the p-nitrophenyl ester. Although the ethyl ester has a somewhat smaller K_{assoc}, we compensated for this by using higher β-cyclodextrin concentrations than did Breslow et al.[2,10] (6.4×10^{-2} M vs. 1.0×10^{-2} M). Under these circumstances, all esters in Table I, including the ethyl ester, are >60% bound. Consequently, the inertness of the ethyl ester cannot be attributed to lack of complex.

If the complexes of the p-nitrophenyl and ethyl esters possessed substantially different structures, then their reactivities might also differ.[13] Two factors render this unlikely. (a) Breslow et al.[2,10] argued that the ferrocenyl moiety seats itself within the β-cyclodextrin cavity (eq 1), so that the geometry of the complex is dictated by the ferrocene unit and not by its ester appendage. (b) The p-nitro*benzyl* ester, although only 31 times less reactive toward OH⁻ than the p-nitrophenyl ester, is stable for 10 days as a complex under conditions where the p-nitrophenyl ester reacts in a few seconds (Table I). Since the two esters differ in structure by only a methylene, the absence of a 3.3×10^5 acceleration with the p-nitrobenzyl ester has likely nothing to do with dissimilar binding.

A clue to the etiology of the "p-nitrophenyl ester syndrome" is provided by the series of phenyl esters in Table I. It is seen that the acceleration, $k_{complex}/k_{un}$, begins to manifest itself when the pK_a of the leaving group drops to that of phenol (9.9). A 10^4–10^5 acceleration is reached only with leaving groups whose pK_a's are 9 or less. How might this be explained? In the case of p-nitrophenyl ester, for example, the tetrahedral intermediate in eq 1 partitions almost exclusively toward product, so that k_{obsd} = k_1. With the ethyl and benzyl esters, partitioning favors reactants, so that k_{obsd} now equals $k_1(k_3/k_2)$ where $k_3/k_2 \ll 1$. The phenyl ester lies in a borderline region where neither step in eq 1 is rate-determining. Surprisingly, the preferential movement of tetrahedral intermediate toward product requires phenols of pK_a < 9 (more than 3 units *below* the pK_a of the reactive β-cyclodextrin hydroxyl[14]). The β-cyclodextrin oxyanion behaves, therefore, as a much better leaving group than one might expect from its pK_a. The reason for this is critical to the understanding of the "p-nitrophenyl ester syndrome". Acylated β-cyclodextrin possesses a high-energy s-cis configuration[15,16] (eq 1) that need not form in simple ester interchanges or hydrolyses. As a result, the tetrahedral intermediate in eq 1 tends to eject the β-cyclodextrin oxyanion and revert to unreacted complex. Clearly, chymotrypsin modelling has disguised its inadequacies by employing substrates whose leaving groups have pK_a values below 9; partitioning toward product then occurs despite the deleterious s-cis effect and despite the absence of electrophilic assistance to the departing entity.

An additional explanation for the data in Table I (consistent with our "spatiotemporal hypothesis"[17]) must be mentioned. Assume that (a) all ester complexes have an identical HO/C=O distance and (b) the "critical distance"[17] for carbonyl addition is smaller for less reactive esters. Therefore, the HO/C=O distance within the complex can be productive for the p-nitrophenyl ester but not for the ethyl ester.

Correcting the above shortcomings via more advantageous positioning of the hydroxyl, in order to catalyze the hydrolysis of authentic substrates, presents a challenge that nature, but not organic chemistry, has already met.

Supplementary Material Available: Analytical, melting point, and spectroscopic data on the new compounds in Table I (second through sixth entries) (4 pages). Ordering information is given on any current masthead page.

(13) Komiyama, M.; Hirai, H. *Chem. Lett.* **1980**, 1467.
(14) VanEtten, R. L.; Clowes, G. A.; Sebastian, J. F.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3253.
(15) Gandour, R. D. *Bioorg. Chem.* **1981**, *10*, 169.
(16) Huisgen, R.; Ott, H. *Tetrahedron* **1959**, *6*, 253.
(17) Menger, F. M. *Acc. Chem. Res.* **1985**, *18*, 128.

