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Stereodefined Tandem Addition Reactions of η^2-Arenes: A Versatile Route to Functionalized Cyclohexenes

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Abstract: A series of anisoles are complexed by pentaammineosmium(II), and the resulting *5,6*-η^2-anisole complexes are treated with activated olefins or acetals in the presence of triflic acid to form 4*H*-anisolium complexes. These intermediates are capable of undergoing inter- or intramolecular nucleophilic addition reactions at C3, and 2-methoxy-1,3-cyclohexadiene complexes are formed. These complexes are readily converted into functionalized cyclohexenones, cyclohexadienes, and cyclohexenes. When $BF_3{\cdot}OEt_2$ is used, it is possible to form a 4*H*-anisolium complex with a pendent boron enolate, which can ultimately undergo intramolecular addition to C1 to form the corresponding [4 + 2] cycloadduct. For cases in which an activated alkyne is added to a C4-alkylated anisole, a migration of the vinyl group occurs, leading to 4-methyl-3-vinylanisoles.

Introduction

Arenes are useful precursors to highly substituted alicyclic compounds as they constitute a cyclic array of fully unsaturated carbons.[1,2] Their aromatic nature makes them highly stable compared to other polyolefinic systems, and readily derivatized through both electrophilic and nucleophilic substitution reactions. However, arenes are much less susceptible to reactions with electrophiles than olefins, and when they do react, the resulting arenium cation usually deprotonates to reform an aromatic system. Methodologies that allow for the selective conversion of an arene to a diene such as the Birch reduction[3,4] or the enzymatic dihydroxylation of arenes[5] have become powerful tools of the synthetic chemist.

Complexation of an arene by an electron-deficient transition metal center greatly modifies the arene reactivity, and this methodology has been the subject of an intense research effort over the past three decades.[6] Typically, the arene is η^6-coordinated to a metal center such as $Cr(CO)_3$,[7] $Mn(CO)_3^+$,[8,9] $Fe(ArH)^{2+}$,[10,11] or $Ru(Cp^*)^+$,[12,13] and coordination activates the arene toward nucleophilic addition. The resulting cyclohexadienyl complex may be oxidized to provide a substituted arene or in selected cases treated with Brønsted acid or other electrophiles to provide disubstituted 1,3-cyclohexadienes. This methodology has been applied to numerous organic syntheses.[7] In a complementary approach, the metal center $Os(NH_3)_5^{2+}$

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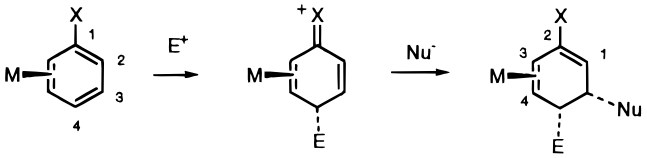
forms η^2-coordinate complexes with aromatic molecules and activates them toward electrophilic addition reactions.[14] Our studies concerning electrophilic addition reactions with η^2-coordinated phenols[15] and anilines[16] illustrate the ease with which electrophiles can be added to C4 of an arene. However, the resulting η^2-4*H*-phenol and 4*H*-anilinium complexes are unexpectedly resistant to nucleophilic addition at C3. To develop a more general route to functionalized dienes from arenes, we have shifted our attention to η^2-anisole osmium complexes, from which the corresponding 4*H*-anisolium species were anticipated to be considerably more reactive than their 4*H*-anilinium or 2,5-dienone counterparts.



Experimental Section

The synthesis and characterization of the complexes **1**−**3**[17] and **5**−**7** and **22**−**24**[18] have been previously reported. All complexes have been isolated and characterized as triflate salts unless otherwise indicated. In some cases, the osmium salts were purified by ion exchange chromatography (Sephadex SP) and analyzed by combustion analysis as their tetraphenylborate salts. Triflate salts were used directly as isolated for all synthetic procedures.

Abbreviations: DDQ = 2,3-dichloro-5,6-dicyanobenzoquinone; DME = 1,2-dimethoxyethane; DMA = *N*,*N*-dimethylacetamide; TBAC = tetra-*n*-butylammonium cyanoborohydride; TBS = *tert*-butyldimethylsilyl; $OTf^- = CF_3SO_3^-$ (triflate); MMTP = 1-methoxy-2-methyl-1-(trimethylsiloxy)propene; TBAH = tetra-*n*-butylammonium hexafluorophosphate; MVK = methyl vinyl ketone; CAN = $Ce(NO_3)_6(NH_4)_2$.

Selected Examples of Compound Syntheses. [Os(NH$_3$)$_5$(3,4-η^2-2-methoxy-6-(1-carbomethoxy-1-methylethyl)-1,3-cyclohexadiene)](OTf)$_2$ (9). Complex 1 (253 mg, 0.37 mmol) was dissolved in CH_3CN (5.0 g), and the solution was cooled to −40 °C. Cold triflic acid (168 mg, 1.12 mmol) in CH_3CN (2.5 g) was added, and the solution immediately turned purple. After ∼20 min, cold MMTP (645 mg, 3.71 mmol) dissolved in CH_3CN (2.7 g) was added, and the solution was allowed to stand for ∼1.5 h. 2,6-Lutidine (625 mg) was added, and the solution was precipitated into ∼200 mL of a 1:1 hexanes/CH_2Cl_2 solution. The resulting slurry was filtered and rinsed with CH_2Cl_2 and then hexanes, and the product was isolated as a white solid (266 mg, 92%). ^{1}H NMR spectra revealed formation of a single diastereomer. ^{1}H NMR (CD_3CN): δ 4.49 (d, 1H, J = 4.5 Hz), 4.14 (br s, 3H, *trans*-NH_3), 3.78 (d, 1H, J = 8.1 Hz), 3.61 (s, 3H), 3.58 (m, 1H), 3.49 (s, 3H), 3.02 (br s, 12 H, *cis*-NH_3), 2.45 (m, 1H), 1.92 (m, 1H), 1.55 (m, 1H), 1.15 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (CD_3CN): δ 178.3 (C), 161.4 (C), 89.9 (CH), 54.2 (CH_3), 51.7 (CH_3), 48.0 (C), 45.4 (CH), 44.6 (CH), 41.7 (CH), 25.7 (CH_2), 22.3 (CH_3), 21.0 (CH_3). Electrochemistry (TBAH, CH_3CN, 100 mV/s): $E_{p,a}$ = 0.66 V.

