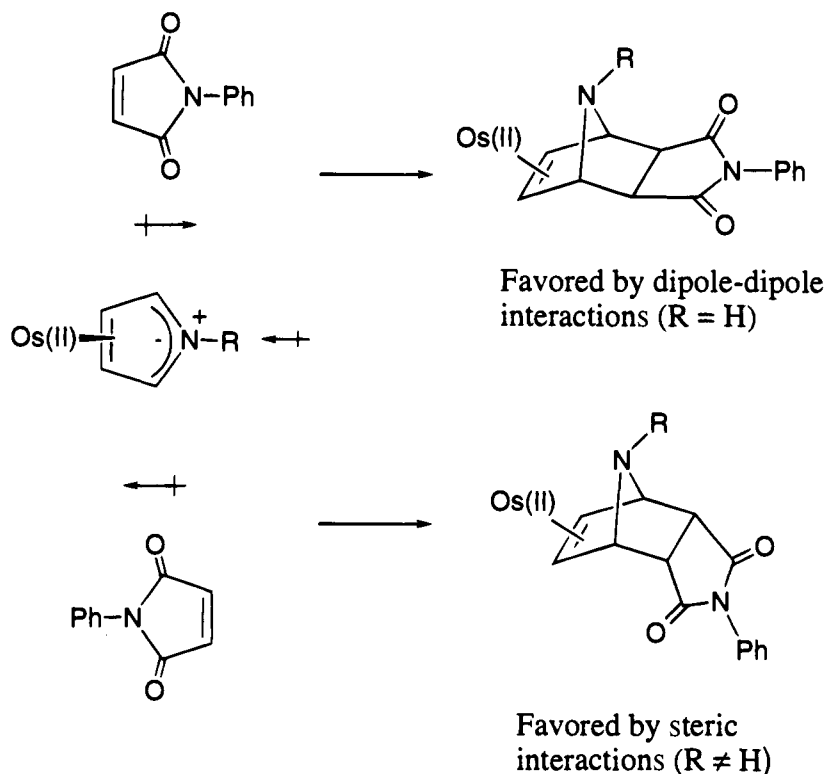


Figure 9. Influence of dipole–dipole vs steric interactions in cycloaddition transition state.

the rearomatization driving force in the cycloreversion process. In dramatic contrast to the behavior observed for free 7-azanorbornenes bearing electron withdrawing groups, the osmium(II) complexes reported herein are highly resistant to retrocycloadditions, even upon moderate heating. Compound **18** is stable in acetonitrile solution at 75 °C for brief periods (~1–2 h) and does not undergo exchange at this temperature with *N*-phenylmaleimide.³⁶

In addition, the bridging nitrogen is protected from certain reactions. Although the cycloadduct complexes may be protonated using triflic acid in acetonitrile, attempts to acylate or quaternize the nitrogen result only in ring-opening under forcing conditions. Inspection of the ORTEP diagrams for the pentaammineosmium complexes of the cycloadducts (Figures 2, 4, and 5) reveals that the bridging nitrogen is severely hindered by the *cis*-ammines on osmium. Further, the N2–N7 distance in **22** is 2.73 Å, an observation which suggests a hydrogen-bonding interaction. The fluxional behavior³⁷ observed for the organic 7-azanorbornanes **34** and **35** is absent in the corresponding pentaammineosmium complexes, indicating the *N*-methyl substituent in the latter is probably locked in an *anti* conformation.

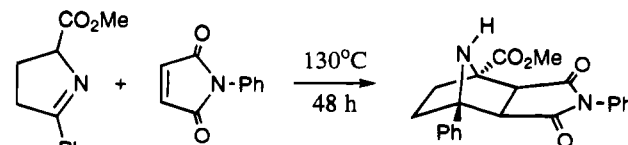
Stereochemistry. In Table 2, the *exo/endo* ratios are listed for a series of pyrrole complexes with the dipolarophile *N*-phenylmaleimide. The pentaammineosmium moiety occupies an *exo* orientation on all cycloadducts, which indicates that cycloaddition takes place *anti* to the face of the pyrrole ring coordinated by the metal. The stereochemistry of the cycloaddition appears to be governed by the steric environment about

the pyrrole nitrogen. For cases where the nitrogen is not substituted, the major product has the electron-withdrawing group in an *exo* configuration. This stereoselectivity, resulting from an *endo* transition state,³⁸ has been observed for 1,3-dipolar cycloaddition reactions of stabilized azomethine ylides lacking *N*-substituents.³⁹ The *endo* selectivity may be explained by consideration of the most favorable orientation of the dipole moments for the azomethine ylide and dipolarophile (Figure 9).⁴⁰ Consistent with this notion is the observation that the *endo* selectivity is decreased with increasing solvent polarity (Table 5) due to a weakening of dipole-dipole interactions between reactants in the more polar solvents.^{41,42}

The stereoselectivity and stereospecificity of this cycloaddition process can be utilized in setting the stereochemistry of substituents on the 7-azanorbornane nucleus. For example, reactions of **3** with the methyl esters of (*Z*)- and (*E*)-3-(3'-pyridyl)acrylates afford, after decomplexation, the corresponding

(38) In the Diels–Alder reactions of cyclopentadiene, an *endo* transition state leads to an *endo*-substituted product. In the dipolar cycloadditions reported here, an *endo* transition state leads to an *exo*-substituted product.

(39) 1,3-Dipoles tautomeric with Δ^1 pyrrolines react with *N*-phenylmaleimide with *endo*-selectivity: (a) Lakhli, T.; Sedqui, A.; Fathi, T.; Laude, B.; Robert, J. F. *Can. J. Chem.* **1994**, *72*, 1417. (b) Mkairi, A.; Hamelin, J. *Tetrahedron Lett.* **1987**, *28*, 1397.



(40) Dipolar interactions have been used to rationalize the unusual *exo*-selectivity of α -methylene lactones and related compounds in the Diels–Alder reaction (Roush, W. R.; Brown, B. B. *J. Org. Chem.* **1992**, *57*, 3380). The high *endo*-selectivity observed in compound **22** is expected based on these arguments.

(41) Similar solvent effects have been observed in other azomethine ylide cycloadditions, see: Grigg, R.; Sridharan, V. *Adv. Cycloaddition* **1993**, *3*, 175, and references cited therein.

(36) After heating for 1 day, an intractable mixture was formed.

(37) The ¹³C NMR spectra of the *endo*-substituted 7-azanorbornanes **34b** and **35b** exhibited severe line broadening of the ethano-bridge ring carbons at room temperature. As the temperature was lowered to 0 °C the resonances coalesced and subsequently split into two sets of resonances at –20 °C. At 50 °C the lines appeared sharp and of almost normal intensity. This effect is probably due to the high barrier of nitrogen inversion that is typical of 7-azanorbornanes (i.e., *syn* and *anti* conformers differing in the position of the *N*-substituent are slowly exchanging; see refs 5b and 7a).

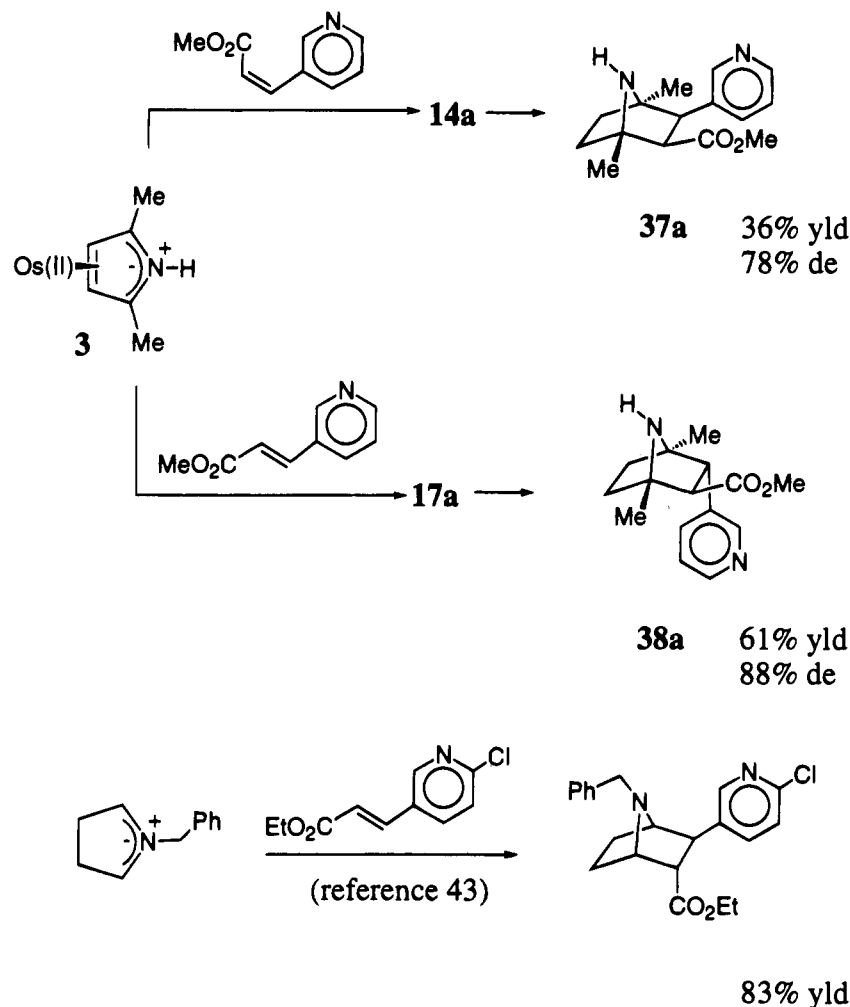


Figure 10. Stereoselective synthesis of epibatidine ring system.

exo and *endo* pyridyl-substituted compounds **37a** and **38a**, respectively (Figure 10). The stereochemistry of **38a** is complementary to that observed in the reaction of a pyrrolidine-derived unstabilized ylide with a related pyridyl acrylate (Figure 10, bottom).^{43,44}

When the nitrogen is substituted, a marked decrease in the *exo/endo* ratio is observed, presumably due to an unfavorable steric interaction with the dipolarophile substituent. This effect is illustrated in the reactions of *N*-phenylmaleimide, for which the *exo/endo* ratio decreases as the steric profile of the nitrogen substituent increases (i.e., the *exo/endo* ratio is 6:1 for L = pyrrole (**1**), 1:6 for L = 1-methylpyrrole (**2**), and <1:20 for L = 1-trimethylsilylpyrrole (**5**); Table 2).⁴⁵ In the case of the very hindered TBS-pyrrole complex, no reaction is observed.

(42) Unlike the pyrrole complexes 1–5, most azomethine ylides reported in the literature that participate in stereoselective cycloadditions have an electron-withdrawing group on one of the ylide carbons. The predominance of products from *endo* transition states has been attributed to secondary orbital interactions between the substituents of dipoles and dipolarophiles (see ref 39a and Tsuge, O.; Kanemasa, S. *Adv. Heterocycl. Chem.* **1989**, *45*, 314).

(43) Pandey, G.; Bagul, T. D.; Lakshmaiah, G. *Tetrahedron Lett.* **1994**, *35*, 7439. The chloropyridyl-substituted intermediate was converted to epibatidine. The stereoselectivity was attributed to steric effects.

(44) Our attempts to synthesize epibatidine have thus far been stymied by the lack of reactivity of the pyrrole (**1**) and *N*-methylpyrrole (**2**) complexes toward compounds such as the pyridyl acrylates shown in Figure 10.

(45) Maleimide, lacking the bulky *N*-phenyl group, reacts with the pyrrole complex (**1**) and the *N*-methylpyrrole complex (**2**) with enhanced *exo* selectivity (*exo/endo* = >20:1 and 1.5:1, respectively). Prof. William Myers, unpublished results.