The First Hydrocarbyl Trinuclear and Tetranuclear Clusters of Tungsten: W₃O(CH₂Ph)(O-i-Pr)₉ and W₃O(R)₂(O-i-Pr)₈ Where R = CH₂Ph, Ph, and W₄(p-tolyl)₂(O-i-Pr)₁₀

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Examples of transition-metal clusters containing alkyl[1] and σ-aryl[2] ligands have been known since the early 1970's but as a class of compounds there are relatively few well-characterized members. Indeed the first structural characterization of an alkyl cluster supported by carbonyl ligands was only just reported.[3] We describe here the synthesis and characterization of the first tungsten clusters bearing hydrocarbyl ligands. These compounds are of particular interest with respect to the development of cluster chemistry supported by alkoxide ligands.[4]

Addition of i-PrOH (5 equiv) to hexane solutions of W₂(p-tolyl)₂(NMe₂)₄[5] at 0 °C affords the green, tetranuclear cluster W₄(p-tolyl)₂(O-i-Pr)₁₀ (1) in ca. 40% isolated crystalline yield according to eq 1.[6] The ¹H and ¹³C{¹H} NMR data[6] for 1 are

$$W_2(p\text{-tolyl})_2(NMe_2)_4 + 5i\text{-PrOH} \rightarrow$$
$$^1/_2 W_4(p\text{-tolyl})_2(O\text{-}i\text{-Pr})_{10} + C_6H_5Me + 4\,HNMe_2 \quad (1)$$
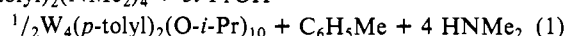
consistent with a static, tetranuclear cluster containing two inequivalent aryl groups and 10 inequivalent O-i-Pr ligands, each having diastereotopic methyl groups. The formation of W₄(p-tolyl)₂(O-i-Pr)₁₀ in eq 1 may be understood in terms of coupling two W₂(p-tolyl)(O-i-Pr)₅(M≡M) compounds in a related manner to the dimerization of two W₂(O-i-Pr)₆(M≡M) species which yields W₄(O-i-Pr)₁₂.[7] The molecular structure of 1[8] is shown in Figure 1 and provides an unprecedented structural type for a 12-electron M₄ cluster.[9] On the basis of M-M distances, one

