Controlled and Selective Introduction of a Cp^*Ru^+ ($Cp^* = C_5Me_5$) Fragment to the 17α-Substituent of 17α-Phenylestradiol

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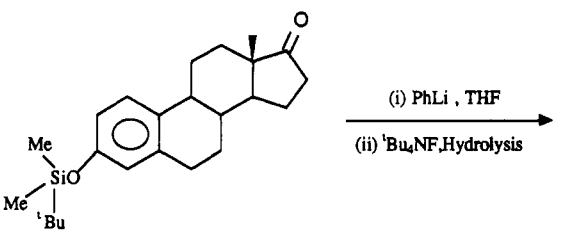
Summary: 17α-Phenylestradiol (**3**) was prepared from 3-*O*-(dimethyl-*tert*-butylsilyl)estrone and PhLi in 67% yield. An X-ray study of **3** shows that it has an orthorhombic unit cell with space group $P2_12_12_1$ and a = 7.325 (4) Å, b = 17.590 (3) Å, c = 18.778 (5) Å, and Z = 4. The ORTEP view of 17α-phenylestradiol (**3**) shows that the phenyl group is on the α-position of the steroid below the plane of the D ring, with the angle θ = 83.8°. When **3** was treated with $[Cp^*Ru(CH_3CN)_3][CF_3SO_3]$ (**1**), the phenolic ring was complexed instead of the 17α-phenyl substituent, thus forming α- and β-[Cp^*Ru(17α-phenyl-η^6-estradiol)]$[CF_3SO_3]$ (**4a,b**). This result suggests that the A ring is more reactive than the 17α-phenyl toward Cp^*Ru^+ coordination. Deactivation of the A ring of **3** by electron-withdrawing groups such as CF_3COO and CH_3COO gave respectively 3-*O*-(trifluoroacetyl)-17α-phenylestradiol (**5a**) and 3-*O*-acetyl-17α-phenylestradiol (**5b**) in quantitative yield. When **5b** was treated with $[Cp^*Ru(CH_3CN)_3][CF_3SO_3]$ (**1**) in a CH_3CN/THF solution and then hydrolyzed with $NaHCO_3$ in MeOH, the target compound [Cp^*Ru(17α-(η^6-phenyl)estradiol)]$[CF_3SO_3]$ (**8**) was isolated and completely characterized by microanalyses and spectroscopic methods (^1H and ^{13}C NMR). These studies help in understanding the factors that control ring preferences toward complexation or/and the selectivity exhibited by $[Cp^*Ru(CH_3CN)_3][CF_3SO_3]$ toward different arene rings in 17α-phenylestradiol (**3**).

The complexation of arenes by Cp^*Ru^+ has been well documented.[1] The common way to prepare the Cp^*Ru^+ fragment utilizes the reduction of $[Cp^*RuCl_2]_2$ to give the Ru(II) species $[Cp^*RuCl]_2$[2] or $[Cp^*Ru(\mu\text{-}Cl)]_4$,[3] depending on the reducing agent. These complexes can be modified to give either $[Cp^*Ru(OMe)]_2$ or $[Cp^*Ru(S)_3]^+X^-$ (S = THF, CH_3CN; X = BF_4, CF_3SO_3), which could react further and complex aromatic rings.

We and others[4] have studied the complexation of some functionalized phenyl rings of steroids such as β-estradiol, methoxyestradiol, and 3-*O*-(hydroxypropyl)estradiol and showed that some of these complexes exhibit reasonable recognition toward the estradiol receptor.[5] Interestingly, our findings on A-ring complexation of β-estradiol by Cp^*Ru^+ match quite well those reported in the literature on phenol coordination,[6] in which the phenolic character is lost in favor of a dienonylic species. So far, few examples have been reported in the literature concerning arene preferences toward Cp*Ru coordination; however, Mann et al. have studied the influence of kinetic and thermodynamic factors on the coordination of polyarenes by CpRu ($Cp = C_5H_5$).[7] In this paper we describe the synthesis and X-ray structure of 17α-phenylestradiol (**3**) as well as the controlled and selective complexation of the less favored 17α-phenyl ring of **3**, thereby deactivating the preferred aromatic A ring. This method can be applied not only to steroid hormones but also to other organic species containing more than one phenyl ring in their skeleton cores.

Scheme I



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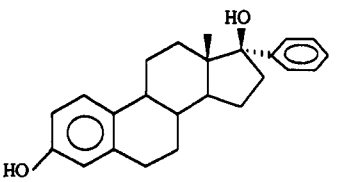

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Results and Discussion

17α-phenylestradiol (**3**) was prepared in 67% yield by following a modified synthetic route.[5b] The product was not purified by chromatography as described previously;[5b] instead, a recrystallization from ether/pentane allowed a higher yield of colorless needles of 17α-phenylestradiol (**3**) (see Scheme I).

The ^1H NMR spectrum of this modified steroid recorded in $CDCl_3$ shows, in addition to the β-estradiol signals, the

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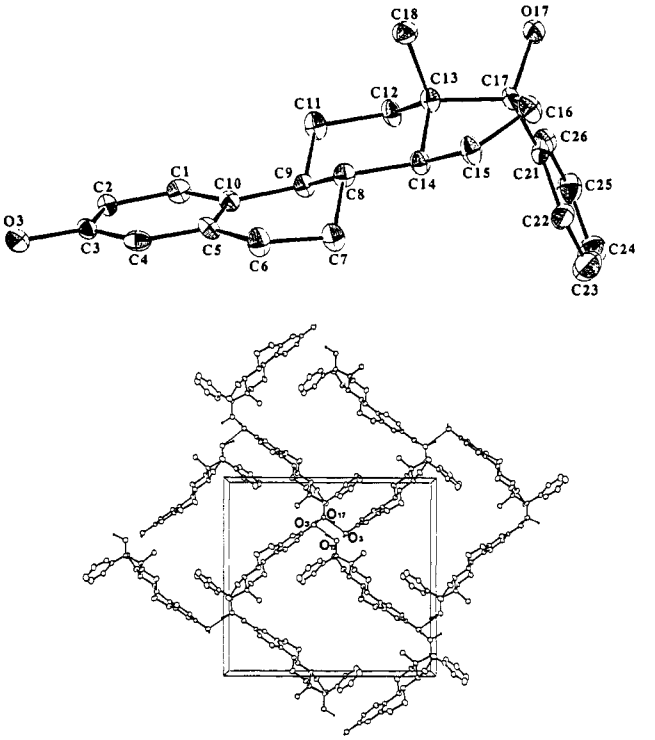


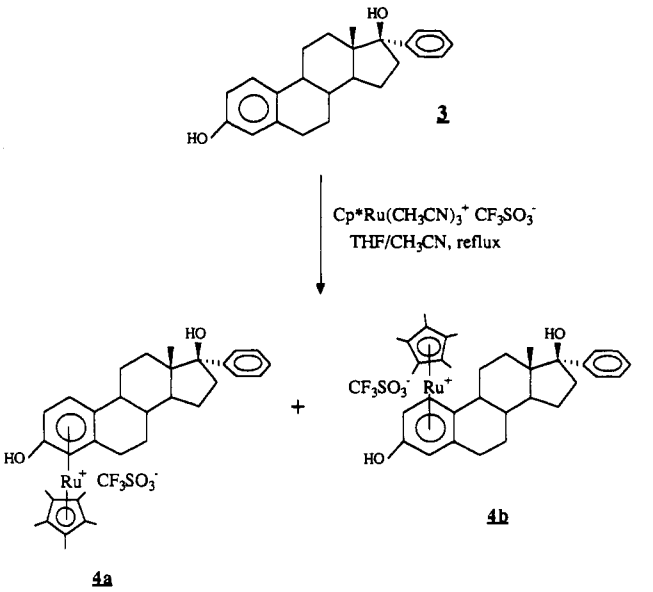
Figure 1. (a, top) X-ray structure of 17α-phenylestradiol (3). Selected bond distances (Å) and angles (deg): C(1)–C(2) = 1.398 (8), C(2)–C(3) = 1.366 (8), C(3)–C(4) = 1.375 (8), C(4)–C(5) = 1.395 (8), C(5)–C(10) = 1.398 (8), C(10)–C(1) = 1.374 (7), C(17)–C(21) = 1.519 (9), C(21)–C(22) = 1.386 (8), C(22)–C(23) = 1.42 (1), C(23)–C(24) = 1.36 (1), C(24)–C(25) = 1.37 (1), C(25)–C(26) = 1.352 (9), C(26)–C(21) = 1.413 (9), C(3)–O(3) = 1.366 (6), C(17)–O(17) = 1.432 (7); O(3)–C(3)–C(4) = 118.6 (5), O(3)–C(3)–C(2) = 122.1 (5), O(17)–C(17)–C(13) = 110.3 (4), O(17)–C(17)–C(16) = 110.6 (5), O(17)–C(17)–C(21) = 108.8 (4), C(26)–C(21)–C(17) = 120.5 (5), C(22)–C(21)–C(17) = 121.4 (5), C(23)–C(22)–C(21) = 118.9 (6), C(25)–C(24)–C(23) = 120.1 (7), C(25)–C(26)–C(21) = 121.9 (6), C(26)–C(21)–C(22) = 118.0 (6), C(24)–C(23)–C(22) = 120.9 (7), C(26)–C(25)–C(24) = 120.2 (7). (b, bottom) ORTEP unit cell representation of **3**. The intermolecular O–H···O hydrogen bonds which link the molecules into infinite chains are indicated by thin lines.

