Synthesis of Oxorhenium(V) Complexes Derived from 7α-Functionalized Testosterone: First Rhenium-Containing Testosterone Derivatives

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In an effort to assist in the preparation of metal-containing ligands for the androgen receptor, we have synthesized the first oxorhenium(V) complexes containing a pendant testosterone moiety. The key step in the synthesis involves the copper-catalysed, α-selective 1,6-Michael addition of a 4-pentenylmagnesium bromide to 6-dehydrotestosterone 17β-acetate. The α-stereoselectivity is governed by the presence of the C-19 methyl group. The absolute configurations of the epimers were investigated by ^{1}H-NMR studies. Further chemical transformations of the 7α-pentenyl spacer introduced the terminal thiol group, needed for complex formation. The complex formation was accomplished by the "3+1" mixed-ligand concept using two different rhenium precursors. The obtained complexes differ with respect to the central donor atom of the tridentate ligand part, namely, S and O.

Introduction

The development of radiolabeled ligands for the androgen receptor may make possible the imaging and detection of androgen-dependent tumors, such as prostate cancer, as well as greatly facilitate the study of androgen action in heterogeneous tissues[1]. Because of its wide availability, convenient half-life and appropriate γ energy, technetium-99m is frequently the radionuclide of choice for diagnostic imaging agents in nuclear medicine[2]. Therefore, the synthesis of technetium- and rhenium-containing steroids that are capable of binding to steroid-hormone receptors with high affinity has been a goal of many investigators[3]. A number of radiolabeled steroid ligands have been prepared as molecular probes for the estrogen and progesterone receptors[4]. A detailed study of the androgen receptor has lagged behind the other sex steroid receptors due in part to the low levels of androgen receptor present in most target tissues, and also to the relatively low stability of this receptor[5][6]. The recent developments of radiolabeled ligands for the androgen receptor involved only syntheses of radiohalogenated, C-11- and 3-H-labeled derivatives of testosterones, 19-nortestosterone and 5α-dihydrotestosterone[6][7][8]. To date, there are no reports using technetium or rhenium as androgen labels.

Recently, it has been shown that the androgen receptor can tolerate a bulky iodide at the 7α position[6]. Moreover, the access to 7α-alkyl and -(phenylalkyl) substituents is well known[9][10]. Therefore, we focused our attention on the introduction of a 7α-alkyl side-chain into the testosterone skeleton bearing a terminal oxorhenium(V) chelate according to the mixed-ligand concept[11][12]. In our preliminary investigations we used rhenium as a surrogate for the radioactive technetium.

Results and Discussion

In this paper we report the synthesis of 17β-hydroxy-7α-(5-mercaptopent-1-yl)-androst-4-en-3-one (**8**) and its conversion into the corresponding oxorhenium(V) "3+1" mixed-ligand complexes. The ω-mercaptoalkyl-functionalized testosterone derivative **8** binds as a monodentate ligand to the oxorhenium(V) core, with the remaining positions at the metal center occupied by a tridentate dithiolate ligand "SXS" . The latter ligand differs with respect to the central donor atom, which can be O or S. The key step of the synthesis of **8** (Scheme 1) involves the diastereoselective introduction of a 4-pentenyl group into the 7α position of the testosterone skeleton. This reaction succeeded by the copper-catalysed, 1,6-conjugate Michael addition of a 4-pentenyl chain to 6-dehydrotestosterone **1**[13]. We used a modification of the procedure by French et al.[10a], replacing pure THF as the solvent and 7 mol-% CuCN (related to 5-bromopentene) instead of a mixture of THF/Et_2O and 0.5 equiv. of CuI. The reaction proceeded with an α/β diastereoselectivity of 4.3:1 which is similar to that of French. The 19β-methyl group in **1** increases the steric bulk of the β face and therefore increases the α selectivity. The separation of both diastereomers of **2** was easily accomplished by flash chromatography to yield the desired diastereomers in 43% (**2a**) and 10% (**2b**). The 4-pentenyl group was used as nucleophilic component containing a masked primary alcohol. This strategy eliminates the need for protecting-group manipulations, contrary to other investigators who have used protected alcohols as nucleophilic compo-

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nents[10b][10c]. The following transformation of **2a** into the required alcohol **5** was achieved by subsequent cleavage of the acetyl group of **2a** and introduction of a TBDMS protecting group followed by a hydroboration/oxidation step using 9-BBN, H_2O_2 and NaOH. The regeneration of the enone system in the A ring of **5** was accomplished by oxidation using *N*-bromoacetamide.