(1) Mertis, K.; Masters, A. F.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1976**, 858.
(2) Bradford, C. W.; Nyholm, R. S.; Gainsford, G. J.; Guss, J. M.; Irland, R. P.; Mason, R. *J. Chem. Soc., Chem. Commun.* **1972**, 87.
(3) Zuffa, J. L.; Gladfelter, W. L. *J. Am. Chem. Soc.* **1986**, *108*, 4669.
(4) Chisholm, M. H. *ACS Symp. Ser.* **1983**, *No. 211*, 243. Buhro, W. E.; Chisholm, M. H. *Adv. Organomet. Chem.*, in press.
(5) Chetcutti, M. J.; Chisholm, M. H.; Folting, K.; Haitko, D. A.; Huffman, J. C.; Janos, J. *J. Am. Chem. Soc.* **1983**, *105*, 1163.
(6) Dry and oxygen-free solvents and atmospheres (N₂) were used throughout. *Selected* NMR data for the compounds are given below; chemical shifts in ppm relative to Me₄Si (relative intensity, multiplicity). (a) W₄(p-tolyl)₂(O-i-Pr)₁₀: ¹H NMR (C₆D₆ at 25 °C) C₆H₄Me, ortho 7.86 7.70 (2, d); C₆H₄Me, meta 7.26, 7.13 (2, d); OCHMe₂, 6.44, 5.09, 5.07, 4.83, 4.75, 4.71, 4.65, 4.43, 4.28, 4.22 (1, septets); C₆H₄Me 2.51, 2.20 (s, 3); 20 equal intensity doublets are observed between 1.9 and 0.7 ppm for the OCHMe₂ groups. ¹³C{¹H} NMR (C₆D₆ at 25 °C) C₆H₄Me, ipso 188.8 (¹J₁₈₃w₋₁₃c = 134 Hz), 181.3 (¹J₁₈₃w₋₁₃c = 123 Hz); OCHMe₂ 83.7, 82.4, 77.9, 77.6, 77.4, 77.2 (intensity 2), 75.1, 74.7, 74.4. (b) W₃O(Ph)₂(O-i-Pr)₈: ¹H NMR (C₆D₆ at 25 °C) C₆H₅, ortho 8.45 (4, d); C₆H₅, meta 7.51 (4, t); C₆H₅; para 7.28 (2, t); OCHMe₂ 5.34, 5.33 (2, septets), 5.49, 5.17, 4.69, 4.16 (1, septets); eight equal intensity doublets are observed between 1.6 and 1.0 ppm for the OCHMe₂ groups. (c) W₃O(CH₂Ph)₂(O-i-Pr)₈: ¹H NMR (C₆D₅, 25 °C) CH₂C₆H₅, ortho 7.38 (4, d); CH₂C₆H₅, meta 7.23 (4, t); CH₂C₆H₅, para 6.87 (2, t); CH₂C₆H₅ 3.39, 3.16 (2, d of an AB quartet, ²J₁₈₃w₋₁H = 6 Hz). (d) W₃O(CH₂Ph)(O-i-Pr)₉: ¹H NMR (C₆D₆ at 25 °C) CH₂C₆H₅, ortho 7.28 (2, d); CH₂C₆H₅, meta 7.19 (2, t); CH₂C₆H₅, para 6.89 (1, t); CH₂C₆H₅, 3.43 (s, 2, ²J₁₈₃w₋₁H = 10 Hz); OCHMe₂ 5.54, 5.32, 4.94 (2, septets), 5.61, 5.26, 4.07 (1, septets); nine equal intensity doublets are observed between 1.7 and 1.1 ppm for the OCHMe₂ groups.
(7) Chisholm, M. H.; Clark, D. L.; Folting, K.; Huffman, J. C. *Angew. Chem., Int. Ed. Engl.*, in press; *Angew. Chem.* **1986**, *25*, 1021.
(8) Crystal data: (a) W₄(p-tolyl)₂(O-i-Pr)₁₀ at −156 °C: a = 12.051 (3) Å, b = 20.339 (3) Å, c = 21.460 (5) Å, β = 94.95 (1)°, Z = 4, d_{calcd} = 1.882 g cm⁻³, and space group Cc. Of 3432 unique reflections (Mo Kα, 6° ⩽ 2θ ⩽ 45°) 3334 reflections having $F > 3\sigma(F)$ were used in the full least-squares refinement. Final residuals are $R(F)$ = 0.053 and $R_w(F)$ = 0.055. (b) W₃O(Ph)₂(O-i-Pr)₈ at −153 °C: a = 12.136 (2) Å, b = 25.217 (6) Å, c = 13.762 (3) Å, β = 92.58 (1)°, Z = 4, d_{calcd} = 1.886 g cm⁻³, and space group $P2_1/n$. Of 5514 unique reflections (Mo Kα, 6° ⩽ 2θ ⩽ 45°) 4336 reflections having $F > 3\sigma(R)$ were used in the full least-squares refinement. Final residuals are $R(F)$ = 0.064 and $R_w(F)$ = 0.061.
(9) Chisholm, M. H.; Errington, R. J.; Folting, K.; Huffman, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 2025 and references therein.
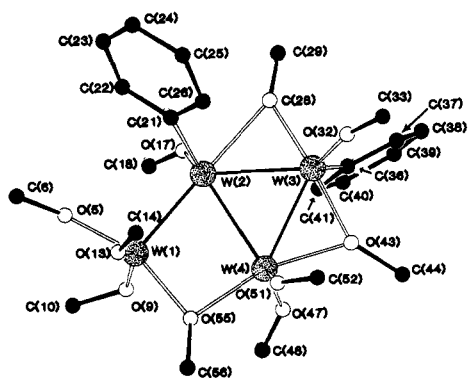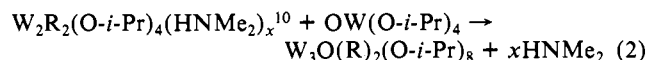
Figure 1. Ball-and-stick drawing of the central $W_4(p\text{-tolyl})_2(OC)_{10}$ core of the $W_4(p\text{-tolyl})_2(O\text{-}i\text{-Pr})_{10}$ molecule. Pertinent bond distances (Å) and bond angles (deg), averaged where appropriate: W(1)–W(2) = 2.4780 (18); W(2)–W(3) = 2.5507 (17); W(3)–W(4) = 2.6088 (18); W(2)–W-(4) = 2.7452 (17); W(1)–W(4) = 3.0105 (17); W–C(aryl) = 2.14 (5); W–O(terminal) = 1.90 (5); W–O(bridging) = 2.05 (5) except W(2)–O-(28) = 2.265 (20) and W(3)–O(28) = 1.949 (20). W(1)–W(2)–W(4) = 70.18 (5); W(3)–W(2)–W(4) = 58.89 (5); W(2)–W(3)–W(4) = 64.28 (5); W(2)–W(4)–W(3) = 56.83 (5).