presence of a phenyl group at δ 7.47 (2 H_{ortho}, d), 7.30 (2 H_{meta}, t), and 7.21 ppm (1 H_{para}, m), which is consistent with a monosubstituted C_6H_5 group. In order to ascertain the stereochemistry of this phenyl group, α or β, an X-ray structure determination for **3** was carried out.

(a) X-ray Structure of 17α-Phenylestradiol (3). Suitable crystals for an X-ray study were obtained by slow diffusion of pentane into an ether solution of **3**. The title compound crystallizes in the $P2_12_12_1$ space group. The ORTEP view, as well as selected bond distances and angles, is shown in Figure 1. The structure of **3** shows that the phenyl group is bound to C17 in the α-position below the D ring with an angle of 83.8° between the average plane of the estradiol skeleton and the phenyl ring. Another important feature is the ability of this estrogen derivative to form intermolecular hydrogen bonds among its subunits via O3 and O17, each molecule bound to four others situated on the lower and upper plane with d(O3–O17) = 2.70 Å. Similar results were reported for the parent estradiol molecule.[8] It is noteworthy that the presence of intermolecular hydrogen bonding among estrogen derivatives is an important criterion for hormone–receptor binding.

The relative binding affinity of this hormone toward the estradiol receptor was determined (RBA = 25%)[5b] with respect to the value of estradiol, taken as 100%.

Scheme II



(b) Preparation of α- and β-[(17α-phenylestradiol)Cp*Ru][CF_3SO_3] (4a,b). When 17α-phenylestradiol was treated with 1 equiv of [Cp*Ru($CH_3CN)_3$][CF_3SO_3] (1) in CH_3CN/THF solution, for 12 h, a dark yellow solution was obtained, from which brown oily products were isolated. Analyses of these compounds by ^{1}H NMR spectroscopy in CD_3CN showed that α- and β-[Cp*Ru(17α-phenylη^6-estradiol)][CF_3SO_3] (**4a,b**) were formed (see Scheme II). We note that the chemical shifts of the aromatic protons of the phenyl ring at C17 did not change with respect to those of the free bioligand **3**, while the aromatic protons of the A ring, notably H1, H2, and H4, were shifted upfield at δ 5.87 (d), 5.68 (dd), and 5.66 ppm (d) for **4a** and δ 5.80 (d), 5.50 (dd), and 5.66 ppm (d) for **4b**. These results are similar to those obtained for α- and β-[Cp*Ru(η^6-estradiol)][CF_3SO_3] species, where Cp^*Ru^+ is complexed to the A ring from the α and β faces, respectively.[9]

These results show that, under same experimental conditions the disubstituted phenol A ring in **3** is favored toward Cp^*Ru^+ coordination rather than the 17α-phenyl group. The difference in reactivity between these two arenes is no doubt related to the high electron density in the phenolic ring compared to that of the phenyl ring. This electron density originates from the resonance effect of the OH group,[10] as well as being due to the alkyl groups at the meta and para positions. Furthermore, the phenolic ring is less hindered than the 17α-phenyl group, as shown in the structure of 17α-phenylestradiol. Consequently, this would enhance the reactivity of the A ring toward Cp^*Ru^+ coordination.

(c) Preparation of [Cp*Ru(3-*O*-acetyl-17α-(η^6-phenyl)estradiol)][CF_3SO_3] (7). In order to attain our target compound [Cp*Ru(17α-(η^6-phenyl)estradiol)][CF_3SO_3] (**8**), we studied the introduction of an electron-withdrawing group at the C-3 position of the A ring to deactivate it; hence, complexation of the phenyl group at the 17α-position becomes possible.