The introduction of a thiol group into the steroid molecule succeeded via a thiobenzoate by the Mitsunobu reaction[14] starting from alcohol **5**. This reaction is the method of choice for the introduction of a sulfur moiety under mild conditions in high yield. By treatment of alcohol **5** with the system PPh_3, DIAD and BzSH the thiobenzoate **6** was obtained in a satisfactory yield of 88%. The cleavage of the TBDMS ether in **6** by treatment with TBAF in THF as the otherwise usual TBDMS deprotecting agent failed. The removal of the silyl ether protecting group succeeded in the system 40% HF/acetonitrile in moderate yield of 68%. The last step of the synthesis involves the saponification of **7** by sodium methoxide in MeOH to give the desired thiol **8**. The overall yield for the end product **8** is 12% based on 6-dehydrotestosterone **1**.

The absolute configurations of the chromatographically separated compounds **2a** (7α isomer) and **2b** (7β isomer) were determined by ^{1}H-NMR measurements[10]. These measurements established the chemical shifts and the coupling pattern of the AB part of the 6α-H, 6β-H and 7-H ABX system of both diastereomers **2a** and **2b**. The assignment of 6α-H (**2a**: δ = 2.32, dd, $^2J_{6\alpha6\beta}$ = 14.3 Hz and $^3J_{6\alpha7\beta}$ = 2.5 Hz; **2b**: δ = 2.30, dd, $^2J_{6\alpha6\beta}$ = 14.5 Hz and $^3J_{6\alpha7\alpha}$ = 5.0 Hz) and 6β-H (**2a**: δ = 2.38, dd, $^2J_{6\alpha6\beta}$ = 14.3 Hz and $^3J_{6\beta7\beta}$ = 5.1 Hz; **2b**: δ = 2.18, dd, $^2J_{6\alpha6\beta}$ = 14.5 Hz and $^3J_{6\beta7\alpha}$ = 12.6 Hz) was confirmed by using the 2D-NOESY and COSY technique.

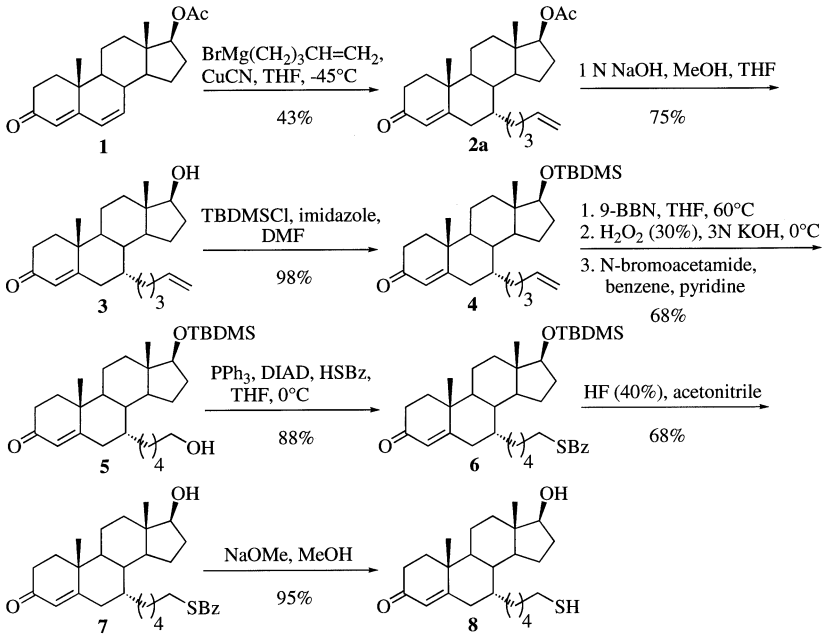
The large $^3J_{\text{axial-axial}}$ coupling constant of 12.6 Hz according to the Karplus curve between 6β-H and 7α-H indicates that the pentyl spacer at the 7-C of **2b** is β-substituted. This led us to the conclusion that compound **2a** therefore must be α-substituted.