may describe the M–M bonding in terms of the valence bond description shown in A. This represents a grossly distorted rhombus of metal atoms.
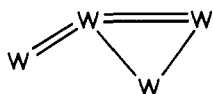

A

A similar strategy can be used to prepare trinuclear-alkyl and σ-bound-aryl tungsten clusters. The comproportionation reaction, eq 2, has been employed in the attempted syntheses of compounds

$$W_2R_2(O\text{-}i\text{-Pr})_4(HNMe_2)_x{}^{10} + OW(O\text{-}i\text{-Pr})_4 \rightarrow$$
$$W_3O(R)_2(O\text{-}i\text{-Pr})_8 + xHNMe_2 \quad (2)$$

2: R = Ph, x = 1; R = CH₂Ph, x = 0

of formula $W_3O(R)_2(O\text{-}i\text{-Pr})_8$ (**2**), but only when R = Ph or CH₂Ph has this proved successful. When R = CH₂-t-Bu and CH₂SiMe₃ reactions proceed via a more complex pathway involving elimination of RH.

The ¹H and ¹³C{¹H} NMR spectra of **2** are consistent with a static structure containing equivalent R groups and one molecular plane of symmetry as shown in B.
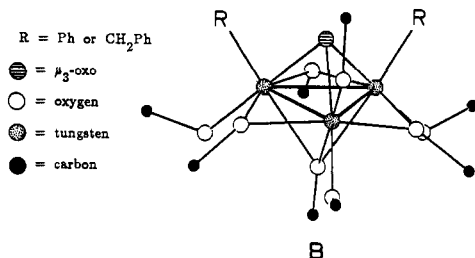
B

Structure B is related to that established for $M_3(\mu_3\text{-O})(\mu_3\text{-OR})(\mu\text{-OR})_3(OR)_6$ compounds (M = Mo and W; R = i-Pr and CH₂-t-Bu)¹¹ where two terminal O-i-Pr ligands cis to the oxo capping ligand are substituted by R groups.

From reactions involving R = Ph, crystals of **2** have been isolated in ca. 30% yield and the proposed structure B has been

confirmed by single-crystal X-ray crystallography.⁸ For R = CH₂Ph, **2** is unstable and a further reaction occurs to give $W_3O(CH_2Ph)(O\text{-}i\text{-Pr})_9$ (**3**) and other as yet uncharacterized tungsten-containing compounds. NMR data⁶ for **3** reliably establish this compound as a six-electron W₃ cluster having the structure diagramatically depicted by C.

C
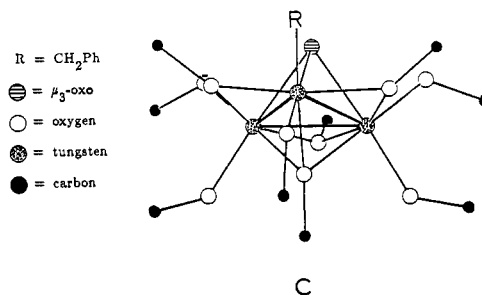
Further studies are in progress.¹²

Supplementary Material Available: Fractional coordinates, anisotropic thermal parameters, and complete listings of bond distances and angles for $W_3O(Ph)_2(O\text{-}i\text{-Pr})_8$ and $W_4(p\text{-tolyl})_2\text{-}(O\text{-}i\text{-Pr})_{10}$ (10 pages). Ordering information is given on any current masthead page.

Total Synthesis of (±)-Grosshemin

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The guaianolide family is one of the largest and most widely distributed groups of naturally occuring sesquiterpene lactones.¹ Until recently no member of this intriguing class of natural products had succumbed to total synthesis and to date only three groups have reported syntheses in this area.² This surprising paucity of activity is in dramatic contrast to the host of synthetic successes that have been forthcoming in the closely related pseudoguaianolide field.³ We wish to report the first total synthesis of (±)-grosshemin (**1**) starting from the readily available seven-membered ring species tropone (**2**).
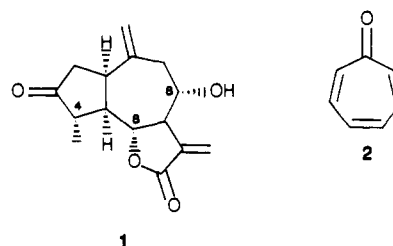
The strategy used in this synthesis focuses on assembling, early in the scheme, a functionalized hydroazulene intermediate which has the A-ring substitution pattern intact in its final form. This approach differs significantly from previous efforts in this area which generally have postponed manipulation of the A ring until the end of the synthesis.²ᵃ,⁴ The γ-butyrolactone unit would then

(10) Chisholm, M. H.; Eichhorn, B. W.; Folting, K.; Huffman, J. C.; Tatz, R. J. *Organometallics* **1986**, *5*, 1599.

(11) Chisholm, M. H.; Folting, K.; Huffman, J. C.; Kirkpatrick, C. C. *Inorg. Chem.* **1984**, *23*, 1021. Chisholm, M. H.; Folting, K.; Huffman, J. C.; Kober, E. M. *Inorg. Chem.* **1985**, *24*, 241.

(12) We thank the Department of Energy, Office of Basic Science, Chemistry Division, and the Wrubel Computing Center for support. B.W.E. is the 1986/1987 Indiana University SOHIO fellow.

(1) Fischer, N. H.; Olivier, E. J.; Fischer, H. D. *Fortschr. Chem. Org. Naturst.* **1979**, *38*, 47.

(2) (a) Rigby, J. H.; Wilson, J. Z. *J. Am. Chem. Soc.* **1984**, *106*, 8217. (b) Devreese, A. A.; Demuynck, M.; DeClercq, P. J.; Vandewalle, M. *Tetrahedron* **1983**, *39*, 3049. (c) Posner, G. H.; Babiak, K. A.; Loomis, G. L.; Frazee, W. J.; Mittal, R. D.; Karle, I. L. *J. Am. Chem. Soc.* **1980**, *102*, 7498.

(3) Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. In *The Total Synthesis of Natural Products*; Apsimon, J. W., Ed. Wiley: New York, 1982; Vol. 5.

(4) For an alternative route into the C_8 oxygenated guaianolide system, see: Rigby, J. H.; Wilson, J. Z. *J. Org. Chem.* **1987**, *52*, 34.