The Osmium(II)-Promoted [4 + 2] Cycloaddition Reaction of Anisole and *N*-Methylmaleimide and Characterization of the η^2-4*H*-Anisolium Intermediate

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Summary: Anisole, when complexed by pentaammineosmium(II), undergoes a [4 + 2] cycloaddition with *N*-methylmaleimide which is shown to be nonconcerted.

Although the Diels–Alder reaction is one of the most powerful synthetic tools available for the formation of bicyclic ring systems, few examples are known where a simple arene serves as the diene fragment.[1] As part of our continuing investigation of the reactivity of dihaptocoordinated aromatic molecules, we hoped to facilitate the cycloaddition of an electron-rich arene and an electron-deficient dienophile by prior coordination of the former with pentaammimeosmium(II). Herein, we wish to report an example of such a reaction with anisole and *N*-methylmaleimide. Under carefully controlled conditions, the indicated cycloadduct is not only isolated as a stable osmium complex, but may be removed from the metal and observed as an intact bicyclo[2.2.2]octadiene prior to its reversion to arene and olefin.

The anisole complex $[Os(NH_3)_5(2,3\text{-}\eta^2\text{-anisole})](OTf)_2$ (**1**) is formed quantitatively from the arene, magnesium, and $Os(NH_3)_5(OTf)_3$ according to literature methods.[2] When an acetonitrile/propionitrile solution of **1** is treated at −50 °C with 1.1 equiv of $BF_3{\cdot}OEt_2$ and 1.9 equiv of *N*-methylmaleimide,[3] the reaction mixture turns purple ($\lambda_{max} \sim 560$ nm). After 10 min, addition of the mixture to ether causes the precipitation of an ivory solid (**2**) that is obtained in 94% yield. ^1H, ^{13}C NMR and electrochemical data support the assignment of **2** as a pentaammineosmium(II) complex of 1-methoxybicyclo[2.2.2]octa-2,5-diene-7,8-methyldicarboximide,[4] formally a [4 + 2] cycloadduct of anisole and the maleimide (Figure 1). Spectral features include two osmium-bound (51.2, 50.9 ppm) and two free (134.1, 127.8 ppm) olefin ^{13}C resonances, bridgehead carbon signals (89.0 and 40.1 ppm), and other features consistent with an intact succinimide ring. NOE data for **2** are consistent with the imide group having an exo orientation.[5] Finally, a cyclic voltammogram of **2** indicates a reversible III/II reduction potential with $E_{1/2} = +0.80$ V (NHE, 100 mV/s), consistent with a metal-coordinated olefin.[6]

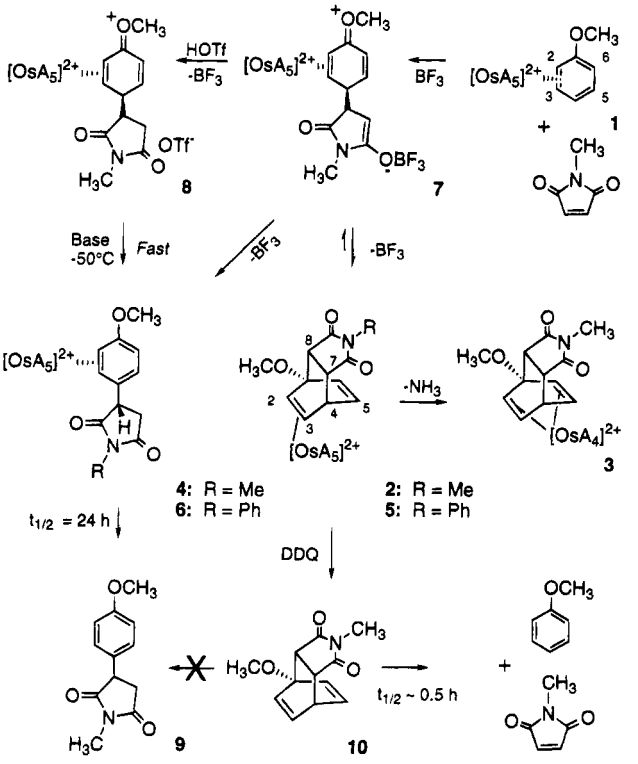

Figure 1. Reaction scheme for the η^2-anisole complex and *N*-methylmaleimide.