17α-Phenylestradiol was first treated with 1 equiv of trifluoroacetic anhydride, $(CF_3COO)_2$, in the presence of

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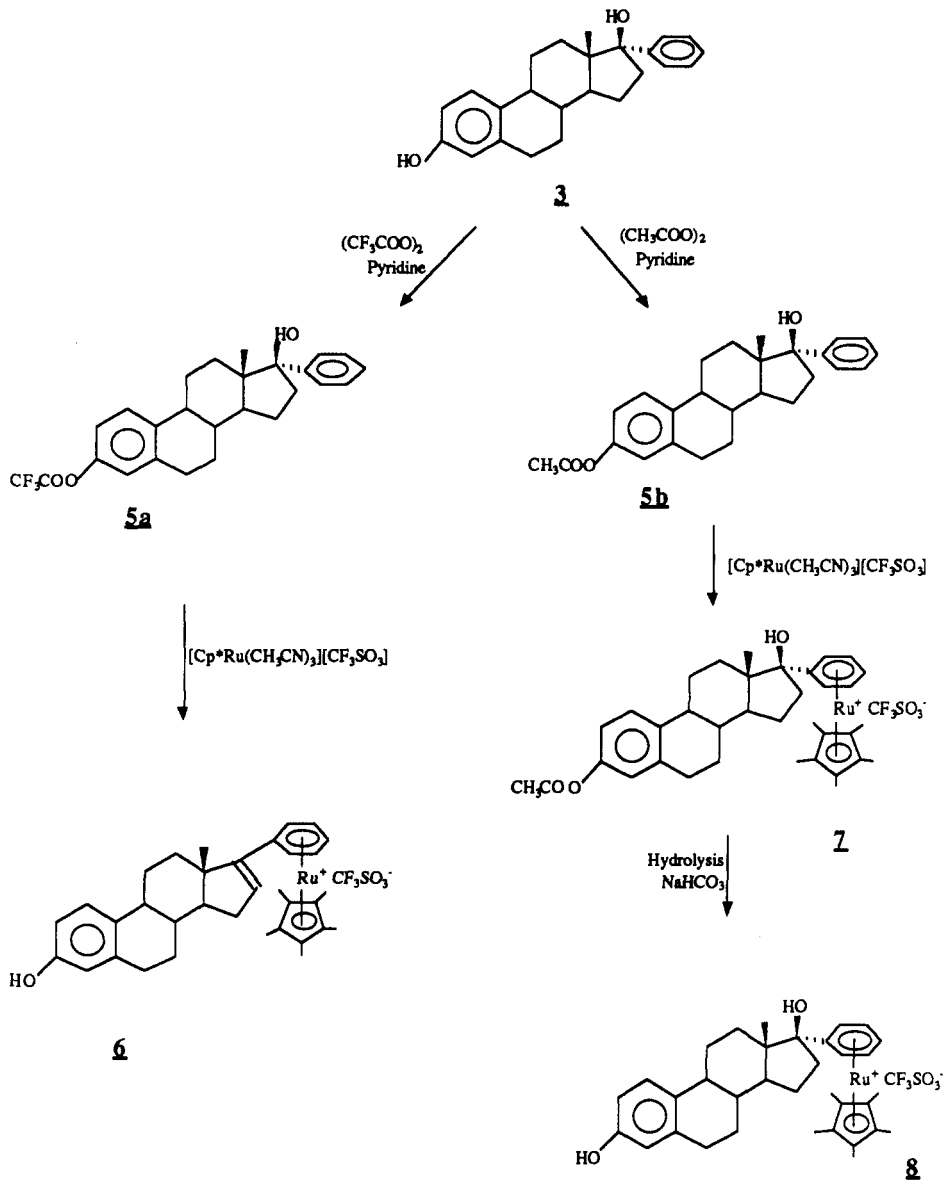
Scheme III



pyridine for 2 h, from which 3-*O*-(trifluoroacetyl)-17α-phenylestradiol (**5a**) was isolated quantitatively. The ^{1}H NMR spectrum of this compound recorded in acetone-d_6 is in agreement with our proposed formula.