The complex formation according to the "3+1" concept by the use of two different rhenium precursors **9**[12] and **10**[15] offers the access to oxorhenium(V) complexes which differ in the central donor atom of the tridentate ligand part, being S for **12** and O for **13**. The corresponding mixed-ligand complexes **12** and **13** could be obtained as reddish-brown and wine-red amorphous glasses in 71% (for **12**) and 14% (for **13**) yield, respectively (Scheme 2).

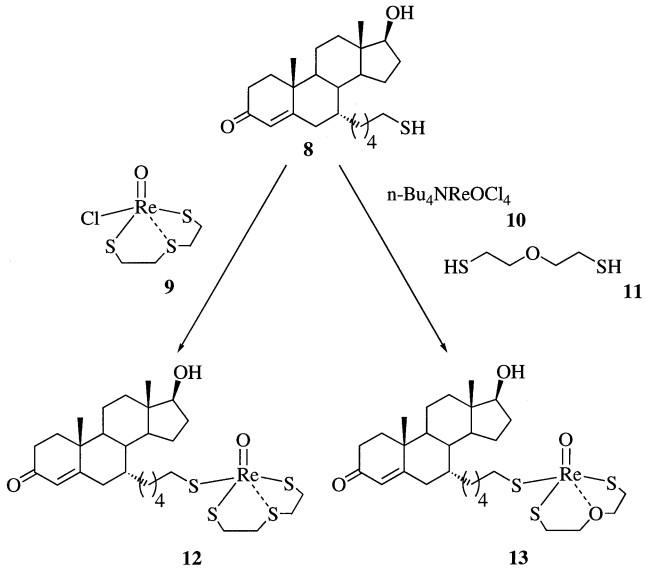
The common reaction of both the tridentate ligand "SOS" **11** and the thiol **8** with the oxorhenium(V) precursor **10** leads to the complex **13**. This reaction occurs immediately at 0°C due to the high reactivity of rhenium precursor **10**. For the preparation of rhenium complex **12** an alternative route is used, based on the chlorine-containing complex **9** as a precursor. The complex formation by exchange of the chlorine atom in **9** by the mercaptide sulfur of **8** requires heating for 2 hours. In the infrared spectra a strong absorption band at 961 cm^{-1} (for **12**) and 969 cm^{-1} (for **13**) is observed, which is indicative of the $Re{=}O^{3+}$ core. The ^{1}H-NMR spectrum of **12** shows at δ = 3.12, 3.91 and 4.30 complex coupling patterns of the tridendate "SSS" ligand protons. By using the "SOS" ligand resulting in complex **13** only broad signals could be observed.

The complexes **12** and **13** represent the first examples of rhenium-containing androgen receptor ligands. Further investigations concerning the biological evaluation of **12** and **13** and their technetium analogues under in vitro and in vivo conditions will be done in order to evaluate the useful-

Scheme 1. Synthesis of thiol **8**



Scheme 2. Oxorhenium(V) complexes **12** (X = S) and **13** (X = O) according to the mixed-ligand concept



ness of complexes like **12** and **13** to act as radiotracers for the image of the androgen receptor.

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Experimental Section

General: Solvents and reagents were purchased from the following commercial sources: Sigma, Fluka and Aldrich. THF was distilled from sodium/benzophenone ketyl prior to use. CuCN and magnesium turnings were dried prior to use. Other reagents were used as received. The synthesis involving air-sensitive compounds were carried out under argon using standard Schlenk technique. The standard workup procedure for product isolation involved quenching of the reaction mixture in an aqueous solution, followed by a thorough extraction with $CHCl_3$, washing of the extract, drying with $MgSO_4$, filtration and evaporation of the solvent under reduced pressure. Flash chromatography was performed according to Still[16], using Merck silica gel (0.040−0.063 mm). − IR: Specord M 80 Carl-Zeiss Jena. − NMR: Bruker DRX-500; Varian Inova-400. For ^1H NMR $CDCl_3$ as solvent $\delta_H = 7.26$; for ^{13}C NMR, $CDCl_3$ $\delta_C = 77.0$. − MS: Finnigan MAT 90.

17β-Acetoxy-7α-(4-penten-1-yl)androst-4-en-3-one (**2a**): 4.51 ml (38.16 mmol) of 5-bromopentene in 15 ml of dry THF was slowly added to 1.29 g (53 mmol) of magnesium turnings under argon. The resulting slurry was diluted with 5 ml of THF and heated for 1 h at 60°C while stirring. Afterwards, additional 60 ml of THF was added to adjust the Grignard solution to 0.75 M. The solution was cooled to −45°C and stirred for 30 min and 245 mg (2.73 mmol) of CuCN was added in one portion and stirring was continued for 30 min. Then 5 g (15.22 mmol) of dienone **1** in 60 ml of THF was added at −40°C over a period of 90 min. The solution was kept at −40 to −45°C for 30 min and then quenched with 5 ml of HOAc followed by filtration of the copper salts and standard workup. The resulting yellow oil contained the two diastereomers **2a** and **2b**. Separation of the diastereomers was accomplished by flash chromatography (EtOAc/*n*-hexane, 5:95). Yield: 2.6 g (43%) of the 7α product **2a** (pale yellow oil) and 0.6 g (10%) of the 7β-product **2b**. − IR ($CHCl_3$): $\tilde{\nu}$ = 1734 cm^{-1} (s, 17β-OAc), 1674 (s, 3-C=O), 1615 (m, C=C). − ^1H NMR ($CDCl_3$): δ = 0.82 (s, 3 H; 18-CH_3), 1.18 (s, 3 H; 19-CH_3), 2.02 (s, 3 H; 17β-$OCOCH_3$), 4.58 (t, ^3J = 8.4 Hz, 1 H; 17-H), 4.91−5.00 (m, 2 H; −CH=CH_2), 5.70 (s, 1 H; 4-H), 5.71−5.76 (m, 1 H; −CH=CH_2). − ^{13}C NMR ($CDCl_3$): δ = 199.0, 171.1, 169.7, 138.5, 125.8, 114.6, 82.4, 47.0, 45.8, 42.4, 38.7, 38.6, 36.6, 36.3, 36.3, 35.9, 33.9, 33.7, 27.3, 26.6, 24.5, 22.8, 21.1, 20.7, 18.0, 11.8. − HRMS (EI, 70 eV): calcd. for $C_{26}H_{28}O_3$ 398.2820, found 398.2812.

17β-Hydroxy-7α-(4-penten-1-yl)androst-4-en-3-one (**3**): 2.6 g (6.5 mmol) of the 17β-acetoxy steroid **2a** was dissolved in 60 ml of MeOH and 30 ml of THF and cooled to 0°C. 30 ml of 1 N NaOH was added drop by drop. The resulting mixture was stirred for 2 h at room temperature and 15 ml of 2 N HCl was added followed by standard workup and flash chromatography (EtOAc/*n*-hexane, 1:2). Yield 1.72 g (75%), m.p. 149−153°C. − IR (KBr): $\tilde{\nu}$ = 3455 cm^{-1} (s, OH), 3077 (w, =C−H), 1658 (s, 3-C=O), 1617 (m, C=C). − ^1H NMR ($CDCl_3$): δ = 0.79 (s, 3 H; 18-CH_3), 1.20 (s, 3 H; 19-CH_3), 3.66 (t, ^3J = 8.4 Hz, 1 H; 17-H), 4.92−5.01 (m, 2 H; CH=CH_2), 5.72 (s, 1 H; 4-H), 5.73−5.80 (m, 1 H; CH=CH_2). − ^{13}C NMR ($CDCl_3$): δ = 199.2, 170.0, 138.6, 125.8, 114.5, 81.6, 47.2, 46.0, 42.8, 39.0, 38.6, 36.6, 36.3, 36.2, 36.0, 34.0, 33.8, 30.3, 26.7, 24.6, 22.8, 20.9, 18.1, 10.9. − $C_{24}H_{36}O_2$ (356.54): calcd. C 80.85, H 10.18; found C 80.50, H 10.14.

17β-(tert-Butyldimethylsilyloxy)-7α-(4-penten-1-yl)androst-4-en-3-one (**4**): 1.24 g (18.2 mmol) of imidazole was dissolved in 12 ml of dry DMF. 1.37 g (9.1 mmol) of TBDMSCl in 6 ml of DMF was slowly added at 0°C. After 30 min, 1.3 g (3.64 mmol) of hydroxysteroid **3** in 5 ml of DMF was added in one portion and the mixture was stirred for 3 h at room temperature. After hydrolysis with a 0.1% K_2CO_3 solution, the mixture was extracted several times with $CHCl_3$, dried with $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (EtOAc/*n*-hexane, 1:3). Yield 1.7 g (98%), m.p. 117−119°C. − IR (KBr): $\tilde{\nu}$ = 3076 cm^{-1} (w, =C−H), 1676 (s, 3-C=O), 1616 (m, C=C). − ^1H NMR ($CDCl_3$): δ = 0.01 [s, 6 H; $Si(CH_3)_2$], 0.75 (s, 3 H; 18-CH_3), 0.88 [s, 9 H; $SiC(CH_3)_3$], 1.20 (s, 3 H; 19-CH_3), 3.57 (t, ^3J = 8.4 Hz, 1 H; 17-H), 4.93−5.01 (m, 2 H; CH=CH_2), 5.72 (s, 1 H; 4-H), 5.75−5.83 (m, 1 H; CH=CH_2). − ^{13}C NMR ($CDCl_3$): δ = 199.3, 170.3, 138.7, 125.8, 114.5, 81.6, 47.3, 45.6, 43.2, 39.1, 38.7, 36.7, 36.6, 36.4, 36.0, 34.1, 33.9, 30.7, 26.8, 25.8, 24.6, 22.9, 20.9, 18.1, 18.1; 11.2, −4.5, −4.8. − $C_{30}H_{50}O_2Si$ (470.81): calcd. C 76.53, H 10.70; found C: 76.35, H 10.46.

17β-(tert-Butyldimethylsilyloxy)-7α-(5-hydroxypent-1-yl)androst-4-en-3-one (**5**): 1.7 g (3.6 mmol) of the steroid **4** was dissolved in 15 ml of dry THF and cooled to 0°C. 44 ml of 9-BBN (0.5 M in THF; 22 mmol) was added dropwise to the stirred solution under argon. After the addition of 9-BBN was complete, the whole mixture was stirred at 60°C for 40 min. At 0°C 15 ml of water was added, followed by 15 ml of 3 N NaOH 5 min later. After another 5 min, 15 ml of 30% H_2O_2 was added very carefully and the mixture was stirred for 30 min. After standard workup using saturated $NaHCO_3$ solution a colorless oil containing the 3-hydroxy-7α-hydroxypentyl steroid was obtained. The residue was dissolved in a mixture of 13 ml of benzene and 26 ml of pyridine, and 0.75 g (5.43 mmol) of *N*-bromoacetamide was added. This was stirred overnight at room temperature. Standard workup involved treatment with 1 N HCl and flash chromatography (EtOAc/*n*-hexane, 1:1). Yield 1.2 g (68%), pale yellow oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3412 cm^{-1} (s, OH), 1673 (s, 3-C=O), 1614 (m, C=C). − ^1H NMR ($CDCl_3$): δ = −0.02 [s, 6 H; $Si(CH_3)_2$], 0.71 (s, 3 H; 18-CH_3), 0.84

[s, 9 H; $SiC(CH_3)_3$], 1.17 (s, 3 H; 19-CH_3), 3.53 (t, ^3J = 8.4 Hz, 1 H; 17-H), 3.59 (t, ^3J = 6.6 Hz, 2 H; CH_2OH), 5.68 (s, 1 H; 4-H). − ^{13}C NMR ($CDCl_3$): δ = 199.4, 170.5, 125.6, 81.5, 62.7, 47.3, 45.5, 43.1, 39.0, 38.6, 36.7, 36.6, 36.3, 35.9, 33.9, 32.6, 30.6, 27.1, 25.9, 25.8, 24.9, 22.8, 20.9, 20.5, 18.0, 18.0, 11.1, −4.6, −4.9. − LRMS (DCI positive, isobutane) for $C_{30}H_{52}O_3Si$: 489 [M+1].

7α-[(S)-5-Benzoylthiopent-1-yl]-17β-(tert-butyldimethylsilyloxy)androst-4-en-3-one (**6**): 880 µl (4.1 mmol) of 90% diisopropyl azodicarboxylate (DIAD) was added to an efficiently stirred solution of 1.08 g (4.1 mmol) of PPh_3 in 11 ml of dry THF at 0°C. The mixture was stirred at 0°C for 30 min and a white precipitate resulted. 1 g (2.05 mmol) of the hydroxy steroid **5** and 532 µl (4.1 mmol) of 95% thiobenzoic acid in 6 ml of dry THF were added dropwise over a period of 10 min and stirring of the mixture was continued for 1 h at 0°C and for 1 h at room temperature. To the resulting yellow solution 100 ml of $CHCl_3$ was added and the mixture was washed with saturated $NaHCO_3$ solution. After drying with $MgSO_4$ and evaporation of the solvent, a pale yellow residue was obtained which was purified by flash chromatography (EtOAc/*n*-hexane, 1:3). Yield 1.1 g (88%), pale yellow oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 1666 cm^{-1} (s, 3-C=O), 1615 (m, C=C). − ^1H NMR ($CDCl_3$): δ = −0.02 [s, 6 H; $Si(CH_3)_2$], 0.73 (s, 3 H; 18-CH_3), 0.87 [s, 9 H; $SiC(CH_3)_3$], 1.18 (s, 3 H; 19-CH_3), 3.05 (t, ^3J = 7.3 Hz, 2 H; CH_2SBz), 3.56 (t, ^3J = 8.4 Hz, 1 H; 17-H), 5.71 (s, 1 H; 4-H), 7.41−7.97 (m, 5 H; $H_{aromat.}$). − ^{13}C NMR ($CDCl_3$): δ = 199.1, 191.9, 170.2, 137.1, 133.2, 128.5, 127.1, 125.7, 81.5, 47.3, 45.6, 43.1, 39.0, 38.6, 36.7, 36.6, 36.3, 35.9, 34.0, 30.6, 29.6, 29.3, 28.9, 26.9, 25.8, 24.9, 22.9, 20.9, 18.0, 18.0, 11.1, −4.6, −4.9. − LRMS (DCI positive, isobutane) for $C_{37}H_{56}O_3SSi$: 609 [M+1].

7α-[(S)-5-Benzoylthiopent-1-yl]-17β-hydroxyandrost-4-en-3-one (**7**): 3.5 ml of 40% aqueous HF was added to a solution of 0.9 g (1.48 mmol) of the steroid **6** in 20 ml of acetonitrile at room temperature. After stirring 1 h at room temperature, 20 ml of saturated $NaHCO_3$ solution was added and the product was extracted with $CHCl_3$. After drying with $MgSO_4$ and evaporation of the solvent, flash chromatography (EtOAc/*n*-hexane, 1:1) was used to isolate pure **7**. