Stabilization of the dienonylic form of the A-ring of .beta.-estradiol by the "Cp*Rh" fragment. X-ray structure of the rhodium complex .alpha.-[(.eta.5-estradienonyl)RhCp*]BF4 (Cp* = C5Me5)

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Stabilization of the Dienonylic Form of the A-Ring of β-Estradiol by the "Cp*Rh" Fragment. X-ray Structure of α-[(η⁵-estradienonyl)RhCp*]BF_4 (Cp* = C_5Me_5)

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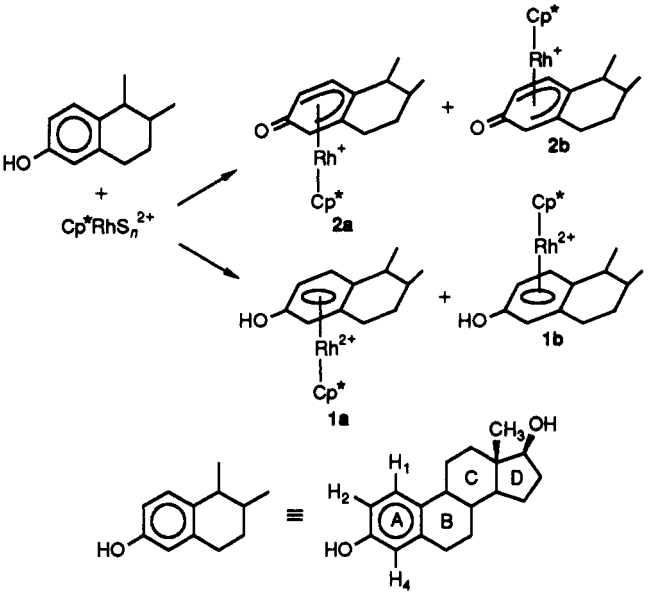
Summary: Treatment of $Cp^*RhS_n^{2+}(BF_4^-)_2$ (S = coordinated solvent) with 1 equiv of β-estradiol in acetone/THF solution afforded the α- and β-isomers of [(η⁶-estradiol)RhCp*]$(BF_4)_2$ (**1a,b**) and the α- and β-isomers of [(η⁵-estradienonyl)RhCp*]BF_4 (**2a,b**), depending on the side of the complexation at the arene ring. Interestingly, the introduction of the $Cp^*RhS_n^{2+}(BF_4^-)_2$ moiety at the A-ring of the β-estradiol modifies its phenolic character to give the corresponding dienonylic form. This result was confirmed by an X-ray structural determination of the α-isomer **2a**. [(η⁵-estradienonyl)RhCp*]BF_4 (**2a**) reacts with HBF_4 to give quantitatively the corresponding complex [(η⁶-estradiol)RhCp*]$(BF_4)_2$ (**1a**); however, in the presence of NEt_3 **2a** was regenerated.

Interest in the solution behavior and reactivity of $Cp^*Rh^{III}(\eta^6\text{-arene})^{2+}$ sandwich compounds has been growing over the last decade.[1,2] These compounds can be reduced to Rh(I) (d^8) and reoxidized to Rh(III) (d^6) reversibly via either electrochemical or chemical routes.[3] In the reduced form the arene ligand changes its hapticity from η^6 to η^4 concomitant with loss of planarity as confirmed by the X-ray structure of $Cp^*Rh^I(\eta^4\text{-}C_6Me_6)$.[4] Analogous to these compounds are species possessing functionalized aromatic rings such as phenols or benzoic acid; however, fewer studies in this area have been documented; we note the example of $[Rh(\eta^6\text{-PhO})(PPh_3)_2]\cdot 2PhOH$ reported by Wilkinson et al. In this complex the phenol ligand is activated to its phenoxo form;[5] most of the chemical properties of phenols may be explained in terms of these two mesomeric forms. Recently Chaudret et al. have reported the synthesis of the compounds $[Cp^*Ru(\eta^6\text{-PhO})]\cdot 2PhOH$ and $[Cp^*Ru(\eta^6\text{-}PhCO_2)]$, defined as zwitterions in which the phenol and benzoic acid ligands are modified to their phenoxo and benzoate forms, respectively. This was proposed on the basis of spectroscopic results; however, no X-ray structural determination was reported.[6] In light of these results and others[7] we have investigated the complexation of the $Cp^*RhS_n^{2+}(BF_4^-)_2$ (S = solvent) fragment at the A-ring of β-estradiol. This type of complex is known to exhibit recognition toward the estradiol receptor; a notable example is the complex α-[(3-*O*-(hydroxypropyl)estradiol]$Cr(CO)_3$,[8] which displays a binding affinity toward the estradiol receptor of RBA = 28% compared to that of free estradiol, taken as 100%. Furthermore, this new series is expected to allow electronic delocalization through the A-ring of the estradiol ligand as well as at the Rh(III) metal center. In this communication we report the synthesis and the X-ray structure of α-[(η⁵-estradienonyl)RhCp*]BF_4 (**2a**), in which the organometallic moiety "Cp*Rh" is coordinated to the α-face of the A-ring of the hormone. In this compound the A-ring loses its planar character by adopting an η^5 coordination mode; however, it remains a six-electron donor ligand to the rhodium center, which is considered as Rh(III). Finally, the reactivity of this species with HBF_4 and NEt_3 is discussed.

Scheme I



When a THF solution of β-estradiol (136 mg, 0.5 mmol) was treated with 0.5 mmol of $RhCp^*S_n^{2+}(BF_4^-)_2$ (S = acetone) in acetone, at room temperature over 2 h, the initial yellow solution decolorized and a white precipitate formed. Analysis of the two phases by ^1H NMR showed a mixture of four products: α-[Cp*Rh(η⁶-estradiol)]$(BF_2)_2$ **1a**, 54%), β-[Cp*Rh(η⁶-estradiol)]$(BF_4)_2$ **1b**, 8.5%), α-[Cp*Rh(η⁵-estradienonyl)]BF_4 (**2a**, 33%), and β-[Cp*Rh-(η⁵-estradienonyl)]BF_4 (**2b**, 4.5%) (Scheme I). $RhCp^*S_n^{2+}(BF_4^-)_2$ (S = solvent) was prepared from $[RhCp^*Cl_2]_2$ and $AgBF_4$ in acetone by following the procedure of Maitlis et al.[9] We would like to draw attention

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Table I. ^{1}H NMR Data for Compounds 1a,b and 2a,b (250 MHz, CD_3CN Solution)[a]

compd	H_1	H_2	H_4	$C^{17}H_3$	Cp*
β-estradiol	7.10 d	6.54 dd	6.50 d	0.73 s	
1a	6.90 d	6.57 dd	6.47 d	0.72 s	2.03 s
1b	6.86 d	6.45 dd	6.53 d	0.73 s	2.08 s
2a	6.42 d	5.47 dd	5.35 d	0.75 s	2.09 s
2b	6.35 d	5.10 dd	5.26 d	0.71 s	1.97 s

[a] In δ (ppm). Abbreviations: d, doublet; dd, doublet of doublets; s singlet. $J_{H_1-H_2}$ = 7.5 Hz, $J_{H_2-H_4}$ = 2.5 Hz, and $J_{H_1-H_4}$ = 0 for all compounds.