When 3-*O*-(trifluoroacetyl)-17α-phenylestradiol (**5a**) was refluxed with 1 equiv of $[Cp^*Ru(CH_3CN)_3][CF_3SO_3]$ in CH_3CN/THF, a yellow solution was obtained from which an oily product was isolated. The ^{1}H NMR spectrum of this compound recorded in acetone-d_6 suggests the formation of $[Cp^*Ru(17\alpha\text{-}(\eta^6\text{-phenyl})C_{19}H_{24}O)][CF_3SO_3]$ (**6**) (see Scheme III). In addition to the usual peaks of 17α-phenylestradiol, we note an upfield shift for the aromatic protons at 6.28 (H_c) and 6.07 ppm (2 $H_{aa'}$ + 2 $H_{bb'}$) of the 17α-phenyl ring, suggesting that complexation by Cp^*Ru^+ has occurred. Further, the presence of a multiplet at δ 6.45 ppm is typical of a vinylic proton. Similar results were reported for the analogous enyne derivatives of $Mo_2Cp_2(CO)_4$(ethynylestradiol) and $Co_2(CO)_6$(ethynylestradiol) obtained by elimination of one molecule of H_2O from the parent carbonium ions, which were stabilized by $Co_2(CO)_6$ and $Mo_2Cp_2(CO)_4$ moieties.[11]

The above reaction suggests that the complexation of the 17α-phenyl ring in **5a** by Cp^*Ru^+ is no doubt followed by elimination of one molecule of H_2O to give the derivative **6** (see Scheme III). It is possible that this elimination reaction is due to the presence of CF_3COOH formed by cleavage of the protecting group of the phenol ring during the complexation reaction. This would later protonate the 17-OH group to give the compound **6**. It appears to us that $(CF_3COO)_2$, although it deactivates the A ring, does not fulfill the conditions necessary to obtain the target compound; hence, we have prepared the analogous 3-acetyl-17α-phenylestradiol (**5b**) by attaching the CH_3COO– fragment to the C-3 position of the 17α-phenylestradiol molecule (**3**).

Treatment of 3-*O*-acetyl-17α-phenylestradiol (**5b**) with 1 equiv of $[Cp^*Ru(CH_3CN)_3][CF_3SO_3]$, in CH_3CN/THF solution for 12 h of reflux, gave a light yellow solution. The solution was concentrated under vacuum. Addition of diethyl ether gave a creamy precipitate (Scheme III). The ^{1}H NMR spectrum of this product recorded at room temperature in acetone-d_6 exhibits two large singlets in the aromatic region at δ 6.24 (H_c, 1 H) and 6.02 ppm (2 $H_{aa'}$ + 2 $H_{bb'}$, 4 H) and 17-OH at δ 4.75 ppm as a large peak, while the signals of H1, H2, and H4 of the A ring did not

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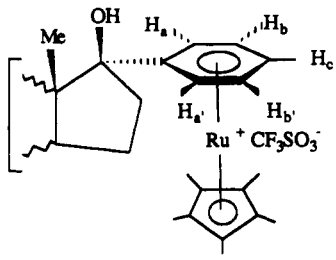

Figure 2.

show any change relative to the free bioligand **5b**. The ^1H NMR spectrum also shows a singlet peak at δ 2.2 ppm (3 H), which is attributed to the Me group of the acetoxy function at C-3 of the A ring. The singlet peak at δ 2.03 ppm, which is integrated for 15 H, is attributed to the C_5Me_5Ru fragment. This suggests the formation of [Cp*Ru(3-*O*-acetyl)(17α-(η^6-phenyl)estradiol][CF_3SO_3] (7).

Hydrolysis of 7 in a methanolic solution of $NaHCO_3$ gave the target compound [Cp*Ru(17α-(η^6-phenyl)estradiol)][CF_3SO_3] (8) (Scheme III). The ^1H NMR spectrum of compound 8 recorded at room temperature in acetone-d_6 shows, in addition to the usual peaks of the estradiol molecule, particularly 17-OH at 4.7 ppm. Further, we note the disappearance of the peak at 2.2 ppm attributed to the acetate group in 7. The ^1H NMR spectrum also shows an upfield shift for the aromatic protons of the 17α-phenyl group. Particularly, two signals are observed at δ 6.01 and 6.22 ppm, which are integrated for 1 H (H_c) and 4 H (2 $H_{aa'}$ + 2 $H_{bb'}$), respectively (Figure 2). Unexpectedly the ^1H NMR signals recorded in the aromatic region for the 17α-phenyl ring of 8, as well as for 6 and 7 (vide supra), do not correspond to the usual A_2B_2C spin system. However, we note that the compound [Cp*Ru(PhOH)][CF_3SO_3] exhibited similar signals in the ^1H NMR spectrum for coordinated phenol ring.[6a]

The ^{13}C NMR spectrum of 8 recorded at room temperature displays an upfield shift for the aromatic carbons C21–26, giving rise to four singlet peaks in the region 87.75–86.79 ppm. This upfield shift is characteristic of Cp^*Ru^+ binding. The ^{13}C NMR spectrum also shows two singlet peaks appearing at δ 97.73 and 11.32 ppm attributed to the pentamethylcyclopentadienyl group of the coordinated Cp^*Ru^+ fragment.

Compound 8 did not show any recognition toward the estradiol receptor (RBA = 0), compared to RBA = 25% for the free estrogen derivative 3. It is possible that the steric effect induced by the Cp^*Ru^+ moiety, as well as the ionic character of this species 8, would impede the approach of 8 to the receptor active site, thereby rendering it inactive.

Conclusion

In this work we have shown that an arene's ability for Cp^*Ru^+ coordination can be altered by diminishing the electron density of the more favored aromatic ring, thereby rendering it less reactive. An example of such a situation is illustrated by the complexation of 17α-phenylestradiol by a Cp^*Ru^+ fragment. This method can be applied to other organic species possessing more than one phenyl group in their skeleton cores.

Experimental Section

Manipulations were carried out on a vacuum line under argon using standard Schlenk techniques; solvents were purified and dried prior to use by conventional distillation techniques under argon. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM 250-MHz instrument, and chemical shifts are relative to Me_4Si; data are presented as proton-decoupled and reported downfield positive with respect to the standard reference. Elemental analyses were performed by the microanalysis service of the CNRS, Gif sur Yvette, France. (Dimethyl-*tert*-butylsilyl)estrone (2) was prepared according to the literature procedure.[12]

17α-Phenylestradiol (3). Compound 3 has already been prepared.[5b,c] However, we have followed a modified synthetic route allowing a higher yield, as described below: 8 mL of a 2 M solution of PhLi in an ether/benzene mixture was added dropwise to 1.2 g (3.12 mmol) of silylestrone in 20 mL of THF, while the temperature of the reaction mixture was kept at T = −78 °C for 2 h. Then the reaction mixture was left overnight with stirring and the solution warmed gradually to attain room temperature. Later a few drops of $^tBu_4NF$ were added. After 30 min the mixture was hydrolyzed by adding 200 mL of saturated NH_4Cl and extracted by CH_2Cl_2, washed with water, and dried over $MgSO_4$. The collected CH_2Cl_2 solution of 3 was evaporated to dryness and then recrystallized from ether/pentane to give white needles of 17α-phenylestradiol (730 mg, yield 67%). IR (KBr pellets): $\nu(OH)_{free}$ 3503 (sharp), $\nu(OH)_{bound}$ 3285 cm^{-1} (broad). ^1H NMR (δ, ppm; acetone-d_6): 7.92 (s, OH phenolic), 7.44 (d, 2 H_{ortho}), 7.30 (t, 2 H_{meta}), 7.21 (d, H_{para}), 6.98 (d, H1), 6.50 (dd, H2), 6.47 (d, H4), 1.1 (s, 18-Me). ^{13}C NMR (δ, ppm; acetone-d_6): 127 (C1), 113.5, 115.97 (C2, C4), 155.57 (C3) 135.00, 132.67 (C5, C10), 128.60, 127.97, 127.43, 127.31 (C_{ipso}, $C_{aa'}$, $C_{bb'}$, C_c), 15.49 (C18).

α- and β-[Cp*Ru(17α-phenyl-η^6-estradiol)][CF_3SO_3] (4a,b). A 0.203-mmol amount of [Cp*Ru(CH_3CN)$_3$][CF_3SO_3] (1) (prepared in situ following Fagan and Calabrese's method[3]) in a mixture of CH_3CN/THF (5 mL/5 mL) was refluxed overnight in the presence of 0.23 mmol (80 mg) of 3. Then, the dark yellow solution was concentrated under vacuum, followed by addition of 20 mL of diethyl ether to give a brown oily residue. The products were washed several times with diethyl ether; overall yield 37% (α:β ratio 70:30). **4a**: ^1H NMR (δ, ppm; acetone-d_6) 7.45 (d, H_c), 7.35 (m, 2 $H_{aa'}$), 7.15 (m, 2 $H_{bb'}$), 5.87 (d, H1), 5.68 (dd, H2), 5.66 (d, H4), 1.8 (s, Cp*), 1.09 (s, 18-Me). **4b**: ^1H NMR (δ, ppm; acetone-d_6) 7.45 (d, H_c), 7.35 (m, 2 $H_{aa'}$), 7.15 (m, 2 $H_{bb'}$), 5.80 (m, H1), 5.5 (dd, H2), 5.66 (d, H4), 1.94 (s, Cp*), 1.21 (s, 18-Me).

3-*O*-(Trifluoroacetyl)-17α-phenylestradiol (5a). A solution mixture of 17α-phenylestradiol (80 mg, 0.229 mmol) in 4 mL of diethyl ether, 37 μL of pyridine (2 equiv), and 65 μL of trifluoroacetic anhydride (2 equiv) was maintained under stirring at T = 0 °C for 1 h. The reaction was warmed gradually to room temperature. Then the mixture was washed several times with water while the pH of the solution was controlled until neutrality was attained. The solution was dried over $MgSO_4$ and purified on silica plates using an ether/pentane (1/1) mixture as eluent (R_f 0.7). The compound is obtained as an oily substance (yield 75%). ^1H NMR (δ, ppm; acetone-d_6): 7.4–7.2 (m, C–H phenyl), 7.32 (d, H1), 7.08 (d, H2), 7.05 (s, H4), 1.26 (s, 18-Me).

3-*O*-Acetyl-17α-phenylestradiol (5b). **5b** was obtained by following a procedure similar to that described for **5a**. A mixture of 400 mg (1.15 mmol) of 17α-phenylestradiol in 25 mL of ether and 0.9 mL of acetic anhydride (10 equiv), in the presence of 1 mL of pyridine, was stirred overnight at room temperature. The mixture was washed with water and the organic phase dried over $MgSO_4$. **5b** was purified on silica plates (eluent ether/pentane (1/1), R_f 0.6) and recrystallized from pentane to give a white powder (overall yield 410 mg, 91%). ^1H NMR (δ, ppm; acetone-d_6): 7.45 (d, 2 H_{ortho}), 7.30 (t, 2 H_{meta}), 7.18 (d, H_{para}), 7.12 (d, H1), 6.76 (dd, H2), 6.74 (d, H4), 2.2 (s, CH_3COO), 1.11 (s, 18-Me).

[Cp*Ru(17α-(η^6-phenyl)$C_{19}H_{24}O$)][CF_3SO_3] (6). A 0.15-mmol amount of [Cp*Ru(CH_3CN)$_3$][CF_3SO_3] (1) (prepared in situ by following Fagan and Calabrese's method[3]) in a THF/CH_3CN solution (5 mL/5 mL) and 0.16 mmol (70 mg) of 3-*O*-(trifluoroacetyl)-1-7α-phenylestradiol were refluxed over 12 h. Then, the reaction was allowed to gradually attain room temperature and concentrated under vacuum. Addition of diethyl ether gave an oily residue, which was separated, washed with diethyl ether, and dried under vacuum (overall yield 50 mg, 45%). ^1H NMR (δ, ppm; acetone-d_6): 7.06 (d, H1), 6.62 (d, H2), 6.55 (s, H4), 6.45 (m, H16), 6.28 (m, H_c), 6.07 (m, 2 $H_{aa'}$ + 2 $H_{bb'}$), 1.96 (s, Cp*), 1.10 (s, 18-Me).

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Table I. Crystallographic Data

chem formula	$C_{24}H_{28}O_2$
fw	348.49
cryst syst	orthorhombic
space group	$P2_12_12_1$
Z	4
a, Å	7.325 (4)
b, Å	17.590 (3)
c, Å	18.778 (5)
V, Å^3	2419 (2)
F(000)	752
ρ(calcd), g cm^{-3}	0.96
μ(Mo Kα), cm^{-1}	0.55
cryst size, mm	0.28 × 0.32 × 0.80
diffractometer	CAD4
monochromator	graphite
radiation	Mo Kα (0.71070 Å)
temp, °C	20
scan type	$\omega/2\theta$
scan range θ, deg	1.5 + 0.34 tan θ
2θ range, deg	2–46
no. of rflns collected	1939
no. of rflns used (criteria)	1213 ($I > 3\sigma(I)$)
R	0.069
R_w[a]	0.073
abs cor[b]	min 0.52, max 1.36
secondary extinctn (×10^6)	509
rms (shift/esd) (last ref)	0.22
least-squares params	237

[a] $R_w = [\Sigma_i w_i(F_o - F_c)^2/\Sigma_i w_i F_o^2]^{1/2}$. [b] See ref 13 (DIFABS).

[Cp*Ru(3-*O*-acetyl-17α-(η^6-phenyl)estradiol)][CF_3SO_3] (7). A 1.02-mmol (400-mg) amount of 3-*O*-acetyl-17α-phenylestradiol (**5b**) in THF was added to 0.92 mmol of [Cp*Ru(CH_3CN)$_3$][CF_3SO_3] (1) prepared in situ in CH_3CN/THF. The reaction mixture was refluxed overnight and then cooled to room temperature. Addition of diethyl ether afforded a gray microcrystalline substance. The product was isolated, washed several times with diethyl ether, and then dried under vacuum (yield 550 mg, 73%). IR (KBr pellets): ν(–OH associated) 3447 cm^{-1}. ^{1}H NMR (δ, ppm; acetone-d_6): 7.18 (d, H1), 6.78 (dd, H2), 6.76 (d, H4), 6.23 (m, H_c), 6.02 (m, 2 $H_{aa'}$ + 2 $H_{bb'}$), 2.20 (s, CH_3COO), 2.03 (s, Cp*), 1.10 (s, 18-Me).

[Cp*Ru(17α-(η^6-phenyl)estradiol)][CF_3SO_3] (8). A 0.129-mmol (100-mg) amount of [Cp*Ru(3-*O*-acetyl-17α-(η^6-phenyl)-estradiol)][CF_3SO_3] (7) was dissolved in 5 mL of methanol with 400 mg of $NaHCO_3$ (3.8 mmol). The reaction mixture was left with stirring overnight, and then dried under vacuum, extracted with CH_2Cl_2, and washed with water. The organic phase was dried over $MgSO_4$ and concentrated under vacuum. Addition of diethyl ether allowed the obtainment of a white microcrystalline product, which was recrystallized from THF/pentane; yield 75 mg (79%). Anal. Calcd for $C_{35}H_{43}O_5SF_3Ru \cdot {}^1/_4CH_2Cl_2$: C, 56.10; H, 5.76. Found: C, 56.28; H, 5.42. ^{1}H NMR (δ, ppm; acetone-d_6): 6.96 (d, H1), 6.53 (H2), 6.50 (d, H4), 6.22 (m, H_c), 6.03 (m, 2 $H_{aa'}$ + 2 $H_{bb'}$), 2.05 (s, Cp*), 1.10 (s, 18-Me), 5.62 (coordinated CH_2Cl_2). ^{13}C NMR (δ, ppm; acetone-d_6): 127.42 (C1); 113.75, 116.17 (C2, C4); 156.06 (C3); 139.42, 132.37 (C5, C10); 87.75, 87.49, 87.11, 86.79 (C_{ipso}, $C_{aa'}$, $C_{bb'}$, C_c); 85.59 (C17); 49.12 (C13); 44.40, 40.79, 49.39 (C9, C8, C14); 30.40, 28.32, 27.20, 37.13, 24.47, 34.42 (C6, C7, C11, C12, C15, C16); 15.58 (C18); 97.73, 11.32 (C_5Me_5).

X-ray Crystal Structure of Compound 3. Intensity data were collected at room temperature on a Nonius CAD4 diffractometer using Mo Kα radiation. The accurate cell dimensions and orientation matrix were obtained from least-squares refinements of the setting angles of 25 well-defined reflections. No decay in the intensities of two standard reflections was observed during the course of data collection. This compound crystallizes in the orthorhombic space group $P2_12_12_1$ with $Z = 4$ and cell dimensions $a = 7.325$ (4) Å, $b = 17.590$ (3) Å, and $c = 18.778$ (5) Å. The usual corrections for Lorentz and polarization effects were applied. An empirical absorption correction (DIFABS[13]) was applied (maximum correction 1.36, minimum correction 0.52).

Computations were performed by using CRYSTALS[14] adapted to a Microvax-II computer. Scattering factors and corrections for anomalous dispersion were from ref 15. The structure was resolved by direct methods (SHELXS[16]) and refined by least squares with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms were then located on a difference Fourier map; however, according to the poor data to variable ratio, they were introduced in fixed positions with an overall refinable isotropic thermal parameter. The structure was refined to $R = 0.069$ and $R_w = 0.073$ with use of 1213 reflections.

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