Presumably, the bulk of the TBS group blocks access to C2 and C5. Since the stereochemistry of the cycloaddition is sensitive to steric effects at the nitrogen substituent, a removable group may be used in the selective synthesis of *endo* cycloadducts. Thus, the stereochemistry of the cycloaddition may be modulated with the use of a TMS group, which is easily cleaved prior to decomposition (Figure 11).

There is strong evidence that the *exo/endo* ratios reported above reflect a kinetic rather than thermodynamic preference for the observed stereochemistry. In the cycloaddition of maleic anhydride and $[\text{Os}(\text{NH}_3)_5(\eta^2\text{-pyrrole})]^{2+}$, the *exo/endo* ratio of reaction products depends on temperature and results in a lower *exo/endo* ratio at -30°C (2:1) than at 20°C (4:1). Subsequent warming of the cold reaction mixture from -30 to 20°C does not alter the 2:1 product ratio.^{13a} In a separate experiment, we find that the acrylate-derived cycloadduct **18** fails to undergo conversion to the maleimide analog **10a** in the presence of an excess of the more reactive dipolarophile *N*-phenylmaleimide, an observation which indicates the cycloaddition is not reversible under the reaction conditions.

The cycloadduct complexes are susceptible to an acid-promoted retro-Mannich reaction in which the final product is a 2*H*-pyrrole species. The vulnerability of the cycloadduct toward ring-opening depends primarily on the stability of the resulting enolate. Most susceptible are those complexes derived from methyl vinyl ketone, for which spontaneous decomposition occurs in solution, even in absence of acid, followed by maleic anhydride, maleimide, esters, or nitriles. This ring-opening reaction is sufficiently slow in acetonitrile that the complexes

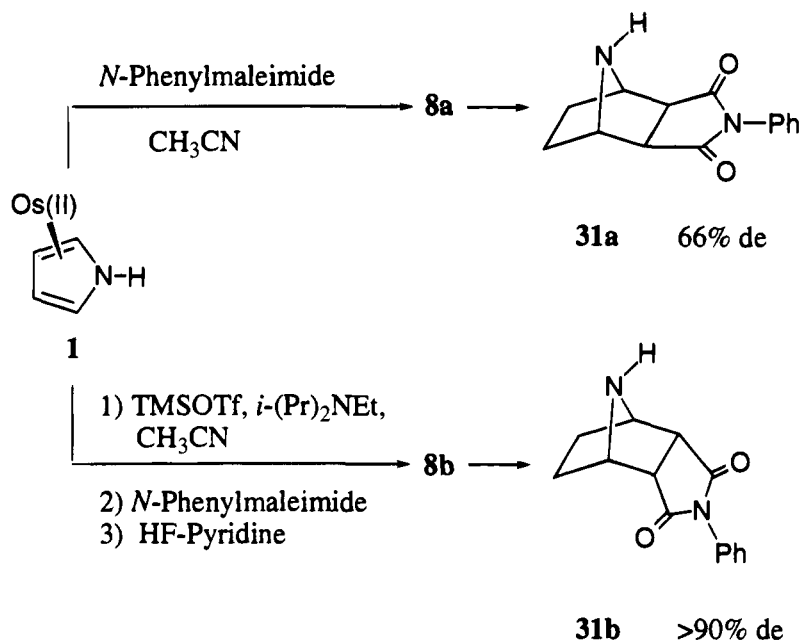


Figure 11. Control of stereochemistry for pyrrole/*N*-phenyl maleimide cycloaddition using a TMS group.⁴⁶

may be protonated prior to decomplexation without appreciable (<10%) ring-opening. In water however, the isomerization is facile even in the absence of acid for many of the cycloadducts, as illustrated in the formation of compounds **26–29**. Treatment of the cycloadduct complexes with 1 equiv of TBSOTf followed by hydrolysis results in facile ring-opening to the 2*H*-pyrrolium complexes, useful intermediates in the construction of pyrrolines and the pyrrolizidine ring system.^{13d,e}

The isomerization of the maleate adduct **13a** to the fumarate adduct **16** in water deserves special comment. The observation that deuterium is not incorporated when the isomerization takes place in D_2O or CD_3OD indicates that epimerization does not occur via a deprotonation/protonation or enolization pathway. Given the mild conditions under which this transformation takes place, it probably occurs through a retro-Mannich/Mannich reaction sequence as shown in Figure 12 (when $\text{Z} = \text{CO}_2\text{CH}_3$). Presumably, such a sequence occurs for the maleimide and anhydride systems as well, but the cyclic nature of these molecules prevents inversion of stereochemistry.

The Cycloaddition/Michael Addition Manifold. As discussed previously,^{13c} the azomethine ylide $[\text{Os}(\text{NH}_3)_5(3,4\text{-}\eta^2\text{-pyrrole})]^{2+}$ is unstable with respect to its 4,5- η^2 tautomer. For the latter, the uncoordinated portion of the heterocycle resembles an enamine, and the expected mode of reaction with an α,β -unsaturated carbonyl compound would be a Michael addition at C3, the β carbon of pyrrole. As described earlier, methyl vinyl ketone combines with the 2,5-dimethylpyrrole complex in acetonitrile at 20 °C to give a 1:1 mixture of cycloaddition and β -Michael addition products. By comparison, the 4,5- η^2 isomer of the 1-methylpyrrole complex (**2**) is less hindered than its 2,5-dimethyl analog (**3**), and as a consequence, the 4,5- η^2 to 3,4- η^2 tautomerization process is expected to be more endothermic for **2** than for **3**, and thus, the equilibrium ratio of 4,5- η^2 to 3,4- η^2 isomers is expected to be greater for **2** than for **3**. This difference in energy is reflected in the rates of both tautomerization and cycloaddition processes (Table 3). It stands to reason that, neglecting any electronic differences between these pyrroles, the 1-methylpyrrole complex (**2**) should show a greater extent of β -Michael reactivity than its 2,5-dimethyl analog (**3**). Indeed, the reaction of **2** with methyl vinyl ketone yields the C3 alkylation product, exclusively.^{13e} A second factor in determining the ratio of β -addition products to cycloadducts

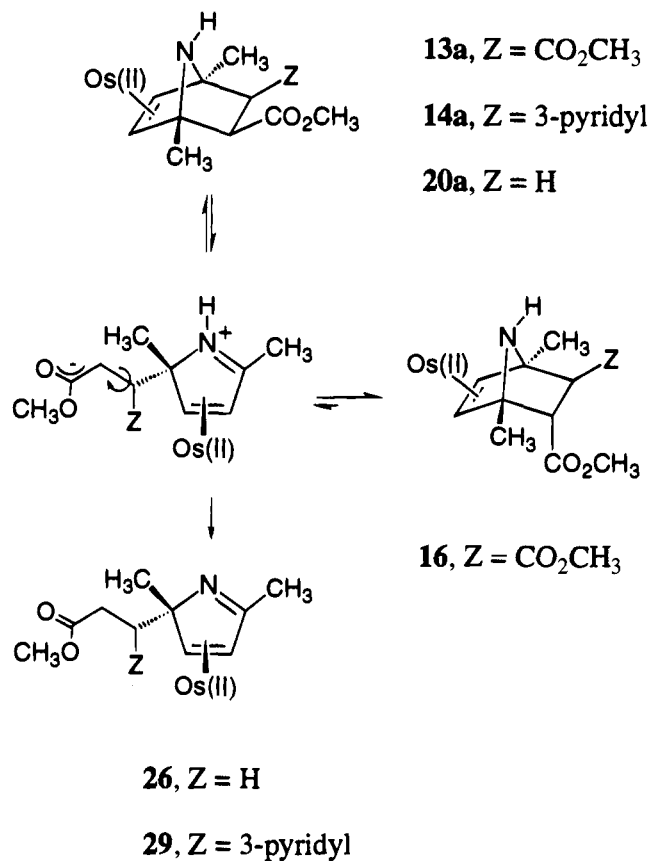


Figure 12. The isomerization or ring-opening of cycloadducts in water via a retro-Mannich reaction.

is the stability of the enolate intermediate formed in the β -Michael reaction. While for methyl vinyl ketone the rate of conjugate addition roughly equals that of cycloaddition, replacement of the methyl ketone functional group by the less electron-withdrawing methyl ester causes the rate of cycloaddition to dominate to such an extent that no conjugate addition is observed. This difference is a direct reflection of the increased stability of the ketone enolate compared to that of the ester. Under conditions where the ester enolate is stabilized by an external Lewis acid, β -Michael adducts are expected to be

formed more easily. Supporting this claim is the observation that methyl acrylate and the 2,5-dimethylpyrrole complex react in the presence of the Lewis acid TBSOTf, to form the β -Michael adduct (a 3*H*-pyrrole), exclusively.^{13e} Since cycloadducts may be ring-opened under acidic conditions to afford 2*H*-pyrroles (α -Michael adducts), the β/α regiochemistry of this Michael reaction may be conveniently controlled by addition of a Lewis acid at the appropriate stage of the reaction. For example, in the reaction of **3** with methyl acrylate, addition of TMSOTf in concert with the dipolarophile affords the β -Michael adduct, whereas addition of TMSOTf after completion of the cycloaddition affords the α -Michael adduct.^{13e}

Applications to the Synthesis of 7-Azanorbornanes. As summarized in Table 6, various substituted 7-azanorbornanes may be synthesized from pyrroles by the sequence of complexation–cycloaddition–decomplexation with typical overall yields of 40–60% for the process. In contrast to the conventional Diels–Alder reaction, requiring reactive acetylenic dienophiles, the [2 + 3] dipolar cycloadditions described herein allow the use of simple alkenes (i.e., bearing one electron-withdrawing group). Use of an alkene allows the construction of one or more stereocenters in the ring-forming step, and this method proves useful in the stereoselective synthesis of substituted 7-azanorbornanes.

In addition, the steps of complex formation, cycloaddition, decomplexation, and hydrogenation may be combined into two one-pot transformations from the commercially-available pyrroles. Although most of the work described in this paper was performed in a glovebox out of convenience (the starting pyrrole complexes **1–7** are air sensitive), the synthesis of compound **35** (from Os(NH₃)₅(OTf)₃ and 1-methylpyrrole) has been routinely performed on the benchtop on a 10 mmol scale taking no special precautions other than maintaining the reaction under nitrogen during the magnesium reduction stage.⁴⁷ The ester **34** and nitrile **35**, obtained in 55–65% overall yield from *N*-methylpyrrole by this procedure, are useful intermediates in the synthesis of biologically-active 7-azanorbornanes with heteroaromatic substituents. A full account of this work is forthcoming.

Conclusions

A new methodology has been described for the stereoselective synthesis of 7-azanorbornanes from pyrroles and α,β -unsaturated carbonyl compounds. The cycloaddition is promoted by the use of an Os(II) complexing agent which transforms the pyrrole into an azomethine ylide fragment capable of 1,3-dipolar cycloadditions. In this approach, addition occurs readily at 20 °C with a variety of dipolarophiles including α,β -unsaturated esters, nitriles, anhydrides, and imides. The metal not only activates the pyrrole ring but also stabilizes the resulting 7-azanorbornene ligand. For the cases examined, the cycloaddition occurs with a preference for *exo* stereochemistry (for the electron-withdrawing substituent) when the pyrrole nitrogen is unsubstituted and for *endo* stereochemistry when the nitrogen is either alkylated or silylated. The principal reaction to compete with the cycloaddition is Michael addition at the β carbon, which is favored when the corresponding enolate intermediate is stabilized by the solvent, carbonyl substituent, or a Lewis acid. The methodology can be applied to the stereoselective synthesis of 7-azanorbornanes and epibatidine analogs in several steps from commercially available pyrroles.

(46) The cycloaddition reactions are stereospecific (i.e., the stereochemistry of the minor diastereomers is 2 α -pyridyl, 3 α -carbomethoxy for **37b** and 2 β -pyridyl, and 3 α -carbomethoxy for **38b**).

(47) The cycloadduct complexes are air stable, so the decomplexations need not be performed under nitrogen.

Experimental Section

General Methods. Routine ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were recorded on a General Electric QE-300 or GN-300 spectrometer and are reported in ppm shift from tetramethylsilane.⁴⁸ Multiplicities for ¹³C NMR resonances were assigned by DEPT. Electrochemical experiments were performed under nitrogen using a PAR Model 362 potentiostat driven by a PAR Model 175 universal programmer. Cyclic voltammograms were recorded (Kipp & Zonen BD90 XY recorder) in a standard three-electrode cell from +1.5 to –1.5 V with a glassy carbon working electrode. All potentials are reported vs NHE and were determined in CH₃CN (~0.5 M TBAH) using ferrocene ($E_{1/2} = 0.55$ V) *in situ* as a calibration standard. The peak-to-peak separation ($E_{p,a} - E_{p,c}$) was between 70 and 100 mV for all reversible couples reported unless otherwise noted. Unless specified otherwise, this work was carried out under a nitrogen atmosphere in a Vacuum Atmospheres Co. glovebox. Separate boxes were used for aqueous and nonaqueous operations unless otherwise noted. All compounds in this study were either achiral or racemic mixtures, and the names and structures describe only the relative stereochemistry of substituents.

Solvents. All distillations were performed under nitrogen, and all solvents were deoxygenated by purging with nitrogen for at least 20 min. Deuterated solvents were deoxygenated by repeated freeze–pump–thaw cycles. Methylene chloride was refluxed for at least 8 h over P₂O₅ and distilled. Diethyl ether was refluxed for at least 8 h over Na/benzophenone and distilled. Methanol was refluxed over Mg(OMe)₂, prepared *in situ* from Mg⁰ activated by iodine, and distilled. Acetonitrile was refluxed over CaH₂ and distilled. DME, DMAc (Aldrich, anhydrous), and acetone (Burdick and Jackson) were deoxygenated prior to use but otherwise were used as supplied.

Reagents. [Os(NH₃)₅(OTf)](OTf)₂ was synthesized from either osmium tetroxide or ammonium hexachloroosmate (Colonial Metals, Inc.) as described by Lay *et al.*⁴⁹ Magnesium powder (Aldrich, 50 mesh) was activated by treating with iodine in DME under nitrogen, stirring for 1 h, and washing with DMAc, acetone, and ether. The pyrrole ligands (Aldrich, Sigma, Pfaltz and Bauer) were distilled over CaH₂ under nitrogen. 2-Ethylpyrrole was obtained from Trans World Chemicals. Commercially available dipolarophiles were either used as supplied (solids) or distilled from CaH₂ under N₂ and stored at –20 °C. The ammonia–methanol (~15 wt %) solution used for chromatography was prepared by saturating methanol with anhydrous ammonia at room temperature (maintained using an ice bath). The silica gel was Merck grade 60, 230–400 mesh. The alumina was Fisher no. A-540 80–200 mesh (sold as “adsorption alumina”; a 1:1 slurry with water has a pH > 9). The preparative TLC plates were 20 × 20 cm, 0.7 mm tapered plates obtained from Analtech.

General Procedure for the Isolation and Purification of Osmium Complexes. The osmium complexes, in the form of their triflate salts, were precipitated from solution by dilution with ether or methylene chloride. In a typical experiment, a solution of a complex (in DMAc, acetonitrile, acetone, methanol, or other highly polar solvent) was added to a larger volume of methylene chloride, ether, or mixtures of the two. Methylene chloride was used in precipitations from DMAc solutions (50–100 mL per g of DMAc) as in the isolation of pyrrole complexes **1–7**; ether was used to precipitate the complexes from their methanol, acetonitrile, or acetone solutions (~10–40 mL per gram of the polar solvent). Occasionally, upon attempted precipitation, an oil or gummy residue formed. In these cases, the supernatant was decanted, and then the oil was dissolved in acetone or acetonitrile and again added dropwise to ether or methylene chloride. The precipitates were filtered using medium or fine fritted glass funnels, washed with several (5–10 mL per mmol of complex) portions of methylene chloride and ether, and then dried under nitrogen or *in vacuo*.

The osmium complexes **2–7** prepared this way are typically >90% pure. The impurities at this stage include up to 5–8% of a binuclear complex, and some solvent (e.g., DMAc).⁵⁰ Most osmium complexes

(48) The ¹³C NMR spectra of the osmium complexes typically show a quartet ($\delta \sim 121$ –122 ppm, $J = 315$ –317 Hz) for the triflate counterion. Due to the low intensity of this signal, it is not always observed and is not reported.

(49) Lay, P. A.; Magnuson, R. H.; Taube, H. *Inorg. Syn.* **1986**, *24*, 269.

reported in this paper may be purified by ion exchange chromatography using Sephadex CM, C-25 (typical loading: 50–200 mg of complex on a 1 × 10 cm column of adsorbent), using aqueous NaCl (0.3–0.35 M) as the mobile phase. The pure complexes may be separated from the mobile phase by addition of a concentrated aqueous solution of sodium tetraphenylborate, which precipitates the complexes as their tetraphenylborate salts.⁵¹

One-Pot Procedure for the Synthesis of Cycloadduct Complexes.

This procedure may be done on the bench. The dipolarophile (e.g., methyl acrylate) was added directly to the reaction mixture following the synthesis of the pyrrole complex. After 1–12 h, the reaction mixture was filtered to remove the magnesium, and the filtrate was added to 1:1 methylene chloride/ether (100 mL per g of DMAc used in the synthesis). The solid was collected by filtration, washed, and dried under nitrogen, affording ~95% yield of the cycloadduct complex containing a variable amount (0.1–1 equiv) of DMAc.

Synthesis of 7-Azanorbornanes. The following procedure was done on the bench: The cycloadduct complex (1.0 mmol) was dissolved in acetonitrile (4 g), protonated with excess triflic acid (3–5 equiv), and treated with DDQ (0.5–1 equiv). The osmium salts that crystallize were removed by filtration (this is optional). The dark solution was transferred to a 50-mL, round-bottom flask with the aid of an additional 20 mL of acetonitrile, then treated with 10% Pd/C (0.25 g, ~20 mol % Pd), and hydrogenated under 1 atm H₂ for 1–2 h. An aliquot was evaporated and analyzed by ¹H NMR in acetone-*d*₆ to check for completion. **Workup A.** The reaction mixture was filtered through Celite, the cake was washed with acetonitrile, and the filtrate was evaporated. The residue was dissolved in water (~10–15 mL), transferred to a separatory funnel, made basic with 10% aqueous Na₂CO₃ (20 mL), and extracted with methylene chloride (3 × 40 mL). The extract was dried over MgSO₄ and evaporated, affording the product. **Workup B.** The hydrogenation reaction mixture was filtered, evaporated, the residue made basic with ammonia–methanol solution or NH₄OH (~1–5 mL), diluted or extracted with methylene chloride or ether (~50 mL), and then filtered directly through a 3 × 3 cm plug of silica gel in a 30-mL medium fritted glass funnel. The flask and silica were washed with an additional 3 × 25 mL of methylene chloride or ether containing ~5–10% NH₃–methanol, and the filtrate evaporated, affording the product. The 7-azanorbornane free bases were purified, and the isomers were separated by column chromatography or preparative TLC.⁵²

Pyrrole Complexes 1–7. The synthesis and characterization of these complexes {Os(NH₃)₅(L)}(OTf)₂ [L = pyrrole (1), 1-methylpyrrole (2), 2,5-dimethylpyrrole (3), 1,2,5-trimethylpyrrole (4), and 2-ethylpyrrole (6)] has been reported.^{13b,c} A slight modification of the original procedure was used for preparations done on a larger scale, as illustrated below for complex 2.

{4,5-η²-[Os(NH₃)₅]-1-methylpyrrole}(OTf)₂ (2). To [Os(NH₃)₅-(OTf)₂] (7.226 g, 10.0 mmol) and activated magnesium (3 g) was added 1-methylpyrrole (9 mL, 100 mmol), DME (20 mL), and DMAc (6 mL) in that order. The mixture was stirred for 45 min to 1 h (the temperature rose to 35–40 °C over the course of 15 min and then gradually dropped after 30 min).⁵³ The brown slurry was filtered through a thin pad of Celite on a 60-mL medium fritted glass funnel, and the cake was washed with ~20 mL DME in small portions. The viscous filtrate was added to methylene chloride (300 mL) with vigorous stirring, and the resulting yellow precipitate filtered through a 150-mL medium fritted funnel and washed with methylene chloride (50 mL)

(50) The pyrrole complex (1) is formed in combination with variable amounts (10–20%) of an unidentified paramagnetic impurity (*E*_{1/2} = -1.0 V).

(51) Some complexes will undergo decomposition upon attempted purification in this manner, in which cases it has not been possible to obtain a satisfactory elemental analysis. Compounds **8b**, **20**, **21**, and **39** were converted to the corresponding organic products **31b**, **34**, **35**, and **40** in order to obtain a full characterization.

(52) Dragendorff's reagent was used to visualize TLC plates (Touchstone, J. C.; Dobbins, M. F. *Practice of Thin Layer Chromatography*, Wiley & Sons: New York, 1978). 7-Azanorbornanes will sometimes stain red-orange on TLC plates using this reagent.

(53) DME is added as a diluent to help control the temperature of the reaction. Under more concentrated conditions (or when the reaction is done on a larger scale) it is necessary to apply external cooling to keep the temperature from rising above 40 °C.

and ether (2 × 50 mL), then dried under nitrogen, affording 6.323 g (97%) of a yellow-tan solid. The characterization of this compound has been reported in ref 13b.

{4,5-η²-[Os(NH₃)₅]-1-trimethylsilylpyrrole}(OTf)₂ (5).⁵⁴ To a solution of pyrrole complex **1** (189 mg, 0.294 mmol) and Proton Sponge (98 mg, 0.46 mmol) in CH₃CN (0.4 g) was added TMSOTf (80 mg, 0.36 mmol). After 35 min the mixture was treated with methylene chloride (40 mL), yielding a tan powder (196 mg, 94%): ¹H NMR (CD₃CN) δ 6.65 (m, 1H), 6.24 (m, 1H), 5.81 (m, 1H), 5.13 (m, 1H), 3.90 (br s, 3H, *trans*-NH₃), 2.73 (br s, 12H, *cis*-NH₃), 0.32 (s, 9H, TMS); ¹³C NMR (CD₃CN) δ 130.6 (CH), 111.4 (CH), 79.6 (CH), 58.6 (CH), 0.2 (TMS); *E*_{p,a} = 0.28 V. Anal. Calcd for C₉H₂₈N₆O₆S₂F₆-SiO_s: C, 15.17; H, 3.96; N, 11.79. Found: C, 14.60; H, 3.72; N, 11.85.⁵¹

{5β,6β-η²-[Os(NH₃)₅]-4β,7β-imino-2-phenyl-3α,4,7,7aα-tetrahydro-1H-isoindole-1,3(2H)-dione}(OTf)₂ (8a). To a solution of the pyrrole complex (**1**) (126 mg, 0.20 mmol) in CD₃CN (0.4 g) was added a solution of *N*-phenylmaleimide (36 mg, 0.21 mmol) in CD₃CN (0.2 g). After 10 min, the solution was added to ether (30 mL) affording a tan powder (136 mg, 85%). This material consisted of a ~6:1 mixture of **8a** to **8b** by ¹H NMR. When this synthesis was carried out on a 1–3 mmol scale in acetonitrile (0.06 M) and the reaction mixture concentrated under reduced pressure, the *exo* isomer (**8a**) crystallized in 41–42% yield. Data for **8a**: ¹H NMR (CD₃CN) δ 7.45–7.28 (m, 5H, Ph), 4.09 (s, 2H, H1, H4), 4.04 (br s, 3H, *trans*-NH₃), 3.23 (br s, 12H, *cis*-NH₃), 3.22 (s, 2H, H5, H6), 3.21 (s, 2H, H2, H3); ¹³C NMR (CD₃CN) δ 176.6 (CO), 134.4 (CH), 132.8 (C), 129.4 (CH), 127.7 (CH), 65.3 (CH), 52.9 (CH), 51.7 (CH); *E*_{p,a} = 0.82 V. This compound was purified by ion-exchange chromatography and isolated as its tetraphenylborate dihydrate salt. Anal. Calcd for C₆₂H₆₇N₇O₂B₂O_s·2H₂O: C, 62.57; H, 6.01; N, 8.24. Found: C, 62.49; H, 6.10; N, 8.38.

{5β,6β-η²-[Os(NH₃)₅]-4β,7β-imino-2-phenyl-3αβ,4,7,7aβ-tetrahydro-1H-isoindole-1,3(2H)-dione}(OTf)₂ (8b). To a solution of **12b** (107 mg, 0.121 mmol) in CH₃CN (0.47 g) was added a solution of HF in pyridine (268 mg of a ~0.7% solution, ~1 equiv of HF; stock solution prepared by mixing 0.30 mL of Aldrich HF/pyridine (~70% HF) with 30 mL of pyridine). After 20 min, the solution was added to 2:1 CH₂Cl₂/Et₂O (75 mL), affording 81 mg (83%) of a purple solid: ¹H NMR (CD₃CN) δ 7.5–7.2 (m, 5H, Ph), 4.10 (br s, 2H), 4.15 (br s, 3H, *trans*-NH₃), 3.41 (br s, 2H), 3.22 (s, 2H), 3.20 (br s, 12H, *cis*-NH₃); ¹³C NMR (CD₃CN) δ 170.0 (CO), 132.4 (C), 129.0 (CH), 128.5 (CH), 127.4 (CH), 63.7 (CH), 50.8 (CH), 46.6 (CH); *E*_{p,a} = 0.85 V. Anal. Calcd for C₁₆H₂₇N₇O₈S₂F₆O_s: C, 23.62; H, 3.34; N, 12.05. Found: C, 22.87; H, 3.12; N, 11.75.⁵¹

{5β,6β-η²-[Os(NH₃)₅]-4β,7β-imino-8-methyl-2-phenyl-3αβ,4,7,7aβ-tetrahydro-1H-isoindole-1,3(2H)-dione}(OTf)₂ (9b). To a solution of the 1-methylpyrrole complex (**2**) (131 mg, 0.20 mmol) in CH₃CN (0.3 g) was added a solution of *N*-phenylmaleimide (36 mg, 0.21 mmol) in CH₃CN (0.1 g). After 5 min the solution was treated with ether (15 mL), affording a 1:6 mixture of **9a** to **9b** as a tan powder (141 mg, 85%). Data for **9b**: ¹H NMR (CD₃CN) δ 7.46–7.20 (m, 5H, Ph), 4.11 (br s, 3H, *trans*-NH₃), 3.86 (dd, *J* = 3.0, 1.5 Hz, 2H, H1, H4), 3.57 (dd, *J* = 3.0, 1.5 Hz, 2H, H5, H6), 3.32 (s, 2H, H2, H3), 3.20 (br s, 12H, *cis*-NH₃), 2.14 (s, 3H, CH₃N); ¹³C NMR (CD₃CN) δ 178.0 (CO), 133.5 (C), 129.8 (CH), 129.3 (CH), 128.2 (CH), 69.4 (CH), 49.9 (CH), 47.9 (CH), 33.5 (CH₃). Data for **9a**: ¹H NMR (CD₃CN) δ 7.46–7.20 (m, 5H, Ph), 4.11 (br s, 3H, *trans*-NH₃), 4.08 (s, 2H, H1, H4), 3.37 (s, 2H, H5, H6), 3.27 (s, 2H, H2, H3), 3.20 (br s, 12H, *cis*-NH₃), 2.36 (s, 3H, CH₃N). Data for the mixture of both isomers: *E*_{1/2} = 0.77 V. Anal. Calcd for C₁₇H₂₉N₇O₈S₂F₆O_s: C, 24.67; H, 3.53; N, 11.85. Found: C, 24.25; H, 3.50; N, 11.14.⁵¹

{5β,6β-η²-[Os(NH₃)₅]-4,7-dimethyl-4β,7β-imino-2-phenyl-3α,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione}(OTf)₂ (10). A mixture of the 2,5-dimethylpyrrole complex (**3**) (401 mg, 0.60 mmol) and *N*-phenylmaleimide (114 mg, 0.66 mmol) was dissolved in CH₃CN (0.5 g). Within minutes a precipitate started to form. After 10 min the mixture was cooled to -20 °C for 1 h and filtered, and the cake washed thoroughly with acetonitrile (5 mL) and ether (5 mL). The resulting tan solid (156 mg) was a 1:1 mixture of isomers by ¹H NMR.

(54) When this complex was prepared from 1-(trimethylsilyl)pyrrole (Fessenden, R.; Crowe, D. F. *J. Org. Chem.* **1960**, *25*, 598), its purity was consistently lower than the material prepared by silylating **1**.

Compound **10b** crystallized in its pure form when the reaction was run under more dilute conditions and allowed to stand for 1 h at room temperature: $^1\text{H NMR}$ (DMSO- d_6) δ 7.43–7.32 (m, 5H, Ph), 4.29 (br s, 3H, *trans*-NH $_3$), 3.59 (br s, 12H, *cis*-NH $_3$), 3.10 (s, 2H, H5, H6), 3.08 (s, 2H, H2, H3), 2.55 (br s, 1H, NH), 1.40 (s, 6H, CH $_3$); $^{13}\text{C NMR}$ (DMSO- d_6) δ 175.7 (CO), 132.5 (C, C1'), 128.7 (CH), 128.1 (CH), 127.2 (CH), 74.5 (C), 59.4 (CH), 51.5 (CH), 18.8 (CH $_3$); $E_{\text{p.a.}} = 0.85$. Anal. Calcd for C $_{18}$ H $_{31}$ N $_7$ O $_8$ S $_2$ F $_6$ Os: C, 25.68; H, 3.71; N, 11.65. Found: C, 25.65; H, 3.81; N, 11.46.

The filtrate from above was added to ether (40 mL), affording **10a** as a light tan solid (291 mg, 58%; combined yield of both isomers: 89%): $^1\text{H NMR}$ (DMSO- d_6) δ 7.42–7.10 (m, 5H, Ph), 4.34 (br s, 3H, *trans*-NH $_3$), 3.50 (br s, 12H, *cis*-NH $_3$), 3.09 (s, 2H, H5, H6), 2.99 (s, 2H, H2, H3), 2.52 (br s, 1H, NH), 1.45 (s, 6H, CH $_3$); $^{13}\text{C NMR}$ (DMSO- d_6) δ 174.0 (CO), 132.8 (C, C1'), 128.4 (CH), 128.0 (CH), 127.6 (CH), 72.7 (C), 58.6 (CH), 57.4 (CH), 15.7 (CH $_3$). A 7% NOE between methine ring resonances at 3.68 and 3.33 ppm in acetone- d_6 is consistent with *exo* stereochemistry; $E_{\text{p.a.}} = 0.81$ V. Anal. Calcd for C $_{18}$ H $_{31}$ N $_7$ O $_8$ S $_2$ F $_6$ Os: C, 25.68; H, 3.71; N, 11.65. Found: C, 25.59; H, 3.43; N, 12.10.

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-4 β ,7 β -imino-2-phenyl-3 α ,4,7,7 α -tetrahydro-4,7,8-trimethyl-1H-isoindole-1,3(2H)-dione}(OTf) $_2$ (11**). To a solution of the 1,2,5-trimethylpyrrole complex (**4**) (200 mg, 0.292 mmol) in CD $_3$ CN (0.4 g) was added a solution of *N*-phenylmaleimide (52 mg, 0.30 mmol) in CD $_3$ CN (0.2 g). After 10 min the orange crystals that formed were filtered, washed with ether, and dried *in vacuo*, affording 155 mg (62%) of a light orange powder. **11b**: $^1\text{H NMR}$ (1:1 acetone- d_6 /DMSO- d_6) δ 7.45–7.25 (m, 5H, Ph), 4.45 (br s, 3H, *trans*-NH $_3$), 3.67 (br s, 12H, *cis*-NH $_3$), 3.39 (s, 2H, H2, H3), 3.32 (s, 2H, H5, H6), 2.16 (s, 3H, NCH $_3$), 1.61 (s, 6H, 2CH $_3$); $^{13}\text{C NMR}$ (1:1 acetone- d_6 /DMSO- d_6) δ 177.2 (CO), 133.6 (C), 129.3 (CH), 129.3 (CH), 127.8 (CH), 77.6 (C), 55.8 (CH), 52.3 (CH), 26.9 (NCH $_3$), 17.1 (CH $_3$). A 7% NOE enhancement of the ring protons upon irradiation of the *N*-methyl substituent is consistent with *endo* stereochemistry.**

The filtrate was added to ether (10 mL) affording compound **11a** as light tan-orange solid (38 mg, 15% yield; 77% yield of both isomers: $^1\text{H NMR}$ (1:1 acetone- d_6 /DMSO- d_6) δ 7.45–7.25 (m, 5H, Ph), 4.53 (br s, 3H, *trans*-NH $_3$), 3.64 (br s, 12H, *cis*-NH $_3$), 3.42 (s, 2H, H2, H3), 3.20 (s, 2H, H5, H6), 2.03 (s, 3H, NCH $_3$), 1.52 (s, 6H, 2CH $_3$); $^{13}\text{C NMR}$ (1:1 acetone- d_6 /DMSO- d_6) δ 175.2 (CO), 128.6 (CH), 128.4 (CH), 127.5 (C), 126.8 (CH), 76.3 (C), 58.9 (CH), 58.0 (CH), 27.6 (NCH $_3$), 14.2 (CH $_3$). Data for the mixture of both isomers: $E_{1/2} = 0.83$ V. Anal. Calcd for C $_{19}$ H $_{33}$ N $_7$ O $_8$ F $_6$ S $_2$ Os: C, 26.67; H, 3.89; N, 11.46. Found: C, 26.48; H, 3.78; N, 11.65.

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-4 β ,7 β -imino-2-phenyl-3 $\alpha\beta$,4,7,7 $\alpha\beta$ -tetrahydro-8-trimethylsilyl-1H-isoindole-1,3(2H)-dione}(OTf) $_2$ (12b**). To a solution of **1** (0.85 g, 1.33 mmol) and Hünig's base (0.28 g, 2.17 mmol) in CH $_3$ CN (1.47 g) was added a solution of TMSOTf (0.41 g, 1.85 mmol) in CH $_3$ CN (0.76 g). After standing for 1.3 h, a solution of *N*-phenylmaleimide (1.52 g, 8.77 mmol) in CH $_3$ CN (1.50 g) was added. After standing for an additional 3 h, the solution was added to 2:1 CH $_2$ Cl $_2$ /Et $_2$ O (225 mL), affording 1.10 g (93%) of **12b** as a purple-brown powder: $^1\text{H NMR}$ (CD $_3$ CN) δ 7.43–7.18 (m, 5H, Ph), 4.35 (dd, $J = 3.0, 1.8$ Hz, 2H, H1, H4), 4.10 (br s, 3H, *trans*-NH $_3$), 3.36 (dd, $J = 3.0$ Hz, 1.8 Hz, 2H, H5, H6), 3.31 (s, 2H, H2, H3), 3.14 (br s, 12H, *cis*-NH $_3$), 0.07 (s, 9H, TMS); $^{13}\text{C NMR}$ (CD $_3$ CN) δ 176.1 (CO), 132.6 (C), 129.0 (CH), 128.6 (CH), 127.4 (CH), 64.7 (CH), 51.5 (CH), 49.2 (CH), -1.0 (TMS); $E_{\text{p.a.}} = 0.86$ V. This compound isomerized to the 2*H*-pyrrole **27** upon attempted purification by ion-exchange chromatography.**

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-2 β ,3 β -bis(carbomethoxy)-1,4-dimethyl-7-azabicyclo-[2.2.1]hept-5-ene}(OTf) $_2$ (13a**). To a solution of 2,5-dimethylpyrrole complex (**3**) (152 mg, 0.227 mmol) in CH $_3$ CN (0.4 g) was added a solution of dimethyl maleate (170 mg, 1.18 mmol) in CH $_3$ CN (0.15 g). Within minutes of mixing, crystals started to form, and after 2 h the orange crystals were filtered, washed with ether, and dried *in vacuo*. A pale orange crystalline solid was obtained (69 mg, 38% yield). $^1\text{H NMR}$ (acetone- d_6) δ 4.63 (br s, 3H, *trans*-NH $_3$), 3.96 (br s, 12H, *cis*-NH $_3$), 3.58 (s, 6H, CH $_3$ O), 3.53 (s, 2H), 3.31 (s, 2H), 1.52 (s, 6H, CH $_3$); $^{13}\text{C NMR}$ (acetone- d_6) δ 172.7 (CO), 74.1 (C, C1, C4), 59.3 (CH), 59.2 (CH), 51.4 (CH $_3$ O), 15.9 (CH $_3$). The filtrate was added to ether (60 mL) affording a mixture of **13a** and **13b** as a tan**

solid (82 mg, 45%; 82% yield of both isomers). Data for **13b**: $^1\text{H NMR}$ (acetone- d_6) δ 4.63 (br s, 3H, *trans*-NH $_3$), 3.93 (br s, 12H, *cis*-NH $_3$), 3.58 (s, 6H, CH $_3$ O), 3.53 (s, 2H, H5, H6), 3.31 (s, 2H, H2, H3), 2.58 (br s, 1H, NH), 1.53 (s, 6H, CH $_3$); $^{13}\text{C NMR}$ (acetone- d_6) δ 172.7 (CO), 74.1 (C, C1, C4), 59.3 (CH), 59.2 (CH), 51.4 (CH $_3$ O), 15.9 (CH $_3$). The ring protons in the succinate moiety of **13a** exhibit a 7% NOE enhancement upon irradiation of the olefinic ring protons, similar to the enhancement observed for the maleimide/trimethylpyrrole adduct **11a**. Data for both isomers: $E_{\text{p.a.}} = 0.80$. Anal. Calcd for C $_{14}$ H $_{32}$ N $_6$ O $_{10}$ S $_2$ F $_6$ Os: C, 20.69; H, 3.97; N, 10.34. Found: C, 20.34; H, 3.90; N, 10.49.

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-1,4-dimethyl-3 β -carbomethoxy-2 β -(3'-pyridyl)-7-azabicyclo[2.2.1]hept-5-ene}(OTf) $_2$ (14a**). The 2,5-dimethylpyrrole complex (**3**) (401 mg, 0.6 mmol) and methyl (Z)-3-(3'-pyridyl)acrylate⁵⁵ (292 mg, 1.79 mmol, 3 equiv) were dissolved in DMAc (0.5 g) and allowed to stand for 18 h. The dark solution was diluted with acetonitrile (1 mL, to reduce the viscosity) and added dropwise to 1:1 methylene chloride–ether (80 mL), affording 413 mg (83%) of a dark tan solid. This solid consisted of a 9:1 mixture of *exo* and *endo* isomers by $^1\text{H NMR}$. Data for **14a**: $^1\text{H NMR}$ (acetone- d_6) δ 8.37 (br s, 2H, overlap of H2' and H6'), 7.61 (d, $J = 8.1$ Hz, 1H, H4'), 7.22 (m, 1H, H5'), 4.63 (br s, 3H, *trans*-NH $_3$), 4.00 (br s, 12H, *cis*-NH $_3$), 3.81 (d, $J = 9$ Hz, 1H), 3.74 (d, $J = 6$ Hz, 1H), 3.62 (br s, NH, 1H), 3.53 (d, $J = 6$ Hz, 1H), 3.37 (d, $J = 9$ Hz, 1H), 3.12 (s, 3H, CH $_3$ O), 1.51 (s, 3H, CH $_3$), 1.24 (s, 3H, CH $_3$); $^{13}\text{C NMR}$ (acetone- d_6) δ 172.9 (CO), 152.0 (CH), 148.1 (CH), 137.5 (CH), 134.6 (C, C3'), 122.6 (CH), 73.9 (C), 73.3 (C), 61.8 (CH), 61.3 (CH), 59.8 (CH), 57.9 (CH), 50.6 (CH $_3$ O), 16.1 (CH $_3$), 15.8 (CH $_3$); $E_{\text{p.a.}} = 0.87$ V. This compound isomerized to the corresponding 2*H*-pyrrole (**29**) upon attempted purification by ion exchange chromatography.**

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-2 β ,3 α -bis(carbomethoxy)-7-azabicyclo[2.2.1]hept-5-ene}(OTf) $_2$ (15**). The pyrrole complex (**1**) (100 mg, 0.156 mmol) and dimethyl fumarate (225 mg, 1.56 mmol) were dissolved in acetonitrile (0.5 g) with stirring and the mixture was allowed to stand for 6 h, while a crystalline solid precipitated. The mixture was diluted with acetonitrile (2 mL) and added to 1:1 ether/methylene chloride (50 mL), affording 95 mg (78%) of a tan solid. Data for **15**: $^1\text{H NMR}$ (CD $_3$ CN) δ 4.07 (br s, 3H, *trans*-NH $_3$), 4.02 (d, $J = 4.2$ Hz, 1H, H1), 3.85 (s, 1H, H4), 3.67 (s, 3H, CH $_3$ O), 3.64 (s, 3H, CH $_3$ O), 3.52 (br s, 1H, NH), 3.22 (br s, 12H, *cis*-NH $_3$), 3.15 (m, 1H), 3.05 (m, 2H), 2.92 (d, $J = 6$ Hz, 1H); $^{13}\text{C NMR}$ (CD $_3$ CN) δ 175.6 (CO), 172.7 (CO), 68.0 (CH), 64.6 (CH), 53.5 (CH), 52.5 (CH $_3$), 52.4 (CH $_3$), 52.1 (CH); $E_{\text{p.a.}} = 0.79$ V. The tetraphenylborate salt was obtained following ion exchange chromatography: Anal. Calcd for C $_{28}$ H $_{48}$ N $_6$ O $_4$ B $_2$ Os: C, 61.92; H, 6.09; N, 7.47. Found: C, 61.72; H, 5.98; N, 7.13.**

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-2 β ,3 α -bis(carbomethoxy)-1,4-dimethyl-7-azabicyclo-[2.2.1]hept-5-ene}(OTf) $_2$ (16**). The 2,5-dimethylpyrrole complex (**3**) (200 mg, 0.3 mmol) and dimethyl fumarate (50 mg, 0.35 mmol) were dissolved in CH $_3$ CN (0.4 g). After 5 min the solution was added to ether (30 mL) affording 207 mg (86%) of an ivory-colored solid. $^1\text{H NMR}$ (acetone- d_6) δ 4.62 (br s, 3H, *trans*-NH $_3$), 3.91 (br s, 12H, *cis*-NH $_3$), 3.68 (s, 3H, CH $_3$ O), 3.64 (s, 3H, CH $_3$ O), 3.50 (d, $J = 5.5$ Hz, 1H), 3.43 (d, $J = 5.5$ Hz, 1H), 3.33 (d, $J = 4.5$ Hz, 1H), 2.93 (d, $J = 4.5$ Hz, 1H), 2.25 (br s, 1H, NH), 1.65 (s, 3H, CH $_3$), 1.33 (s, 3H, CH $_3$); $^{13}\text{C NMR}$ (acetone- d_6) δ 175.3 (CO), 172.0 (CO), 76.4 (C), 74.8 (C), 63.2 (CH), 59.0 (CH), 58.3 (CH), 54.4 (CH), 51.9 (CH $_3$ O), 51.8 (CH $_3$ O), 18.5 (CH $_3$), 16.1 (CH $_3$); $E_{1/2} = 0.78$ V. The tetraphenylborate salt was obtained following ion exchange chromatography. Anal. Calcd for C $_{26}$ H $_{42}$ N $_6$ O $_4$ B $_2$ Os: C, 62.50; H, 6.29; N, 7.29. Found: C, 62.60; H, 6.11; N, 6.97.**

{5 β ,6 β - η^2 -[Os(NH $_3$) $_5$]-1,4-dimethyl-3 β -carbomethoxy-2 α -(3'-pyridyl)-7-azabicyclo[2.2.1]hept-5-ene}(OTf) $_2$ (17a**). The 2,5-dimethylpyrrole complex (**3**) (669 mg, 1.0 mmol) and methyl (*E*)-3-(3'-**

(55) Methyl (Z)-3-(3'-pyridyl)acrylate was prepared from nicotinaldehyde using the Still–Gennari procedure (Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405) as described for the 6-chloro derivative.^{6c} In order to obtain high selectivity (*Z*:*E* > 10:1), however, it is essential to use pure THF as the reaction solvent (Dr. Sidduri Achyutha Rao, personal communication; ref 6c). In our hands, addition of the commercially available 0.5 M toluene solution of potassium hexamethyldisilazide to the other reagents in THF solution as described by Still and Gennari (approximate toluene content of the reaction mixture: 10%) led to a complete reversal of the expected stereoselectivity (*Z*:*E* = 1:9).

pyridyl)acrylate⁵⁶ (750 mg, 4.6 mmol) were dissolved in methanol (0.65 g) and allowed to stand for 14 h. The dark solution was diluted with acetonitrile (2 mL) and methylene chloride (5 mL), and added to ether (50 mL), affording 774 mg (93%) of a dark tan solid.⁵⁷ This material consisted of a 94:6 ratio of isomers by ¹H NMR. Data for **17a**: ¹H NMR (acetone-*d*₆) δ 8.55 (s, 1H, H^{2'}), 8.42 (d, *J* = 4.5 Hz, 1H, H^{6'}), 7.8 (d, *J* = 7.8 Hz, H^{4'}), 7.24 (dd, *J* = 7.8, 4.5 Hz, H^{5'}), 4.65 (br s, 3H, *trans*-NH₃), 3.98 (br s, 12H, *cis*-NH₃), 3.81 (d, *J* = 6.2 Hz, 1H), 3.64 (s, 3H, CH₃O), 3.45 (d, *J* = 6.2 Hz, 1H), 3.27 (d, *J* = 5.3 Hz, 1H), 3.20 (d, *J* = 5.3 Hz, 1H), 1.42 (s, 3H, CH₃), 1.40 (s, 3H, CH₃); ¹³C NMR (acetone-*d*₆) δ 175.0 (CO), 149.9 (CH), 147.7 (CH), 136.2 (CH), 134.8 (C), 123.1 (CH), 75.9 (C), 74.2 (C), 62.4 (CH), 61.6 (CH), 57.6 (CH), 52.5 (CH), 51.1 (CH₃), 16.6 (CH₃), 15.5 (CH₃); *E*_{pa} = 0.89 V. The tetraphenylborate monohydrate salt was obtained following ion exchange chromatography. Anal. Calcd for C₆₃H₇₇N₇O₇B₂Os·H₂O: C, 63.58; H, 6.35; N, 8.24. Found: C, 63.95; H, 6.27; N, 8.23.

[5β,6β-η²-[Os(NH₃)₅]-2β-carbomethoxy-1,4-dimethyl-7-azabicyclo[2.2.1]-hept-5-ene](OTf)₂ (18a). The 2,4-dimethylpyrrole complex (**3**) (669 mg, 1.0 mmol) was suspended in methyl acrylate (2 g), and the slurry was stirred for 1 h. Acetonitrile (~1 mL) was added to dissolve the solids, and the resulting solution was added to ether (50 mL), affording 730 mg (97%) of an off-white powder. This solid consisted of a 92:8 mixture of **18a** and **18b**, respectively, by ¹H NMR (the NMR data for **18a** has been previously reported).^{13d} *E*_{pa} = 0.69 V. Anal. Calcd for C₁₂H₃₀N₆O₈S₂F₆Os: C, 19.10; H, 4.01; N, 11.14. Found: C, 18.57; H, 3.96; N, 11.02.

[5β,6β-η²-[Os(NH₃)₅]-2-cyano-1,4-dimethyl-7-azabicyclo[2.2.1]-hept-5-ene](OTf)₂ (19). The 2,5-dimethylpyrrole complex (**3**) (201 mg, 0.3 mmol) was dissolved in acrylonitrile (0.5 g, 9.42 mmol), the solution was allowed to stand for 30 min and then added to ether (40 mL), affording 180 mg (83%) of a tan precipitate. This product was found to be a 5:1 mixture of isomers by ¹H NMR. Major (*exo*) isomer (**19a**):⁵⁸ ¹H NMR (CD₃CN) δ 4.01 (br s, 3H, *trans*-NH₃), 3.33 (br s, 12H, *cis*-NH₃), 3.18 (d, *J* = 5.5 Hz, 1H), 3.11 (d, *J* = 5.5 Hz, 1H), 2.90 (dd, *J* = 8.5, 4.7 Hz, 1H, H₂), 2.29 (dd, *J* = 12.2, 8.5 Hz, 1H, H_{3α}), 1.76 (br s, 1H, NH), 1.65 (dd, *J* = 12.2, 4.7 Hz, 1H, H_{3β}), 1.51 (s, 3H, CH₃), 1.37 (s, 3H, CH₃); ¹³C NMR (CD₃CN) δ 122.0 (CN), 74.5 (C), 71.8 (C), 58.1 (CH), 56.7 (CH), 48.3 (CH₂), 41.3 (CH), 18.1 (CH₃), 16.7 (CH₃); *E*_{1/2} = 0.77 V. The tetraphenylborate salt was obtained following ion exchange chromatography. Anal. Calcd for C₅₇H₆₇N₇B₂Os·H₂O: C, 63.39; H, 6.44; N, 9.08. Found: C, 63.0; H, 6.05; N, 9.01.

[5β,6β-η²-[Os(NH₃)₅]-1,4-dimethyl-spiro(7-azabicyclo[2.2.1]hept-5-ene-2,3'-(1β)-dihydro-2-[3H]furanone)](OTf)₂ (22a). To a solution of the 2,5-dimethylpyrrole complex (**3**) (801 mg, 1.20 mmol) in CH₃CN (1 g) was added α-methylene-γ-butyrolactone (824 mg, 8.40 mmol). After 45 min, the solution was added to ether (50 mL), yielding 883 mg (96%) of an ivory-colored solid: ¹H NMR (CD₃CN) δ 4.30 (ddd, *J* = 13.2, 7.4, 4.2 Hz, 1H, CH₂O), 4.17 (ddd, *J* = 13.2, 8.6, 8.4 Hz, 1H, CH₂O), 4.02 (br s, 3H, *trans*-NH₃), 3.37 (br s, 13H, *cis*-NH₃ overlap with H₆), 3.26 (d, *J* = 5.4 Hz, 1H, H₅), 2.56 (ddd, *J* = 9.0, 8.4, 7.4 Hz, 1H), 2.27 (ddd, *J* = 9.0, 8.6, 4.2 Hz, 1H), 1.95 (d, *J* = 12.0 Hz, 1H), 1.86 (d, *J* = 12.0 Hz, 1H), 1.34 (s, 3H, CH₃), 1.27 (s, 3H, CH₃); ¹³C NMR (CD₃CN) δ 183.0 (C), 76.7 (C), 71.4 (C), 66.5 (CH₂), 59.9 (CH), 57.5 (C), 55.9 (CH₂), 53.4 (CH), 31.8 (CH₂), 18.7 (CH₃), 14.0 (CH₃). When the downfield olefinic ring proton resonance is irradiated in acetone-*d*₆, it generates a 12% NOE enhancement with one and a 6% NOE enhancement with the other diastereotopic methylene proton on C^{4'} of the spiro lactone ring; *E*_{pa} = 0.76 V. Anal.

(56) Methyl (*E*)-3-(3'-pyridyl)acrylate was prepared from the acid and methanol in 92% yield as described (Wenkert, E.; Halls, T. D. J.; Kunesch, G.; Orito, K.; Stephens, R. L.; Temple, W. A.; Yadav, J. S. *J. Am. Chem. Soc.* **1979**, *101*, 5370), except the use of benzene as a cosolvent proved to be unnecessary.

(57) Under the same concentrations in DMAc, the reaction was considerably faster (<2 h), but after precipitation the resulting product remained contaminated with small amounts (e.g. 5–10%) of this solvent. In this case the stereoselectivity of the reaction did not vary significantly (<5%) as a function of the solvent.

(58) This stereochemical assignment is based on the value of *J*_{H₂,H_{3α}} (*vide supra*).

Calcd for C₁₃H₃₀N₆O₈S₂F₆Os: C, 20.37; H, 3.94; N, 10.96. Found: C, 20.47; H, 4.09; N, 10.60.

[5β,6β-η²-[Os(NH₃)₅]-4,7-dihydro-4β,7β-imino-3α,7α-propano-1H,3H-isobenzofuran-1,3-dione](OTf)₂ (23a). Acetonitrile (0.2 g) was added to a mixture of 1,2-cyclopentenedicarboxylic acid anhydride (35 mg, 0.25 mmol) and complex **3** (67 mg, 0.1 mmol). After 20 min, the mixture was diluted with acetonitrile (1 mL) and added to ether (20 mL), yielding a tan solid (68 mg, 84%).⁵⁹ ¹H NMR (DMSO-*d*₆) δ 4.34 (br s, 3H, *trans*-NH₃), 3.57 (br s, 12H, *cis*-NH₃), 3.40 (s, 2H, H₅, H₆), 2.92 (br s, 1H, NH), 2.14 (m, 3H), 1.8 (m, 3H), 1.26 (s, 6H, 2CH₃); ¹³C NMR (DMSO-*d*₆) δ 173.7 (CO), 76.4 (C), 74.8 (C), 53.2 (CH), 32.0 (CH₂), 30.1 (CH₂), 14.9 (CH₃); *E*_{1/2} = 0.85 V. The recrystallized material was purified further by ion exchange chromatography and isolated as the tetraphenylborate dihydrate salt; IR (KBr) 1858, 1827, 1769 cm⁻¹. Anal. Calcd for C₆₁H₇₀N₆O₃B₂Os·2H₂O: C, 61.93; H, 6.30; N, 7.10. Found: C, 62.29; H, 6.17; N, 7.06.

[3β,4β-η²-[Os(NH₃)₅]-2α-(*N*-phenylsuccinimid-3'-yl)-2H-pyrrole](OTf)₂ (27). This compound was formed in the attempted purification of compound **12b** and was also prepared in the following manner: A solution of complex **12b** (89 mg, 0.10 mmol) in acetone (0.4 g) was treated with a solution of triflic acid (17 mg, 0.11 mmol) in a mixture of water (0.4 g) and acetone (0.2 g). After 7 min, the reaction mixture was added to ether (40 mL), affording 85 mg of a purple solid. A solution of this material in acetone (0.4 g) was treated with a solution of Proton Sponge (24 mg, 0.11 mmol) in acetone (0.2 g), and after 10 min the solution added to methylene chloride (50 mL), affording 45 mg (63%) of the title product: ¹H NMR (CD₃CN) δ 8.17 (s, 1H, H₅), 7.5–7.2 (m, 5H, Ph), 4.93 (d, *J* = 4.8 Hz, 1H), 4.40 (d, *J* = 4.8 Hz, 1H), 4.31 (br s, 3H, *trans*-NH₃), 3.82 (ddd, *J* = 9.2, 4.6, 2.5 Hz, 1H, H_{3'}), 3.09 (d, *J* = 2.5 Hz, 1H, H₂), 2.96 (br s, 12 H, *cis*-NH₃), 2.71 (dd, *J* = 18.3, 9.2 Hz, 1H), 2.42 (dd, *J* = 18.3, 4.6 Hz, 1H). Compound **27** was isolated as a tetraphenylborate monohydrate salt following the attempted chromatography of **12b**. Anal. Calcd for C₆₂H₆₇N₇B₂Os·H₂O: C, 63.53; H, 5.93; N, 8.37. Found: C, 63.35; H, 5.99; N, 8.03.

[3β,4β-η²-[Os(NH₃)₅]-2β,5-dimethyl-2α-(1-[3'-pyridyl]-3-carbomethoxy-ethyl)-2H-pyrrole](OTf)₂ (29a). This compound was formed in the attempted purification of compound **14** and could also be prepared in the following manner: The cycloadduct complex **14a** (110 mg, 0.132 mmol) was dissolved in acetonitrile (0.5 g), treated with TBSOTf (69 mg, 0.261 mmol), and after 5 min quenched with water (69 mg, 3.83 mmol). After standing for 40 min the solution was made basic with excess Hünig's base (0.3 g) and added to methylene chloride (50 mL), affording 75 mg (68%) of a tan-brown powder: ¹H NMR (CD₃CN) δ 8.41 (s, 1H, H^{2'}), 8.35 (d, *J* = 3.6 Hz, 1H, H^{6'}), 7.69 (d, *J* = 7.5 Hz, 1H, H^{4'}), 7.23 (dd, *J* = 7.5, 3.6 Hz, 1H, H^{5'}), 4.68 (d, *J* = 4 Hz, 1H), 4.47 (d, *J* = 4 Hz, 1H), 4.42 (br s, 3H, *trans*-NH₃), 3.43 (s, 3H, CH₃), 3.4–3.0 (br s, m overlap, 14 H, *cis*-NH₃ + 2 × CH), 2.65 (dd, *J* = 15.6, 11.7 Hz, 1H), 1.83 (s, 3H, CH₃), 0.87 (s, 3H, CH₃); ¹³C NMR (CD₃CN) δ 180.2 (C, C₅), 172.7 (CO), 151.3 (CH), 147.4 (CH), 137.1 (CH), 136.7 (C, C_{3'}), 122.4 (CH), 79.0 (C, C₂), 63.8 (CH), 60.2 (CH), 51.0 (CH₃O), 50.4 (CH), 35.1 (CH₂), 19.4 (CH₃), 19.1 (CH₃). This compound was isolated as its tetraphenylborate monohydrate salt following the chromatography of **14a**. Anal. Calcd for C₆₃H₇₃N₇O₂B₂Os·H₂O: C, 63.58; H, 6.35; N, 8.24. Found: C, 63.64; H, 6.53; N, 8.16.

3α,4α,5,6,7α,7α-Hexahydro-2-phenyl-4β,7β-imino-1H-isolindole-1,3(2H)-dione (31a). The crude cycloadduct complex **8** (814 mg, 1.0 mmol) was protonated, oxidized (1 equiv DDQ),⁶⁰ and hydrogenated in methanol using 28 mol % of 10% Pd/C according to the general procedure described above. After 2 h, the reaction was complete. Workup B (eluent: 4:1 ether–methanol, 2% NH₄OH) afforded the title compound (95 mg, 39%) as a 5:1 mixture of *exo* and *endo* isomers. This material was recrystallized from ethyl acetate/petroleum ether,

(59) Under more concentrated conditions (e.g., 1 M in both reactants), the reaction was complete in less than 1 min by cyclic voltammetry, and the product crystallized on standing over the course of 15 min in 35–40% yield.

(60) Data for the protonated 7-azanorbornene **30a**: ¹H NMR (CD₃CN) δ 7.75 (br s, 1H, NH), 7.6–7.4 (m, 5H, ArH), 6.85 (br s, 1H, NH), 6.63 (s, 2H, H₅, H₆), 5.08 (s, 2H, H₁, H₄), 3.37 (s, 2H, H₂, H₃); ¹³C NMR (CD₃CN) δ 171.8 (CO), 134.4 (CH, C₅, C₆), 131.9 (C), 128.9 (2 × CH overlap), 126.8 (CH), 62.9 (CH, C₁, C₄), 44.9 (CH).

affording 42 mg (17%) of **31a** as colorless crystals (mp 206–209×a1C): ¹H NMR (CDCl₃) δ 7.5–7.3 (m, 5H, Ph), 4.15 (t, *J* = 2 Hz, 2H, H1, H4), 2.86 (s, 2H, H2, H3), 1.7 (m, 4H, 2 × CH₂), 1.54 (br s, 1H, NH); ¹³C NMR (CDCl₃) δ 177.3 (CO), 132.1 (C), 129.0 (CH), 128.5 (CH), 126.5 (CH), 59.9 (CH, C1, C4), 49.0 (CH, C2, C3), 29.5 (CH₂). Anal. Calcd for C₁₄H₁₄N₂O₂: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.29; H, 5.90; N, 11.74.

3α,4α,5,6,7α,7β-Hexahydro-2-phenyl-4β,7β-imino-1H-isoindole-1,3(2H)-dione (31b). Compound **8b** (0.82 g, 1.01 mmol) was treated as described for **8a** using 1 equiv of DDQ. The hydrogenation was complete in 1.5 h in acetonitrile using 25 mol % of 10% Pd/C. The crude material (149 mg) obtained using workup A was chromatographed on silica gel (ether and then 10% NH₃–CH₃OH in ether as the eluent), affording the product (99 mg, 41%). Recrystallization from ethyl acetate/petroleum ether afforded analytically pure material (mp 137–138 °C): ¹H NMR δ 7.6–7.2 (m, 5H, Ph), 4.18 (br s, 2H, H1 and H4), 3.64 (br s, 1H, NH), 3.41 (br s, 2H, H2 and H3), 1.8–1.6 (m, 4H); ¹³C NMR (CDCl₃) δ 175.9 (C), 132.0 (C), 129.7 (CH), 129.3 (CH), 126.9 (CH), 59.6 (CH), 51.5 (CH), 26.5 (CH₂). Anal. Calcd for C₁₄H₁₄N₂O₂: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.42; H, 5.75; N, 11.32.

8-Ethyl-3α,4,5,6,7α,7β-hexahydro-2-phenyl-4β,7β-imino-1H-isoindole-1,3(2H)-dione (32a). The procedure used in the synthesis of compound **31a** was repeated on a 1.0 mmol scale using acetonitrile instead of methanol as the hydrogenation solvent. After 18 h, the crude product was isolated using method A, and chromatographed on silica gel (3.5 × 13 cm column). Elution with ether yielded 56 mg (21%) of **32a** (*R*_f 0.8; ether containing ~1% NH₄OH). Further elution with 1:3:30 NH₄OH/methanol/ether yielded compound **31a** (69 mg, 29%) (*R*_f 0.2; ether containing ~1% NH₄OH). The first fraction was treated with decolorizing charcoal, filtered, and evaporated, and the residue was recrystallized from ethyl acetate/petroleum ether, affording colorless crystals of **32a** (21 mg, 8%): mp 126–128 °C; ¹H NMR (CDCl₃) δ 7.5–7.25 (m, 5H, Ph), 3.82 (t, *J* = 2.2 Hz, 2H, H1, H4), 2.80 (s, 2H, H2, H3), 2.37 (q, *J* = 7.2 Hz, 2H, NCH₂), 1.93 (m, 2H, H5_β, H6_β), 1.51 (m, 2H, H5_α, H6_α), 1.04 (t, *J* = 7.2 Hz, 3H, CH₃); ¹³C NMR (CDCl₃) δ 177.8 (CO), 132.4 (C, C1'), 129.1 (CH), 128.5 (CH), 126.7 (CH), 62.6 (CH, C1, C4), 49.5 (CH, C2, C3), 40.4 (CH₂N), 25.0 (CH₂), 14.5 (CH₃). Anal. Calcd for C₁₆H₁₈N₂O₂: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.49; H, 7.03; N, 10.09.

2β,3α-Bis(carbomethoxy)-7-azabicyclo[2.2.1]heptane (33). To a solution of cycloadduct **15** (235 mg, 0.30 mmol) and triflic acid (73 mg, 0.49 mmol) in acetonitrile (0.57 g) was added a solution of DDQ (69 mg, 0.30 mmol) in acetonitrile (0.56 g). The acetonitrile was evaporated, and the hydrogenation was carried out in methanol as described in the synthesis of compound **31a**. Purification by preparative TLC (1:1:8 methanol/HMDS/methylene chloride) afforded 27 mg (42%) of the title product as a clear oil. ¹H NMR (CDCl₃) δ 3.95 (t, *J* = 4.5 Hz, 1H, H4), 3.84 (d, *J* = 4.8 Hz, 1H, H1), 3.70 (s, 3H, CH₃O), 3.695 (s, 3H, CH₃O), 3.22 (td, *J* = 4.8, 1.8 Hz, 1H, H3), 3.03 (d, *J* = 4.8 Hz, 1H, H2), 2.55 (br s, 1H, NH), 1.8–1.3 (overlapping m, 4H); ¹³C NMR (CDCl₃) δ 174.8 (CO), 172.1 (CO), 61.8 (CH, C1 or C4), 59.1 (CH, C4 or C1), 52.3 (CH), 52.1 (CH₃, CH₃O), 52.0 (CH₃, CH₃O), 50.1 (CH), 28.7 (CH₂), 24.9 (CH₂).²⁷

2-(Carbomethoxy)-7-methyl-7-azabicyclo[2.2.1]heptane (34). A solution of the 1-methylpyrrole complex (**2**) (6.323 g, 0.966 mmol) in methyl acrylate (20 mL) and DMAc (3 mL) was allowed to stand for 9 h. The solution was added to methylene chloride (300 mL), affording **20** (6.197 g, 84%) as a 1:1 mixture of diastereomers. The oxidation and hydrogenation steps were done as described in the synthesis of **35** (workup B), affording the isomers in a combined yield of 914 mg (65% from **20**, 55% overall) after chromatographic separation (silica gel, 5% NH₃–methanol/ether). *Exo* isomer (**34a**): *R*_f 0.76; ¹H NMR (CDCl₃) δ 3.66 (s, 3H, CH₃O), 3.62 (d, *J* = 4.2 Hz, 1H, H1), 3.30 (t, *J* = 4.0 Hz, 1H, H4), 2.40 (dd, *J* = 9.6, 5.4 Hz, 1H, H2), 2.21 (s, 3H, CH₃N), 2.18 (m, 1H), 1.86 (m, 2H), 1.57 (dd, *J* = 12.6, 9.6 Hz, 1H, H3_α), 1.33 (m, 2H); ¹³C NMR (CDCl₃) δ 174.6 (CO), 64.2 (CH), 61.1 (CH), 51.9 (CH₃, CH₃O), 47.4 (CH, C2), 34.5 (CH₃, CH₃N), 33.3 (CH₂), 26.7 (CH₂), 26.2 (CH₂). *Endo* isomer (**34b**): *R*_f 0.62; ¹H NMR (CDCl₃) δ 3.65 (s, 3H, CH₃O), 3.44 (t, *J* = 4.5 Hz, 1H, H1 or H4), 3.21 (t, *J* = 4.5 Hz, 1H, H4 or H1), 3.08 (m, 1H, H2), 2.26 (s, 3H, CH₃N), 1.95 (m, 1H), 1.75 (m, overlap, 3H), 1.36 (m, 2H); ¹³C NMR (CDCl₃,

50×a1C) δ 174.3 (C, CO), 64.1 (CH, C1 or C4), 62.1 (CH, C4 or C1), 51.4 (CH₃, CH₃O), 45.2 (CH, C2), 34.4 (CH₃, CH₃N), 30.6 (CH₂), 28.0 (CH₂), 24.2 (CH₂). The picrate salt (both isomers combined) was crystallized from wet ethanol (mp 102–108 °C). Anal. Calcd for C₁₅H₁₈N₄O₉: C, 45.23; H, 4.55; N, 14.07. Found: C, 45.42; H, 4.59; N, 14.10.

2-Cyano-7-methyl-7-azabicyclo[2.2.1]heptane (35). The following was done on the benchtop: A 50-mL, three-necked flask with a thermometer, septum, and nitrogen inlet (connected to a bubbler) was charged with Os(NH₃)₅(OTf)₃ (7.226 g, 10.0 mmol) and activated magnesium (3 g). The vessel was thoroughly flushed with nitrogen for 10 min and then degassed 1-methylpyrrole (8 mL) and DMAc (6 mL) were introduced via syringe in that order. The mixture was shaken to help dissolve the osmium, then stirred, and cooled in a water bath (to maintain a temperature of 25–30 °C) for 45 min. Degassed acrylonitrile (8 mL) was added by syringe, and the reaction was allowed to proceed without agitation for an additional 3 h. The mixture containing the air-stable cycloadduct complex **20** was filtered through a 150-mL medium fritted funnel, using ~20 mL acetone in small portions to wash the magnesium filter cake. The filtrate was added to methylene chloride (600 mL), the mixture was diluted with ether (400 mL), and the resulting precipitate was filtered, washed with methylene chloride (3 × 30 mL) and ether (2 × 30 mL), and then dried under a blanket of nitrogen. The product (**20**) was obtained as a tan solid (7.23 g of material containing ~15 mol % DMAc by ¹H NMR integration). Compound **20** was dissolved in acetonitrile (15 mL) and treated at 0–5 °C (ice bath) with a solution of triflic acid (2.5 mL) in acetonitrile (5 mL). The resulting protonated complex was treated with a solution of DDQ (2.35 g, 10.35 mmol) in acetonitrile (5 mL). The reaction was allowed to stand at this temperature for 1 h, while a solid precipitated from solution. The slurry was filtered, and the cake was washed with acetonitrile (60 mL) in small portions and dried, leaving 5.86 g of an osmium-containing solid. The filtrate was treated with 10% Pd/C (2.34 g, ~20 mol % Pd) and stirred under hydrogen for 1 h. (An aliquot was evaporated, and the residue taken up in CD₃CN to check the progress of the reaction.) The mixture was filtered through Celite, the solvent was evaporated, and the residue was made basic with 15% NH₃–methanol (30 mL). The mixture was treated with ether (300 mL), and an additional quantity of precipitated salts removed (3.25 g). The solvent was evaporated, and the residue was chromatographed on silica gel (3 × 10 cm column, gradient elution of ether containing up to 7% NH₃–methanol), yielding 466 mg of **35a** and 447 mg of **35b** (combined overall yield is 67%) (Analytical TLC using 1:1:8 HMDS/methanol/methylene chloride). *Exo* isomer (**35a**): *R*_f 0.71; ¹H NMR (CDCl₃) δ 3.53 (d, *J* = 3.3 Hz, 1H, H1), 3.37 (t, *J* = 3.8 Hz, 1H, H4), 2.44 (dd, *J* = 9.3, 5.1 Hz, 1H, H2), 2.36 (s, 3H, CH₃N), 2.1 (m, 1H), 1.83 (m, 2H), 1.75 (dd, *J* = 12.6, 9.3 Hz, 1H, H3_α), 1.3 (m, 2H); ¹³C NMR (CDCl₃) δ 122.7 (CN), 65.5 (CH), 60.8 (CH), 35.7 (CH₂), 35.3 (CH₃), 31.9 (CH), 27.5 (CH₂), 26.9 (CH₂). *Endo* isomer (**35b**): *R*_f 0.55; ¹H NMR (CDCl₃) δ 3.44 (t, *J* = 4.5 Hz, 1H, H1 or H4), 3.29 (t, *J* = 4.5 Hz, 1H, H4 or H1), 2.92 (dtd [11 line pattern], *J* = 12, ~4.8, 1.8 Hz, 1H, H2), 2.26 (s, m overlap, 4H, CH₃N and H3_β), 2.0–1.8 (m, 3H), 1.57 (dd, *J* = 12.3, 5.1 Hz, 1H, H3_α), 1.45 (m, 1H); ¹³C NMR (CDCl₃, 50 °C) δ 121.7 (CN), 63.8 (CH), 61.6 (CH), 34.6 (CH₂), 34.4 (CH₃, CH₃N), 29.2 (CH, C2), 27.9 (CH₂), 24.1 (CH₂). The picrate salt (both isomers combined) was crystallized from ethanol (mp 218–224 °C). Anal. Calcd for C₁₄H₁₅N₃O₇: C, 46.03; H, 4.14; N, 19.17. Found: C, 45.85; H, 4.08; N, 18.88.

1,4-Dimethyl-2β-(carbomethoxy)-7-azabicyclo[2.2.1]heptane (36). The cycloadduct (**18**) (2.611 g, 3.46 mmol) was dissolved in acetonitrile (5 mL) and protonated with triflic acid (1.557 g, 10.4 mmol) in acetonitrile (2.5 mL). After 5 min, a solution of DDQ (393 mg, 1.73 mmol) in acetonitrile (2.5 mL) was added. After 30 min, the solution was concentrated under reduced pressure, the slurry filtered, and the filter cake was washed with acetonitrile (4 × 5 mL), leaving 1.658 g of osmium salts. The filtrate⁶¹ was treated with 10% Pd/C (733 mg,

(61) An aliquot of the filtrate was evaporated and analyzed in CD₃CN, showing the 7-azanorbornene salt: ¹H NMR (CD₃CN) δ 6.33 (d, *J* = 6 Hz, 1H), 6.20 (d, *J* = 6 Hz, 1H), 3.75 (s, 3H, CH₃O), 2.80 (t, *J* = 6.3 Hz, 1H), 2.08 (m, 2H), 1.72 (s, 3H, CH₃), 1.72 (s, 3H, CH₃); ¹³C NMR (CD₃CN) δ 175.0 (CO), 139.0 (CH), 136.2 (CH), 74.6 (C), 72.2 (C), 53.4 (CH₃, CH₃O), 46.4 (CH), 37.7 (CH₂), 16.3 (CH₃), 14.3 (CH₃).

20 mol %) and reduced over 1 atm hydrogen for 12 h (an aliquot taken after 30 min showed the reaction was ~50% complete). Workup B afforded 0.513 g of a black syrup containing a 92:8 mixture of *exo/endo* isomers. This oil was chromatographed on neutral alumina (2.5 × 22 cm column) using methylene chloride, affording 382 mg (60%) of **36a** (R_f 0.7 on TLC using 1:10 NH₃-ethanol(8%)/methylene chloride) containing ~4% of the *endo* isomer. Data for **36a**: ¹H NMR data has been reported (ref 13c); ¹³C NMR (CDCl₃) δ 176.5 (CO), 67.7 (C), 63.4 (C), 53.0 (CH), 51.3 (CH₃, CH₃O), 44.0 (CH₂), 38.3 (CH₂), 36.7 (CH₂), 20.5 (CH₃), 18.3 (CH₃). This compound was purified further by crystallization of the picrate salt from anhydrous ethanol: mp 171–173 °C. Anal. Calcd for C₁₆H₂₀N₄O₉: C, 46.60; H, 4.89; N, 13.59. Found: C, 46.90; H, 4.97; N, 13.50.

1,4-Dimethyl-2β-(3'-pyridyl)-3β-carbomethoxy-7-azabicyclo[2.2.1]heptane (37a). Compound **14** (189 mg, 0.227 mmol) was dissolved in acetonitrile (3 g), protonated with triflic acid (157 mg, 1.05 mmol), and added to a solution of DDQ (32 mg, 0.141 mmol) in acetonitrile (1 g). The acetonitrile was evaporated,⁶² and the solid residue was dissolved in methanol (4 g) and hydrogenated under 1 atm H₂ and 10% Pd/C (0.15 g, 60 mol %) for 16 h. Workup A gave 40 mg of resin, that after preparative TLC (1:1:10 methanol/HMDS/methylene chloride) afforded **37a** (24 mg, 41%; R_f 0.79) and **37b** (3 mg, 5%; R_f 0.63). Data for **37a**: ¹H NMR (CDCl₃) δ 8.43 (d, J = 4.5 Hz, 1H, H6'), 8.37 (s, 1H, H2'), 7.66 (d, J = 7.8 Hz, H4'), 7.18 (dd, J = 7.8, 4.5 Hz, 1H, H5'), 3.38 (d, J = 9.6 Hz, 1H), 3.18 (d, J = 9.6 Hz, 1H), 3.09 (s, 3H, CH₃O), 1.70 (m, 5H, 2 × CH₂ + NH), 1.57 (s, 3H, CH₃), 1.14 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 171.5 (CO), 151.3 (CH), 148.1 (CH), 137.0 (CH), 134.7 (C, C3'), 122.3 (CH), 66.5 (C), 65.2 (C), 60.6 (CH), 55.8 (CH), 50.7 (CH₃O), 41.0 (CH₂), 39.0 (CH₂), 19.0 (CH₃), 18.4 (CH₃). The bis-picrate salt was crystallized from ethanol (mp 206.5–208.5 °C). Anal. Calcd for C₂₇H₂₆N₈O₁₆: C, 45.13; H, 3.65; N, 15.59. Found: C, 45.13; H, 3.89; N, 15.41.

Partial characterization of **37b**: ¹H NMR (CDCl₃) δ 8.58 (d, J = 4.2 Hz, 1H, H6'), 8.42 (s, 1H, H2'), 7.46 (d, J = 8.1 Hz, 1H, H4'), 7.31 (dd, J = 8.1, 4.2 Hz, 1H, H5'), 3.89 (d, J = 12 Hz, 1H), 3.71 (d, J = 12 Hz, 1H), 3.38 (s, 3H, CH₃O), 2.94 (m, 1H), 2.1 (m, 1H), 2.0–1.9 (m, 3H), 1.77 (s, 3H, CH₃), 1.52 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 170.9, 151.0, 149.5, 136.2, 131.8, 123.5, 71.6, 69.8, 52.9, 51.9, 51.4, 30.3, 30.1, 19.7, 19.1; mass spectrum (EI) m/e 261 (M + 1), 97.

1,4-Dimethyl-2α-(3'-pyridyl)-3β-carbomethoxy-7-azabicyclo[2.2.1]heptane (38a) and its β-Pyridyl-α-carbomethoxy isomer (38b). The procedure described for the decomplexation of **18** was followed exactly for **17**, yielding a chromatographically-inseparable 94:6 mixture of **38a** to **38b** (1:10 NH₃ (8%) in ethanol/methylene chloride; R_f 0.45) in 69% yield. For **38a**: ¹H NMR (CDCl₃) δ 8.45 (m, 2H, H2' and H6' overlap), 7.49 (dt, J = 7.8, 1.5 Hz, 1H, H4'), 7.23 (dd, J = 7.8, 4.8 Hz, 1H, H5'), 3.64 (s, 3H, CH₃O), 3.29 (dd, J = 5.9, 2.1 Hz, 1H, H2), 2.95 (d, J = 5.9 Hz, 1H, H3), 2.62 (br s, 1H, NH), 1.85–1.6 (m, 2H, CH₂'s), 1.5 (m, 1H), 1.35 (m, 1H), 1.29 (s, 3H, CH₃), 1.26 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 175.7 (CO), 149.8 (CH), 148.2 (CH), 135.3 (CH), 134.1 (C), 123.1 (CH), 67.6 (2 × C overlap), 58.7 (CH), 58.3 (CH), 51.7 (CH₃O), 38.6 (CH₂), 30.3 (CH₂), 19.3 (CH₃), 18.7 (CH₃).

(62) The residue was analyzed by ¹H NMR (CD₃CN); diagnostic resonances of protonated 7-azanorbornene: δ 6.64 (d, J = 6 Hz, 1H), 6.38 (d, J = 6 Hz, 1H), 4.0 (d, J = 9 Hz, 1H), 3.50 (d, J = 9 Hz, 1H).

Diagnostic features of **38b**: δ 3.36 (d, J = 6 Hz, H2), 2.8 (dd, J = 6, 2 Hz, H3). The bis-picrate salt of **38a** was crystallized from ethanol (mp 204–205 °C). Anal. Calcd for C₂₇H₂₆N₈O₁₆: C, 45.13; H, 3.65; N, 15.59. Found: C, 45.29; H, 3.83; N, 15.49.

{5β,6β-η²-[Os(NH₃)₅]-1,4-dimethyl-2β-(hydroxymethyl)-7-azabicyclo-[2.2.1]hept-5-ene}(OTf)₂ (39). The acrylate cycloadduct (**16**) (730 mg, 0.967 mmol) was dissolved in lithium 9BBN-H (1M in THF; 2.0 g, 2.18 mmol). After 45 min, the reaction was quenched with water (0.1 g) and added to ether (100 mL), affording 627 mg (89%) of **27** as an ivory-white solid: ¹H NMR (CD₃CN) δ 3.98 (br s, *trans*-NH₃), 3.6 (m, 2H, CH₂OH), 3.42 (br s, 12H, *cis*-NH₃), 3.1 (m, 2H), 2.95 (br s, 1H, NH), 1.9 (m, 1H), 1.6 (m, 1H), 1.3 (s, 6H, 2 × CH₃), 1.3 (m, overlap, 1H). ¹³C NMR (CD₃CN) δ 73.0 (C), 70.3 (C), 62.5 (CH₂), 60.2 (CH), 60.0 (CH), 51.2 (CH), 45.3 (CH₂), 19.1 (CH₃), 16.0 (CH₃); E = 0.71 V. Anal. Calcd for C₁₁H₃₀N₆O₇S₂F₆Os: C, 18.18; H, 4.16; N, 11.57. Found: C, 18.57; H, 4.34; N, 10.88.⁵¹

1,4-Dimethyl-2β-(hydroxymethyl)-7-azabicyclo[2.2.1]hept-5-ene (40). A solution of the reduced complex (**39**) (727 mg 1.0 mmol) in acetonitrile (2 g) was protonated with excess triflic acid (250 mg, 1.67 mmol) and treated at –10 °C with a cold solution of ceric ammonium nitrate (560 mg, 1.02 mmol) and triflic acid (560 mg, 3.73 mmol) in acetonitrile (2 g). Workup A afforded 147 mg of brown oil. The crude material was purified by silica gel column chromatography using 1:10 of 15 wt % NH₃ in methanol/CH₂Cl₂ (R_f 0.5), affording 62 mg (41%): ¹H NMR (CDCl₃) δ 6.31 (d, J = 5.3 Hz, 1H), 6.09 (d, J = 5.3 Hz, 1H), 3.99 (dd, J = 10.3, 2.1 Hz, 1H), 3.67 (dd, J = 10.3, 2.1, 1H), 3.6–2.8 (br, *2H, OH and NH), 1.4–1.8 (m, 3H), 1.48 (s, 3H), 1.47 (s, 3H); ¹³C NMR (CDCl₃) δ 145.2 (CH), 141.5 (CH), 69.9 (C), 67.0 (C), 61.5 (CH₂), 41.7 (CH), 37.0 (CH₂), 18.9 (CH₃), 15.7 (CH₃). This material was further characterized by conversion to the picrate salt, which was recrystallized from ethanol (mp 186–188 °C). Anal. Calcd for C₁₅H₁₈N₄O₈: C, 47.12; H, 4.75; N, 14.65. Found: C, 46.96; H, 4.52; N, 14.66.

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Supplementary Material Available: Tables of experimental details, atomic position parameters, thermal parameters, bond distances and angles, and ORTEP drawings for **8a**, **13a**, and **22a** (27 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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