[Os(NH$_3$)$_5$(3,4-η^2-2-methoxy-6-(2-(1-methylpyrrolyl))-1,3-cyclohexadiene)](OTf)$_2$ (11). Complex **1** (253 mg, 0.37 mmol) was dissolved in CH_3CN (4.3 g), and the solution was cooled to −40 °C. Cold triflic acid (172 mg, 1.15 mmol) dissolved in CH_3CN (2.5 g) was added, and the solution immediately turned purple. After ∼20 min, a cold solution of *N*-methylpyrrole (306 mg, 3.78 mmol) in CH_3CN (2.8 g) was added, and the solution was allowed to stand at −40 °C for ∼18 h. After this time, 2,6-lutidine (204 mg, 1.91 mmol) was added, and the solution was added to ∼100 mL of a 1:1 hexanes/CH_2Cl_2 solution. The slurry was filtered, and the product was isolated as an off-white powder (259 mg, 92%). ^{1}H NMR (acetone-d_6): δ 6.51 (t, J = 2.1 Hz, 1H), 5.88 (m, 2H), 4.79 (br s, 3H, *cis*-NH_3), 4.11 (d, J = 8.7 Hz, 1H), 3.85−3.89 (m, 1H), 3.68 (br s, 12H, *trans*-NH_3), 3.59 (s, 3H), 3.56 (s, 3H), 2.88−2.97 (m, 1H), 2.72−2.85 (m, 1H), 2.18 (dq, J = 3.0, 15.0 Hz, 1H). ^{13}C NMR (acetone-d_6): δ 161.6 (C), 138.3 (C), 122.3 (CH), 107.2 (CH), 106.6 (CH), 93.2 (CH), 55.0 (CH_3), 46.4 (CH), 44.8 (CH), 34.3 (CH_3), 32.9 (CH_2), 32.8 (CH). Electrochemistry (TBAH, CH_3CN, 100 mV/s): $E_{p,a}$ = 1.40 V, $E_{1/2}$ = 0.67 V.

[Os(NH$_3$)$_5$(2,3-η^2-(methyl 5-(1-carbomethoxy-1-methylethyl)-2-cyclohexen -1-onium)](OTf)$_3$ (13). Complex **9** (220 mg, 0.28 mmol) was dissolved in CH_3CN (1.6 g), and the solution was cooled to −40 °C. A cold solution of triflic acid (62 mg, 0.41 mmol) in CH_3CN (398 mg) was added, and the solution color immediately darkened. After ∼10 min, the solution was added to ∼100 mL stirring ether, and the slurry was filtered. The resulting filter cake was rinsed with ether and dried in vacuo to yield the product (**13**, 240 mg, 92%) as a purple powder. ^{1}H NMR (CD_3CN): δ 5.76−5.79 (m, 1H), 5.13 (d, J = 7.2 Hz, 1H), 5.00 (br s, 3H, *trans*-NH_3), 4.29 (s, 3H), 3.84 (br s, 12H, *cis*-NH_3), 3.66 (s, 3H), 3.08 (d, J = 23.7 Hz, 1H), 2.77−2.87 (m, 2H), 1.99−2.02 (m, 1H), 1.00 (m, 1H), 1.12(s, 3H), 1.10(s, 3H). ^{13}C NMR (CD_3CN): δ 214.5 (C), 178.0 (C), 64.0 (CH_3), 62.7 (CH), 54.1 (CH), 53.3 (CH_3), 46.0 (C), 38.4 (CH), 32.0 (CH_2), 27.6 (CH_2), 23.9 (CH_3), 22.8 (CH_3).

[Os(NH$_3$)$_5$(2,3-η^2-5-(1-carbomethoxy-1-methylethyl)-2-cyclohexen-1-one)](OTf)$_2$ (14). Compound **13** (60 mg, 0.65 mmol) was dissolved in CH_3CN and treated with a drop of H_2O (18 mg, 1.2 mmol). The reaction mixture immediately changed color to light orange. Upon addition to ether (∼40 mL) a light tan precipitate was collected, washed with ether, and dried in vacuo (42 mg, 85%). ^{1}H NMR (CD_3CN): δ 4.65 (br s, 3H, *trans*-NH_3), 3.95 (m, 1H), 3.85 (d, 1H, J = 7.5 Hz), 3.51 (s, 3H), 3.35 (br s, 12 H, *cis*-NH_3), 2.61 (m, 1H), 1.75−2.0 (m, 3H), 1.40 (m, 1H), 1.12 (s, 3H), 1.10 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 214.2 (C), 177.9 (C), 52.5 (CH_3), 51.6 (CH), 50.0 (CH), 45.7 (CH), 45.2 (C), 38.1 (CH_2), 26.7 (CH_2), 23.2 (2 × CH_3). Electrochemistry (TBAH, CH_3CN, 100 mV/s): $E_{p,a}$ = 0.97 V.

5-(1-Carbomethoxy-1-methylethyl)-2-cyclohexen-1-one (15). Compound **14** (214 mg, 0.23 mmol) was dissolved in water (3.5 g). After ∼15 min, ether (5 mL) was added followed by CAN (256 mg, 0.47 mmol) in water (1.5 g). The mixture was allowed to stir for ∼15 min, and the aqueous phase was separated off. The organic phase was washed with 10 mL of brine solution, and the organic phase was separated off and dried (Na_2SO_4). The solvent was evaporated, and the residue was purified on a preparative TLC plate (9:1 petroleum ether/EtOAc). The product was isolated as a clear liquid (34 mg, 75%). ^{1}H NMR (CD_3CN): δ 6.96 (m, 1H), 5.98 (d, 1H, J = 9.6 Hz), 3.64 (s, 3H), 2.0−2.4 (m, 5H), 1.15 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 199.0 (C), 176.5 (C), 149.4 (CH), 128.9 (CH), 51.4 (CH_3), 44.3 (C), 41.8 (CH), 39.3 (CH_2), 27.0 (CH_2), 21.8 (CH_3), 21.4 (CH_3). The spectrum of this compound matches the spectrum of the previously synthesized material.[19]

[Os(NH$_3$)$_5$(1,2,3-η^3-5-(1-carbomethoxy-1-methylethyl)-4*H*-1,3-cyclohexadienium)](OTf)$_3$ (17). Complex **16** (150 mg, 0.20 mmol) was dissolved in CH_3CN (1.7 g), and triflic acid (40 mg, 0.27 mmol) was added. After ∼5 min, the solution was added to ∼100 mL of stirring ether, and the resulting slurry was filtered. The solid was rinsed with ether and dried in vacuo (155 mg, 86%). Partial characterization only. ^{1}H NMR (CD_3CN): δ 5.62−5.65 (m, 2H), 5.25 (br s, 3H, *cis*-NH_3), 5.17−5.22 (m, 1H), 3.97 (br s, 12H, *trans*-NH_3), 3.62 (s, 3H), 2.66 (dd, J = 12.6, 16.8 Hz, 2H), 1.72−1.81 (m, 2H), 1.09 (s, 6H), 0.40−0.52 (m, 1H).

[Os(NH$_3$)$_5$(5,6-η^2-7-methoxy-4a-methyl-3,4,4a,8a-tetrahydro-1*H*-naphthal-2-one)](OTf)$_2$ (21). Complex **20** (830 mg, 0.906 mmol) was dissolved in CH_3OH (5.6 g) containing triflic anhydride (799 mg, 2.832 mmol). After being stirred for 0.25 h, the purple color of the reaction mixture disappears and the solution is precipitated by addition to ether to give a dark solid (677.3 mg). This solid was dissolved in CH_3CN and cooled to −40 °C. Excess pyridine was then added, and after 15

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min, the reaction mixture was added to ether/CH_2Cl_2 to give a tan precipitate which was collected, washed with ether, and dried in vacuo (530.7 mg, 95%). ^{1}H NMR (CD_3CN): δ 4.40 (m, 1H), 4.19 (br s, 3H, *cis*-NH_3), 3.75 (m, 1H), 3.69 (d, 1H, J = 8.1 Hz), 3.58 (d, 1H, J = 8.1 Hz), 3.47 (s, 3H), 3.17 (br s, 12 H, *trans*-NH_3), 1.10−2.90 (m, 6H), 1.40 (s, 3H). ^{13}C NMR (acetone-d_6): δ 210.7 (C), 161.8 (C), 90.9 (CH), 58.2 (CH), 55.0 (CH_3), 45.2 (CH), 44.8 (CH_2), 43.0 (C), 42.0 (CH), 41.1 (CH_2), 38.6 (CH_2), 23.1 (CH_3). Anal. Calcd for $C_{60}H_{71}O_2N_5B_2Os\cdot 2H_2O$: C, 63.10; H, 6.62; N, 6.13. Found: C, 63.36; H, 6.76; N, 6.43.

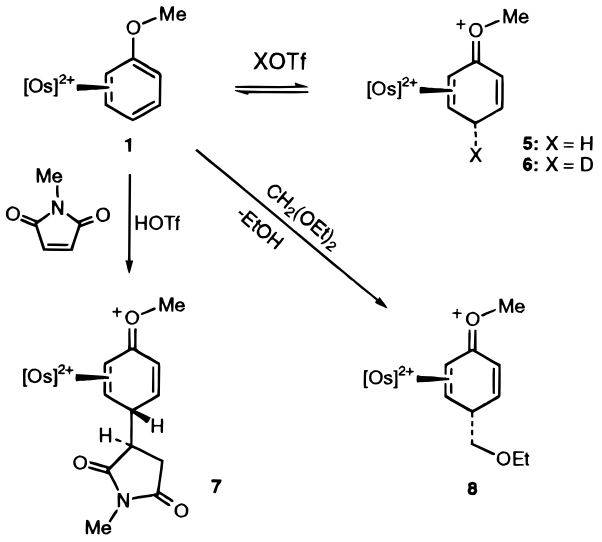
[Os(NH$_3$)$_5$(5,6-η^2-(methyl 4,4a,8,8a-tetrahydro-4a-methyl-1*H*,3*H*-naphthaldionium)](OTf)$_3$ (22). Compound **21** (588, mg, 0.642 mmol) was dissolved in CH_3OH (1 g) and cooled to 0 °C. This solution was added dropwise to a solution (MeOH, 1.0 g) of triflic acid (195 mg, 1.30 mmol), and the reaction mixture was warmed to room temperature and stirred for 2.5 h. Addition to ether (350 mL) gave a gray precipitate which was collected, washed with ether, and dried in vacuo to yield **22** (523 mg, 90% mass recovery). ^{1}H NMR (CD_3CN): δ 5.87 (d, 1H, J = 7.2 Hz), 5.35 (d, 1H, J = 7.2 Hz), 5.04 (br s, 3H, *cis*-NH_3), 4.30 (s, 3H), 3.93 (br s, 12 H, *trans*-NH_3), 2.05−2.90 (m, 9H), 1.52 (s, 3H). ^{13}C NMR (CD_3CN): δ 211.3 (C), 210.3 (C), 69.3 (CH), 64.0 (CH_3), 54.5 (CH), 42.2 (CH_2), 41.2 (C), 41.0 (CH_2), 38.2 (CH_2), 37.1 (CH), 33.7 (CH_2), 21.7 (CH_3).

[Os(NH$_3$)$_5$(5,6-η^2-(4,4a,8,8a-tetrahydro-4a-methyl-1*H*,3*H*-naphthaldione)](OTf)$_2$ (23). Compound **22** (593, mg, 0.648 mmol) was dissolved in CH_3OH (2.0 g) and cooled to 0 °C. H_2O (100 mg) was added, and the reaction was stirred at room temperature overnight (12 h). Addition to ether (400 mL) gave a tan precipitate which was collected, washed with ether, and dried in vacuo to yield **23** (473 mg, 97% mass recovery). ^{1}H NMR (CD_3CN): δ 4.44 (br s, 3H, *cis*-NH_3), 4.23 (d, 1H, J = 8.1 Hz), 4.12 (d, 1H, J = 8.1 Hz), 3.39 (br s, 12 H, *trans*-NH_3), 2.10−2.90 (m, 9H), 1.49 (s, 3H). ^{13}C NMR (CD_3CN): δ 213.8 (C), 211.3 (C), 62.3 (CH), 51.1 (CH), 43.4 (CH_2), 41.2 (CH_2), 40.8 (CH_2), 39.9 (C), 38.6 (CH_2), 38.5 (CH), 22.9 (CH_3). Anal. Calcd for $C_{59}H_{69}O_2N_5B_2Os\cdot H_2O$: C, 63.84; H, 6.45; N, 6.31. Found: C, 63.71; H, 6.25; N, 6.36.

[Os(NH$_3$)$_4$(2,3,5,6-η^4-1-methoxy-4-methyl-7-acetyl[2.2.2]bicycloocta-2,5,7-triene]](OTf)$_2$ (30). Compound **3** (250 mg, 0.360 mmol) was dissolved in CH_3CN (3.0 g), and 3-butyn-2-one (190.0 mg, 2.79 mmol) was added. The reaction mixture was cooled to −40 °C, and cold $BF_3\cdot OEt_2$ (53 mg, 0.373 mmol) was added. The reaction mixture instantly turned dark purple. After 2 h, addition of excess CH_3OH (650 mg) caused the purple color to fade to orange. Addition to ether (50 mL) gave an orange precipitate (260 mg, 95% mass recovery) which was collected, washed with ether, and dried in vacuo. ^{1}H NMR (CD_3CN): δ 6.77 (s, 1H), 4.65 (br s, 3H), 4.40 (br s, 3H), 4.10 (d, 2H, J = 5.7 Hz), 3.78 (d, 2H, J = 5.7 Hz), 3.40 (s, 3H), 3.25 (br s, 3H), 3.10 (br s, 3H), 2.28 (s, 3H), 1.73 (s, 3H). ^{13}C NMR (CD_3CN): δ 196.4 (C), 157.2 (CH), 145.5 (C), 97.2 (C), 54.5 (CH_3), 51.2 (2 × CH), 50.8 (C), 50.4 (2 × CH), 28.2 (CH_3), 20.2 (CH_3). Electrochemistry (TBAH, CH_3CN, 100 mV/s): $E_{p,a}$ = 1.70 V. Anal. Calcd for $C_{60}H_{66}O_2N_4B_2Os\cdot 2H_2O$: C, 64.17; H, 6.28; N, 4.99. Found: C, 64.43; H, 6.30; N, 5.67.

[Os(NH$_3$)$_5$(5,6-η^2-3-(3-oxobutenyl)-4-methylanisole)](OTf)$_2$ (32). Compound **3** (60.0 mg, 0.086 mmol) was dissolved in CH_3CN (1.5 g), and 3-butyn-2-one (50.0 mg, 0.734 mmol) was added. The reaction mixture was cooled to −40 °C, $BF_3\cdot OEt_2$ (12.4 mg, 0.087 mmol) was added, and the reaction mixture turned purple. After 4 h, addition of excess CH_3OH (400 mg) caused the purple color to fade to orange. Addition to ether (50 mL) gave an orange precipitate (57 mg, 86%) which was collected, washed with ether, and dried in vacuo. ^{1}H NMR (CD_3CN): δ 7.70 (d, 1H, J = 15.9 Hz), 6.38 (d, 1H, J = 15.9 Hz), 5.83 (s, 1H), 5.20 (d, 1H, J = 7.8 Hz), 5.05 (d, 1H, J = 7.8 Hz), 4.20 (br s, 3H), 3.71 (s, 3H), 3.03 (br s, 12H), 2.47 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (CD_3CN): δ 198.6 (C), 166.1 (C), 154.4 (C), 139.2 (CH), 123.8 (CH), 122.7 (C), 89.9 (CH), 63.9 (CH), 56.0 (CH), 55.1 (CH_3), 27.0 (CH_3), 19.9 (CH_3). Electrochemistry (TBAH, CH_3CN, 100 mV/s): $E_{p,a}$ = 0.55 V.

Scheme 1. Electrophilic Addition Reactions at C4 of an η^2-Anisole Complex



Results and Discussion

The one-electron reduction of $Os(NH_3)_5(OTf)_3$ in the presence of various anisole ligands yields complexes of the form [$Os(NH_3)_5(\eta^2$-L)](OTf)$_2$ [L = anisole (**1**), 3-methylanisole (**2**), 4-methylanisole (**3**), and 3,4-dimethylanisole (**4**)] in high yield.[17] In all cases, the metal preferentially binds to the unsubstituted ortho and meta carbons, and all complexes appear static at 20 °C in a 300-MHz proton NMR spectrum.

When a solution of the anisole complex (**1**) in CD_3CN is cooled to −40 °C and treated with HOTf or DOTf, the reaction solution changes from yellow to deep blue indicating the formation of the η^2-4*H*-anisolium (**5**) and η^2-4D_{exo}-anisolium (**6**) cations, respectively (Scheme 1).[20] Correspondingly, the reaction of the η^2-anisole complex **1** with various carbon electrophiles and triflic acid provides a number of 4-substituted 4*H*-anisolium complexes. The scope of electrophiles includes a variety of Michael acceptors and acetals, all of which react with η^2-anisole complexes to form 4-substituted 4*H*-anisoliums.[17] Although these highly electrophilic intermediates are generally unstable at 20 °C, they can be observed in solution at reduced temperatures (−40 °C). Two examples include the addition products of *N*-methylmaleimide (**7**)[18] and diethoxymethane (**8**) shown in Scheme 1. Whereas arenium complexes produced from η^2-aniline or η^2-phenol complexes are highly resistant to addition of carbon nucleophiles at C3,[15,16] anisolium complexes such as **5**−**8** are considerably more electrophilic at C3 and undergo reactions with mild carbon nucleophiles.

C4−C3 Tandem Addition Reactions. When complex **1** is combined with triflic acid and the silyl ketene acetal MMTP at −40 °C, a new species (**9**) is obtained (92%) whose ^{1}H and ^{13}C NMR and electrochemical data support the assignment of **9** as the methoxydiene complex shown in Scheme 2. Irradiation of the sample at the *cis*-ammine frequency results in a moderate NOE (4%) with the proton at C3 indicating that addition of the silyl ketene acetal occurs anti to the metal center. In a similar fashion, when the anisolium species **5** is prepared at low temperature and then combined with either *N*-methylpyrrole (−40 °C) or 2-trimethylsiloxyfuran (−80 °C), addition products **11** and **12** are formed. In all three cases, ^{13}C and ^{1}H NMR and DEPT data as well as electrochemical data support the assign-

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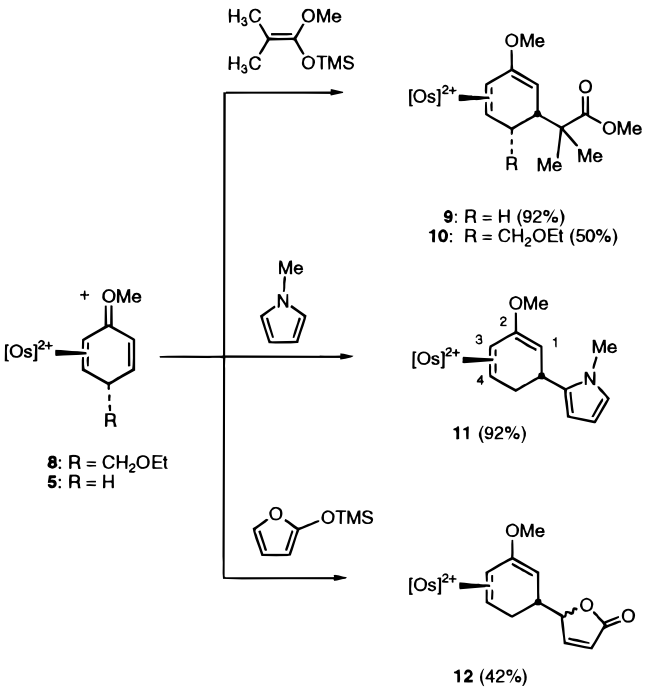
Scheme 2. Nucleophilic Addition Reactions at C3 of η^3-4*H*-Anisolium Complexes

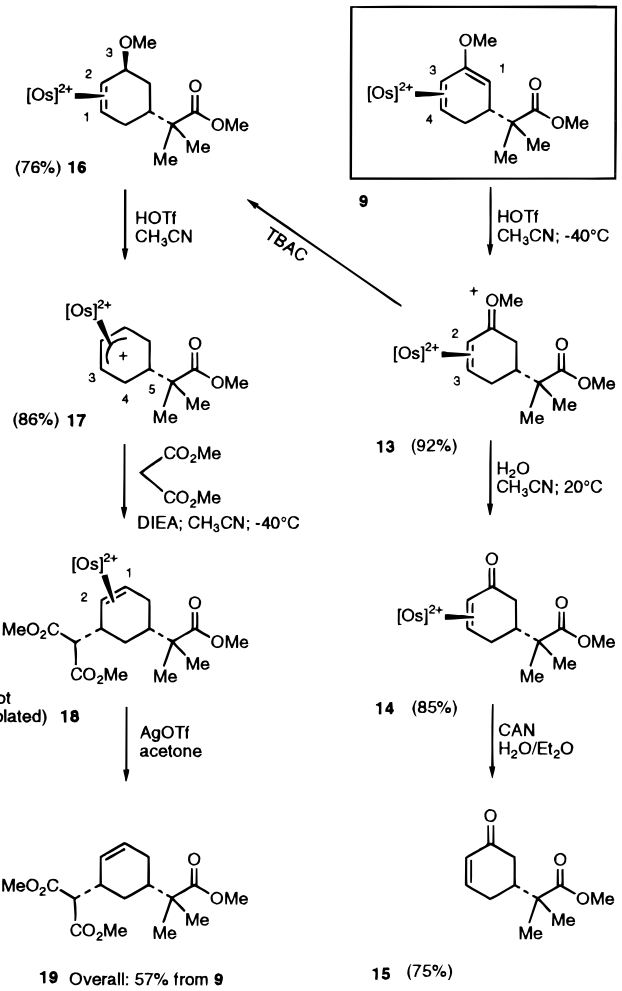


ment of **9**−**12** as 6-substituted 2-methoxy-1,3-cyclohexadiene complexes. All complexes are formed as single diastereomers (>10:1) which are assumed to correspond to the product of exo nucleophilic addition, as observed for η^2-anisolium systems.[16] For **12**, the additional stereogenic center created in the heterocycle is also formed stereoselectively. The reaction with the silyloxy furan yields a mixture of **12** and the anisole complex (**1**), indicating that deprotonation at C4 is competitive with nucleophilic addition at C3 in this case. Although the yields are >90% for complexes **9** and **11**, these species also contain small amounts of **1**, and separation of the products from starting material proved difficult. Nonetheless, according to ^{13}C and ^{1}H NMR, and electrochemical data, the only impurity for complexes **9**−**12** is **1**. Nucleophiles which fail to react with the anisolium complex under these conditions include furans, β-diketones, allylsilanes, and stannanes.

The vicinal addition of two carbon substituents can also be achieved, provided that the electrophile and nucleophile are not too sterically encumbering. For example, when the 4-(ethoxymethyl)-4*H*-anisolium complex (**8**) is generated from **1** at −40 °C and is combined with MMTP, an ivory solid is isolated from solution. The ^{1}H and ^{13}C NMR and electrochemical data are consistent with the formation of a single diastereomer (>10:1) of the methoxydiene complex **10**. Homonuclear decoupling and HETCOR data further support the structure depicted in Scheme 2.

2-Methoxy-1,3-diene complexes such as those shown in Scheme 2 are expected to have the methoxy group oriented in the plane defined by the uncoordinated olefin (C2, C1, H1) pointing *away* from the pentaammineosmium(II) system. This expectation is gained from inspection of molecular models which predict a significant steric interaction between the ammine ligands and the methoxy group, if the latter was oriented toward the metal. Correspondingly, these complexes are considerably less reactive at C1 with carbon electrophiles than their η^2-arene precursors. However, they are easily protonated to form η^2-(methyl cyclohexenonium) complexes. When an acetonitrile solution of complex **9** is treated with triflic acid at −40 °C, a

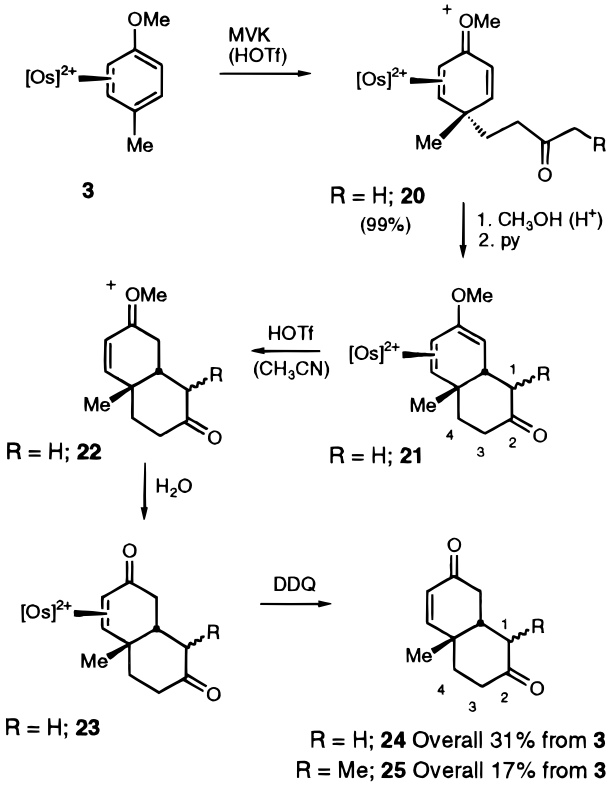
Scheme 3. Elaboration of an η^2-Methoxydiene Complex To Form a Substituted Cyclohexenone and Cyclohexene



purple solid (**13**) is isolated whose ^{1}H NMR spectrum exhibits a methoxy (4.29 ppm) and cis (3.84 ppm) and trans (5.00 ppm) ammine resonances shifted downfield from their positions in the spectrum of **9**. ^{13}C NMR data include a carbonyl resonance at 214.5 ppm as well as other signals consistent with the structure proposed in Scheme 3. In contrast to the sluggish rate of hydrolysis observed for 4*H*-anisolium complexes (vide infra), the methyl cyclohexenonium complex **13** readily hydrolyzes in acetonitrile to produce the cyclohexenone complex **14**. Finally, when complex **14** is treated with CAN in a water/Et_2O biphasic mixture, the cyclohexenone **15** is isolated in 75% yield. This represents a 51% overall yield from anisole for six isolated steps (Scheme 3; 89%/step). If the methyl cyclohexenonium intermediate **13** is treated with a hydride reagent (TBAC) a new product is isolated whose ^{1}H NMR spectrum is consistent with the methoxycyclohexene complex **16** shown in Scheme 3. Significant ^{1}H NMR features include three proton signals in the range 4.0−4.7 ppm assigned to the bound olefin protons and the methine proton adjacent to the methoxy group. These features are similar to those of the 3-methoxycyclohexene complex obtained from hydrogenation of the anisole complex (**1**).[21] As initially demonstrated for the latter compound, complex **16** readily reacts with acid to form an allyl species **17**. π-Allyl complexes of pentaammineosmium(II) are considerably more stable with respect to deprotonation than the corresponding arenium sytems and undergo reactions with a

(21) Harman, W. D.; Taube, H. *J. Am. Chem. Soc.* **1989**, *111*, 2261.

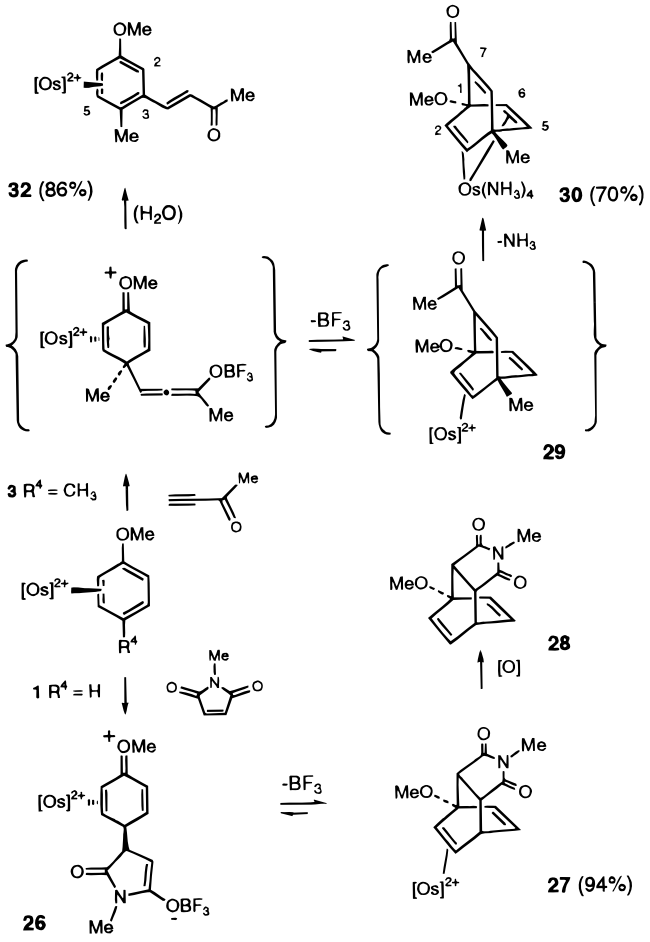
Scheme 4. Michael−Michael Ring-Closure Reaction To Form a Decalin Core



wide range of nucleophiles that include phosphines, pyridines, alkoxides, and stabilized enolates.[22] For example, the allyl species **17** reacts with dimethyl malonate to form a single diastereomer of the cyclohexene complex **18**, which is oxidized in situ to liberate the 1,3-disubstituted cyclohexene product (**19**; Scheme 3). Although the overall yield is poor if each intermediate is isolated (due to incomplete precipitation), repeating the reaction sequence *without* isolation of intermediates starting from complex **13** delivers the substituted cyclohexene product (**18**) in 62% yield. This represents an overall yield from anisole of 50% (or 57% from compound **9**) for eight chemical steps (>91%/step). Most importantly, by starting from the arene complex **1**, the sequence to generate **19** represents the sequential addition of two electrophiles and three nucleophiles to the aromatic ring. All but one of the original arene carbons have undergone addition reactions.

An important extension of this methodology includes intramolecular nucleophilic additions to synthesize β-tetralones. For example, the Michael addition product (**20**) of MVK and the 4-methylanisole complex (**3**) offers the possibility of an intramolecular nucleophilic addition at C3 (Scheme 4). When a sample of **20** is dissolved in acidic methanol (generated from triflic anhydride to ensure anhydrous conditions), the dark blue color discharges over a 15-min period to give a brown solution. After treatment with pyridine and addition to ether/CH_2Cl_2, a light tan solid (**21**) is obtained. ^{1}H NMR, ^{13}C NMR, and DEPT data support the assignment of **21** as a complex of 1,2,3,4,4a,-8a-hexahydro-7-methoxy-4-methylnaphthalene, the product of an intramolecular nucleophilic addition at C3. Treatment of a solution of **21** with triflic acid in methanol results in conversion to the cyclohexenonium species **22**, and subsequent hydrolysis to **23** and oxidative decomplexation yields the organic decalin

Scheme 5. C1−C4 Cyclization Reactions of Anisoles with Olefins or Alkynes



24 in an overall yield of 31% from **3**. Electrochemical evaluation of the series of complexes **20**−**24** indicates that the majority of the product loss is due to a competing metal-centered oxidation that occurs during the cyclization step. The ^{1}H NMR of the organic decalin product (**24**) shows an angular methyl resonance at 1.38 ppm indicative of a *cis*-decalin ring juncture.[23] When this reaction sequence is repeated using ethyl vinyl ketone as the Michael acceptor, the methyl-substituted analogue of **24** is obtained (**25**) as a 6:1 ratio of diastereomers (overall yield from **3**: 17%). ^{1}H NMR data of **25** again are supportive of a *cis*-decalin with an angular methyl group.

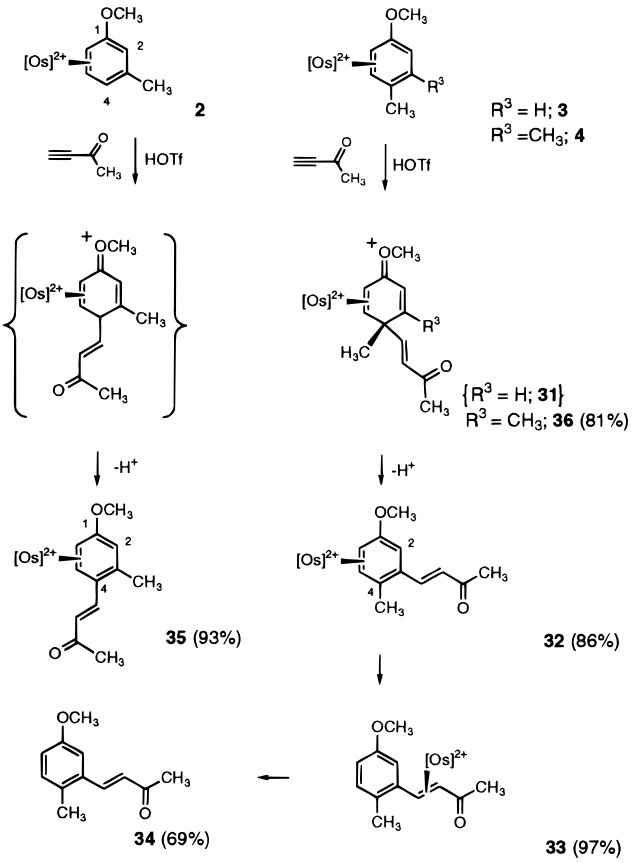
[4 + 2] Cycloaddition Reactions. When a Lewis acid is used to promote the Michael addition between *N*-methylmaleimide and the anisole complex (**1**), it is possible to observe the initial intermediate 4*H*-anisolium species trapped as a boron enolate (**26**; Scheme 5). As we have previously described,[18] if the enolate is left undisturbed, it reacts with the highly electrophilic C1 to give what is formally a Diels−Alder cycloadduct, **27.** Oxidation of this material (DDQ) renders the intact organic cycloadduct **28**. Cycloadducts are successfully formed from *N*-methylmaleimide and **1** (94%), **2** (88%), **3** (89%), **4** (65%), and **5** (98%).[24] Although the [4 + 2] cycloaddition reaction appears general with respect to the range of alkylated anisoles, the scope of dienophiles is limited. Under reaction conditions similar to those used for maleimides, the potential dienophiles MVK, 3-butyn-2-one, and maleic anhydride all react with **1** to form C4-alkylated anisolium species.

(22) Harman, W. D.; Hasegawa, T.; Taube, H. *Inorg. Chem.* **1991**, *30*, 453.

(23) Boger, D. L. *Tetrahedron Lett.* **1978**, 17.

(24) Kopach, M. E. Ph.D. Dissertation, University of Virginia, 1995.

Scheme 6. Formation of C3 and C4-Vinylanisole Complexes from the Michael Addition of 3-Butyn-2-one



However, after workup, C4-substituted anisole complexes are the only products isolated. For less reactive dienophiles such as methyl acrylate or acrylonitrile, only starting materials are recovered. However, when the 4-methylanisole complex **3** is treated with 3-butyn-2-one and $BF_3{\cdot}OEt_2$ at −40 °C, a [4 + 2] cycloaddition readily occurs (Scheme 5). Apparently the putative intermediate **29** readily loses an ammonia ligand. After workup with methanol, the tetraammine **30** (Scheme 5) is isolated in 70% yield after purification. Key spectral features for the tetraammine barrelene complex (**30**) include four nonequivalent ammine resonances (4.65, 4.40, 3.25, and 3.10 ppm), an olefin signal, (6.77 ppm), and two upfield metal-coordinated proton resonances (4.10 and 3.78 ppm, 2H each). In addition, ^{13}C NMR data reveal a bridgehead carbon (97.2 ppm), two metal coordinated carbons (51.2 and 50.4 ppm), and a carbonyl signal (196.4 ppm). A cyclic voltammogram taken immediately after isolation reveals a reversible oxidation wave at +0.80 V that likely corresponds to the pentaammineosmium η^2-cycloadduct (**29**).[18] After 15 min, a second cyclic voltammogram reveals complete conversion to the tetraammine species (**30**) ($E_{p,a}$ = 1.70 V).

The synthesis of the η^4-barrelene **30** was never successfully carried out in greater than 70% yield, despite extensive efforts to optimize the yield of this reaction.[24] In the presence of a proton source (e.g., trace H_2O), the boron enolate is probably quenched, and the resulting 4,4-disubstituted 4*H*-anisolium species (**31**; inferred) appears to undergo a C4-to-C3 alkyl migration. The structure of the resulting disubstituted anisole complex **32** was confirmed by ^1H, ^{13}C, and $^1H/^1H$ coupling data for the complex as well as its linkage isomer, **33**, which forms when **32** is treated with acid. The corresponding organic ligand **34** may be obtained by the air oxidation of **33**. A ^1H NMR spectrum of **34** (*trans*-4-(5′-methoxy-2′-methylphenyl)-3-buten-2-one) reveals W coupling between the two ortho protons consistent with a 3,4-disubstituted anisole. To rule out a product resulting from methyl migration, the pentaammineosmium(II) complex of *trans*-4-(4-methoxy-2-methylphenyl)-3-buten-2-one (**35**) was independently prepared through the reaction of **2** with 3-butyn-2-one. ^1H and ^{13}C NMR for both the complex and ligand confirm that **32** is a 3,4-disubstituted anisole complex with the same substituents as, but different from, the arene ligand of **35** (Scheme 6). Finally, when the osmium complex of 3,4-dimethyl anisole is combined with 3-butyn-2-one and acid, a para alkylation product (**36**) is formed that resists rearrangement to a 3,4-disubstituted anisole.

Conclusion

4*H*-Anisolium complexes of pentaammineosmium(II), prepared directly from anisole, are shown to be exceptional synthons to a diverse array of functionalized mono- and polycyclic systems. Both electrophilic and nucleophilic addition reactions occur with an exceptional level of both regio- and stereocontrol with yields averaging between 80 and 90% per chemical transformation. The low number of carbons required for η^2 coordination allows for the sequential addition to multiple carbons of the arene system with a single application of the metal.[25]

Acknowledgment. Acknowledgment is made to the Camille and Henry Dreyfus Foundation, the National Science Foundation (CHE-9509883 and the NYI program), the Alfred P. Sloan Foundation, and Colonial Metals Inc. (Elkton, MD; OsO_4) for their generous support of this work.

Supporting Information Available: Experimental details (7 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(25) We note that OsO_4 may be purchased at an economical price (Colonial Metals) and may be converted to $Os(NH_3)_5(OTf)_3$ in 98% overall yield. Using these procedures, the cost of any of the final organic products presented in this text fall in the range $30−50 per gram. This reflects the cost of osmium over the entire process (taking into account yields) and assumes no recovery of the metal.