Over time ($t_{1/2} = 3$ h), an acetonitrile solution of the cycloadduct **2** (20 °C) converts to a new species, **3**, which, judging from ^1H, ^{13}C NMR and combustion analysis, is the tetraammine analog of **2** where the diene is bound η^4 to the osmium.[7] Key spectral data for **3** include four nonequivalent ammine ^1H NMR resonances, four osmium-bound olefin ^{13}C resonances (46–55 ppm), and an irreversible oxidation wave with $E_{p,a} = +1.87$ V (cf. $[Os(NH_3)_4(CH_2{=}CH_2)_2]^{2+} = 1.7$ V, NHE).[8]

When the reaction of **1** and *N*-methylmaleimide is repeated under conditions identical to those for the preparation of **2**, but for an extended reaction period (2 h), the intense blue color observed upon mixing fades to a light brown. Addition of ether induces the precipitation of a new compound, **4**.[9] Judging from ^1H and ^{13}C NMR as well as electrochemical data, **4** is an osmium(II) complex of a *para*-substituted arene, the product of

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(1) (a) Ciganek, E. *Tetrahedron Lett.* **1967**, *34*, 3321. (b) Miller, R. G.; Stiles, M. *J. Am. Chem. Soc.* **1963**, *85*, 1798. (c) Weis, C. D. *J. Org. Chem.* **1963**, 28, 74. (d) Krespan, C. G.; McKusick, B. C.; Cairns, T. L. *J. Am. Chem. Soc.* **1961**, 83, 3428. (e) Hart, H.; Du, F. C.-J.; Mohebalian, J. *J. Org. Chem.* **1988**, *53*, 2720. (f) Tabushi, I.; Yamada, H.; Yohida, Z.; Oda, R. *Bull Chem. Soc. Jpn.* **1977**, *50*, 285.

(2) Harman, W. D.; Sekine, M.; Taube, H. *J. Am. Chem. Soc.* **1988**, *110*, 5725.

(3) Attempts to prepare the cycloadduct **2** using catalytic BF_3 conditions have failed.

(4) All reactions were carried out under nitrogen. Synthesis of **2**: Compound **1** (165 mg, 0.242 mmol) was dissolved in CH_3CN/CH_3CH_2CN (8:1; 2.25 g) and combined first with $BF_3{\cdot}OEt_2$ (37.0 mg, 0.260 mmol) and then *N*-methyl maleimide (50.0 mg, 0.450 mmol; CH_3CH_2CN) at −50 °C. After 10 min, CH_3OH (400 mg) was added and the reaction mixture was poured directly into ether (20 mL). The ivory white precipitate was collected, washed with ether, and dried *in vacuo* (180 mg, 94%). ^1H NMR (CD_3CN): δ 5.65 (d, 2H, $J = 10$ Hz), 4.08 (br s, 3H), 3.78 (d, 1H, $J = 8.1$ Hz), 3.72 (s, 3H), 3.64 (m, 1H), 3.53 (d, 1H, $J = 7.8$ Hz), 3.48 (dd, 1H, $J = 8.1$, 4.5 Hz), 3.35 (dd, 1H, $J = 7.8$, 4.5 Hz), 3.11 (br s, 12 H), 2.74 (s, 3H). ^{13}C NMR (CD_3CN): δ 177.9 (CO), 175.4 (CO), 134.1 (CH), 127.8 (CH), 89.0 (C), 51.2 (CH), 51.1 (OCH_3), 50.9 (CH), 48.6 (CH), 47.1 (CH), 40.1 (CH), 24.4 (NCH_3). Cyclic voltammetry $E_{p,a} = 0.80$ V. Anal. (BPh_4^- salt) ($C_{60}H_{68}O_3N_6B_2Os$): C, H, N.

(5) Priority is assigned to the metalated double bond. NOE enhancements are as follows: between H(2) and H(8), 3%; H(3) and H(7), 3%; NH_3(cis) and H(2), 7%; NH_3(cis) and H(3), 14%.

(6) Harman, W. D.; Taube, H. *J. Am. Chem. Soc.* **1990**, *112*, 2682.

(7) Compound **2** also converts to **3** (90%) and **1** (10%) over a period of 24 h in the solid state.

(8) Taube, H.; Nunes, F. S. *Inorg. Chem.* **1994**, *33*, 3116.