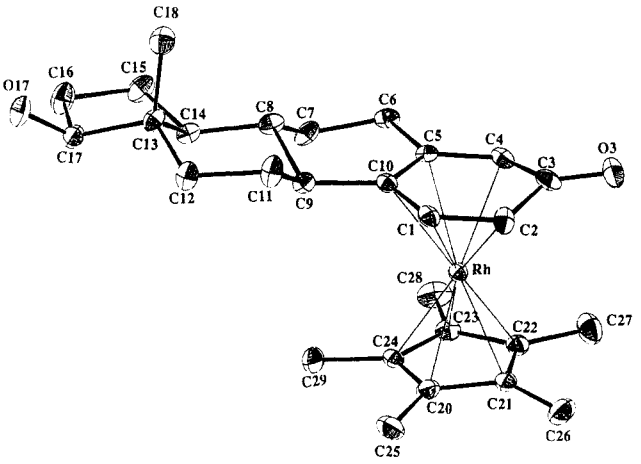


Figure 1. X-ray structure of α-Cp*Rh(η^5-estradienonyl)]$^+$ (**2a**). Selected bond distances (Å) and angles (deg): Rh(1)–C(1) = 2.195 (8), Rh (1)–C(2) = 2.224 (9), Rh(1)–C(4) = 2.233 (8), Rh(1)–C(5) = 2.231 (8), Rh(1)–C(1)–C(10) = 2.240 (8), Rh(1)–C(3) = 2.495 (9), Rh(1)–C(20) = 2.186 (8), Rh(1)–C(21) = 2.157 (8), Rh(1)–C(22) = 2.143 (8), Rh(1)–C(23) = 2.155 (8), Rh(1)–C(24) = 2.190 (8), C(1)–C2) = 1.38 (1), C(2)–C(3) = 1.48 (1), C(3)–C(4) = 1.46 (1), C(5)–C(10) = 1.43 (1), C(1)–C(10) = 1.42 (1), C(3)–O(3) = 1.20 (1), C(4)–C(5) = 1.39 (1); C(10)–C(1)–C(2) = 122.8 (8), O(3)–C-(3)–C(2) = 124.7 (10), C(4)–C(3)–O(3) = 125.3 (10), C(10)–C-(5)–C(4) = 119.6 (8), C(3)–C(2)–C(1) = 122.8 (9), C(4)–C(3)–C(2) - 109.7 (8), C(5)–C(4)–C(3) = 125.4 (8).

to a new high-yield route to the starting material $[RhCp^*Cl_2]_2$, by starting from $[Rh(cod)Cl]_2$ and HCp* in methanol, in the presence of concentrated HCl as oxidizing agent.[10]

Compounds **1a,b** and **2a,b** were separated by fractional crystallization, and these complexes were characterized by microanalyses and spectroscopic methods. In the ^{1}H NMR spectra of compounds **1a,b** and **2a,b**, the resonances for the aromatic protons H_1, H_2, and H_4 occur at high field relative to those of the free ligand (see Table I). In general, arene coordination to a transition metal results in a loss of π-electron density at the arene ligand and a concomitant increase in the anisotropic magnetic shielding component, manifested as a high-field shift in the resonances of the aromatic protons.[11,12]

The ^{1}H NMR spectra of **2a,b**, recorded in CD_3CN, show a further upfield shift, relative to that of **1a,b** (see Table I). We interpret these results as indicative of a loss of

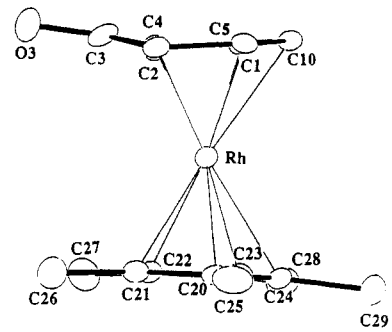
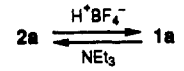


Figure 2. Perspective view of the molecular structure of **2a** showing the Cp*Rh fragment coordinated to only the A-ring of β-estradiol.

Scheme II



aromaticity in favor of a vinylic description for the arene coordination; this description implies that activation of the hydroxyl group to its ketonic form has occurred. Similar results were reported by Chaudret et al. in comparing the two species [Cp*Ru(η^6-PhO)]·2PhOH and [Cp*Ru(η^6-PhOH)]CF_3SO_3.[6] It should be pointed out, however, that the chemical shifts of protons H_2 and H_4 in compounds **1a** and **2a** are permuted relative to those of **1b** and **2b**; this is due to the anisotropic magnetic shielding, which operates differently depending on whether the compound is the α- or the β-species[12] (see Table I).

Recrystallization of a mixture of **1a** and **2a** in a CH_3CN/ether solution afforded yellow crystals of the more stable species **2a**.[13] The structure of **2a**, determined by X-ray crystallography (Figure 1), shows that the rhodium center is coordinated to only five carbons of the steroid A-ring. The bond distance Rh–C_3 is 2.495 (9) Å, thus excluding any interaction between the metal center and C_3 of the A-ring, while the C_3–O_3 bond of 1.20 Å is typical of a double bond. The latter distance is shorter than that reported for the compounds [Rh(η^5-2,6tBu$_2$-4-MeC$_6$H$_2$O)(PPh$_3$)$_2$] (1.28 Å) and [Ru(η^5-2,6-tBu$_2$C$_6$H$_3$O)-Cp*] (1.256 Å).[14,15] Loss of aromatic character in the A-ring is reflected in (i) the elongation of the bonds C_2–C_3 (1.48 (1) Å) and C_3–C_4 (1.46 (1) Å) compared to C_1–C_2 (1.38 Å), C_4–C_5 (1.39 Å), C_1–C_{10} (1.42 Å), and C_5–C_{10} (1.43 Å) and (ii) the dihedral angle along the C_2–C_4 axis of 16° (Figure 2). This angle is similar to that observed for the

(10) Synthesis of $[RhCp^*Cl_2]_2$: 1 mL of concentrated HCl (35%) was added to a Schlenk tube containing a suspension of $[Rh(cod)Cl]_2$ (498 mg, 1 mmol) in 20 mL of methanol and 0.5 mL (3.2 mmol) of pentamethylcyclopentadiene. The reaction mixture was refluxed under argon for 2 h, during which time a burgundy microcrystalline species crystallized out of solution; the precipitate was separated and identified as $[RhCp^*Cl_2]_2$, yield 565 mg (91%). Anal. Calcd for $C_{20}H_{30}Cl_4Rh_2$: C, 38.83; H, 4,85; Cl, 22.97; Rh, 33.3. Found: C, 38.87; H, 4.78; Cl, 23.46; Rh, 33.06. ^{1}H NMR ($CDCl_3$): δ 1.62 (C_5Me_5, s).

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(13) Anal. Calcd for $C_{28}H_{38}O_2BF_4Rh$ (**2a**): C, 56.37; H, 6.37; B, 1.8; F, 12.75. Found: C, 56.52; H, 6.35; B, 1.78; F, 12.46. IR (KBr, ν(C=O), **2a**): 1596 cm^{-1} (strong). X-ray diffraction data for **1a**: yellow crystals, 0.2 × 0.2 × 0.7 mm; space group orthorhombic $P2_12_12_1$, a = 8.3248 (1) Å, b = 12.404 (2) Å, c = 25.189 (3) Å, V = 2602 Å^3, Z = 4, ρ_{calcd} = 1.52 g/cm^3, μ(Mo Kα) = 6.96 cm^{-1}; Nonius CAD4F diffractometer, graphite monochromated; Mo Kα radiation (λ = 0.7170 Å), room temperature, 2614 reflections collected ($3 < 2\theta < 50°$), 2160 reflections used ($I > 3\sigma(I)$); R = 0.04, R_w = 0.046 (w = 1); 301 variables. Computations were performed by using Crystals[13a] adapted for a Microvax-II computer. Scattering factors and corrections for anomalous dispersion were from ref 13b. Solution of the structure was accomplished by standard Patterson–Fourier techniques; all non-hydrogen atoms were refined anisotropically, and 33 H atoms were located on a difference Fourier map (except for OH). They were included as fixed contributors (with U_{iso}(H) = 1.2U_{eq} of the bonded carbon) so as to improve the data to variable ratio. (a) Watkin D. J.; Carruthers, J. R.; Betteridge, P. W. *CRYSTALS User Guide*; Chemical Crystallography Laboratory, University of Oxford: Oxford, England, 1986. (b) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV.

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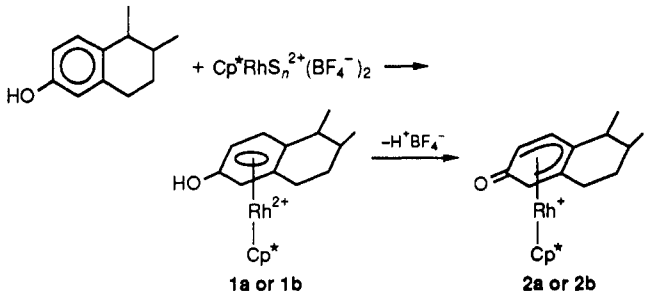
Scheme III



complex [Ru(η^5-2,6-t$Bu_2C_6H_3O$)Cp*] (19.1°).[15]

In order to investigate the solution behavior of the complexes **2a,b**, we have studied their reactivity with HBF_4. Treatment of [Cp*Rh(η^5-estradienonyl)]BF_4 with HBF_4 yielded [Cp*Rh(η^6-estradiol)]$(BF_4)_2$ (**1a,b**) quantitatively, while in the presence of NEt_3 the initial species was regenerated (Scheme II). In addition, we note that in strongly coordinating basic solvents, such as DMSO, compounds **1a,b** were transformed immediately to the conjugated dienonylic form, **2a,b**. In CH_3CN, this transformation was slower, occurring over a 10-h period. Due to solubility limitations, other solvents were not studied. It is possible that the driving force for this transformation (**1a,b** → **2a,b**) could be related to the high oxidation state of the rhodium metal in the organometallic moiety Cp*Rh^{III}, which pulls electronic density from the A-ring of β-estradiol and renders the phenol group more acidic.

Repetition of the initial reaction of β-estradiol and RhCp*S$_n^{2+}$(BF$_4^-$)$_2$ (S = acetone, Scheme I), in the presence of HBF_4, led to the formation of complex **1a**[16] as the major compound. Upon recrystallization in acetone/ether solution, however, this unstable species gave **2a** in 20% yield. This indicates that a possible route for the synthesis of the species **2a,b** involves initial formation of the kinetically favored species **1a,b**, with subsequent loss of one molecule of HBF_4 to give the thermodynamically more stable species, either **2a** or **2b** (Scheme III).

Studies on the reactivity of these complexes and their electrochemical behavior are currently in progress.

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Supplementary Material Available: Tables of positional and thermal parameters and complete bond distances and angles (5 pages); a listing of calculated and observed structure factors (9 pages). Ordering information is given on any current masthead page.

(16) Anal. Calcd. for $C_{28}H_{39}O_2B_2F_8Rh$ (**1a**): C, 49.12; H, 5.70. Found: C, 49.70; H, 5.69.

Relative Magnitude of the β-Effect of Silyl, Germyl, and Stannyl Groups in the Stabilization of Vinyl Cations

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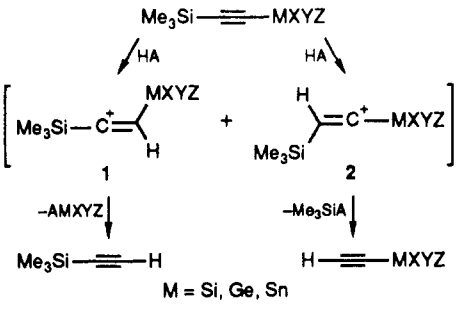
Summary: The competitive addition of acids to 1,2-dimetalated acetylene compounds shows that the relative degree of hyperconjugative stabilization (β-effect) of vinyl cations follows the general trend Sn > Ge > Si but can be altered to a degree by the appropriate modification of the other groups borne by the metal.

The stabilization of vinyl cation intermediates, including hyperconjugative stabilization by a β-silyl group (β-effect), has been reviewed.[1,2] However, examples of the ability of the lower group 14 (group IVA) elements Ge and Sn to stabilize such species have not been reported. We have, therefore, undertaken experiments that allow a comparison of the degree to which the ligands borne by the metal and the metal itself change the magnitude of the β-effect for vinyl cations.

The premise of the experiment is that competitive protonation of a dimetalated acetylene will proceed via the most stable β-carbocation (stronger β-effect) and lead, after loss of the better stabilizing group, to a monometalated acetylene (Scheme I).

Scheme I



We chose to use the $SiMe_3$ group as a reference point. A series of metalated (trimethylsilyl)acetylenes was prepared by the reaction of lithium (trimethylsilyl)acetylide (1.1 equiv) with the appropriate silyl/germyl/stannyl chloride (1.0 equiv, 1–5 M, THF or ether, 0–25 °C, nitrogen atmosphere). The protonations were carried out in $CDCl_3$ solution with several acids, including F_3CSO_3H, $MeSO_3H$, F_3CCOOH, Cl_3CCOOH, $Cl_2HCCOOH$, and $ClCH_2COOH$.

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