0022-3263/94/1959-6506$04.50/0

conjugate addition and subsequent deprotonation at C(4) of anisole (Figure 1).[10]

In order to determine if cycloadduct **2** is an intermediate in the formation of the arene substitution product (**4**), an isolated sample of the former was dissolved in acetonitrile/propionitrile with an excess of *N*-phenylmaleimide (~10 equiv) and the reaction mixture cooled to −50 °C. Subsequent addition of BF_3·OEt_2 (1.0 equiv) and reprecipitation of products (3 h; Et_2O) yielded a 9:1 mixture of the arene complex, **4**, and its phenyl-substituted analog, **6**, respectively. In a complementary experiment, the *N*-phenylmaleimide cycloadduct **5**[11] was treated with an excess of *N*-methylmaleimide (~10 equiv) under otherwise identical reaction conditions. Here, the product mixture was a 1:9 ratio of the arene complexes **4** and **6**.[12] The minor amount of scrambling in each case indicated that these η^2-cycloadducts (**2** and **5**) do not undergo a significant retrocycloaddition under the indicated reaction conditions and, therefore, were likely to be reaction intermediates in the conjugate addition process. However, the purple color of the reaction mixture (λ_{max} = 560 nm [ϵ > 600 cm^{-1} M^{-1}]),[13] 710 nm (sh)) prior to addition of ether suggested that an intermediate *other than a cycloadduct* was present at early reaction times, and this observation prompted us to monitor by ^1H NMR the reaction of **1** and *N*-methylmaleimide with BF_3 at a lower temperature. After 10 min, a poorly resolved ^1H NMR spectrum (CD_3CN/CD_2Cl_2/50 °C) revealed a new species, **7**, with ammine (3.69, 5.00 ppm) and olefin (7.35, 6.81 ppm) ^1H resonances similar to the 4*H*-anisolium complex that is obtained from direct protonation of anisole (λ_{max} = 548 nm; 710 nm (sh)).[14,15] Over time, this species gives way to the cycloadduct **2**. In a separate experiment, a solution of **7** (prepared *in situ*) was treated with 1 equiv of triflic acid (−40 °C) to generate **8**, a species spectroscopically similar to its precursor but with an intact succinimide ring.[16] Subsequent addition of 2,6-lutidine to the solution of **8** resulted in quantitative formation of the *para*-disubstituted arene complex **4**, which over a period of 24 h underwent solvolysis (CH_3CN) to give the free arene **9**. Taken together, these observations suggest the reaction sequence shown in Figure 1.

Thus, the 4*H*-anisolium species, **7**, is a common intermediate for both cycloaddition and electrophilic-substitution reactions. At early reaction times this anisolium species undergoes a ring closure with the borane−enolate to form the cycloadduct **2**. Over time, however, the anisolium species (still accessible from the cycloadduct in the presence of BF_3), undergoes a proton transfer from C(4) to the succinimide ring to generate the *para*-substituted arene, **4** (91%).

When 1.0 equiv of DDQ is used as the oxidant, the pentaammineosmium fragment of **2** can be removed (−40 °C/CH_3CN) and the intact bicyclo[2.2.2]octadiene, **10**, isolated (overall yield from **1**: ~25%).[17] With time ($t_{1/2}$ = 0.5 h at 20 °C), **10** suffers a retrocycloaddition to give only anisole and *N*-methylmaleimide as final products.

Preliminary studies suggest that cycloaddition products may be formed for a variety of substituted anisoles and dienophiles. When C(5) and C(6) or C(4) are methylated, the corresponding cycloadducts analogous to **2** have increased stability with regard to forming η^2-Michael adducts; however, the 2,3-dimethylanisole species is more susceptible than **2** to loss of ammonia and readily forms the η^4-bicyclooctadiene complex at room temperature. For the electrophiles maleic anhydride, methyl vinyl ketone, and 3-penten-2-one, η^2-cycloadduct intermediates with **1** are not observed. However, when the 4-methylanisole derivative of **1** is combined with 3-butyn-2-one both η^2- and η^4-bicyclo[2.2.2]octatriene (barrelene) species may be obtained. Thus, dihaptocoordination renders an arene a potentially useful synthon for the preparation of highly functionalized, unsaturated bicyclo[2.2.2]octanes. The scope of this reaction is currently under investigation.

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(9) Characterization of **4**. ^1H NMR (CD_3CN): δ 6.38 (d, 1H, J = 6.9 Hz), 5.52 (d, 1H, J = 6.9 Hz), 5.12 (d, 1H, J = 8.1 Hz), 4.96 (d, 1H, J = 8.1 Hz), 4.18 (br s, 3H), 3.83 (dd, 1H, J = 9.3, 4.5 Hz), 3.64 (s, 3H), 3.11 (br s, 12 H), 3.00 (dd, 1H, J = 18.3, 9.3 Hz) , 2.90 (s, 3H), 2.61 (dd, 1H, J = 18.3 Hz, 4.5 Hz). ^{13}C NMR (CD_3CN): δ 183.5 (CO), 177.1 (CO), 169.3 (C), 136.5 (C), 118.8 (CH), 93.5 (CH), 63.6 (OCH_3), 56.1 (CH), 55.6 (CH), 45.9 (CH), 40.1 (CH_2), 25.0 (NCH_3). Cyclic voltammetry $E_{p,a}$ = 0.45 V. Anal. (BPh_4^- salt) ($C_{60}H_{68}O_3N_6B_2Os$): C, H, N.

(10) For other examples of C(4) conjugate addition with η^2-arene complexes see: (a) Kopach, M. E., Gonzalez, J.; Harman, W. D. *J. Am. Chem. Soc.* **1991**, 113, 8972. (b) Kopach, M. E.; Kelsh, L. P.; Stork, K.; Harman, W. D. *J. Am. Chem. Soc.* **1993**, *115*, 5322. (c) Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 6581. (d) Kolis, S. P.; Gonzalez, J.; Harman, W. D. Manuscript in preparation.

(11) Cycloadduct **5** was prepared by a method analogous to that for **2**. Yield: 88%.

(12) When the η^2-anisole complex was combined with an equimolar mixture of *N*-phenyl- and *N*-methylmaleimide (BF_3·OEt_2; 3 h), workup of the reaction mixture revealed a 1:1 ratio of η^2-C(4) Michael products which were readily distinguishable by ^1H NMR.

(13) The solution of **7** was unstable over the course of this measurement. For comparison, the complex [$Os(NH_3)_5$(2,3-η^2-4-methyl-4-(3-oxobutyl)-4*H*-anisolium)]$^{2+}$, which is stable in acetonitrile at 20 °C, has a λ_{max} = 556 nm with ϵ = 780 cm^{-1} M^{-1}.

(14) The η^2-4H-anisolium complex is readily formed by direct protonation at −40 °C in CH_3CN. Partial characterization. ^1H NMR (CD_3CN): δ 7.72 (br s, 1H), 6.75 (br s, 1H), 5.74 (br s, 1H), 5.13 (br s, 1H), 4.80 (br s, 3H, *trans*-NH_3), 4.31 (s, 3H), 3.47 (br s, 12H, cis-NH_3), 2.56 (d, 1H, J = 27.9 Hz), 1.41 (d, 1H, J = 27.9 Hz).

(15) The hypothesized 4*H*-anisolium complex is analogous to several 4*H*-anilinium species previously reported. Gonzalez, J.; Sabat, M.; Harman, W. D. *J. Am. Chem. Soc.* **1993**, *115*, 8857.

(16) Characterization of **8**. ^1H NMR (CD_3CN): δ 7.31 (dd, 1H, J = 10.5, 3.0 Hz), 6.80 (d, 1H, J = 10.5 Hz), 5.76 (d, 1H, J = 6.9 Hz), 5.29 (d, 1H, J = 6.9 Hz), 4.96 (br s, 3H), 4.35 (s, 3H), 4.00 (m, 1H), 3.63 (br s, 12 H), 3.56 (m, 1H), 3.05 (m, 1H), 3.03 (s, 3H), 2.90 (m, 1H). ^{13}C: 198.6 (CO) 172.0 (CH), 122.3 (CH), 63.6 (OCH3), 57.6 (CH), 51.8CH), 43.6 (CH), 40.3 (CH), 30.0 (CH_2), 23.6 (NCH_3). (Maleimide carbonyl signals were not observed.)

(17) NMR yield for this reaction is ~80%. The low isolated yield (25%) reflects a considerable amount of retrocycloaddition for **10** during workup. Characterization of **10**. ^1H NMR ($CDCl_3$): δ 6.63 (d, 1H, J = 7.8 Hz), 6.50 (d, 1H, J = 6.0 Hz), 6.45 (d, 1H, J = 9.6 Hz), 6.29 (dd, 1H, J = 7.8, 6.0 Hz), 4.00 (dd, 1H, J = 9.6, 4.5 Hz), 3.70 (s, 3H), 3.69 (m, 1H) , 3.09 (m, 1H), 2.90 (s, 3H).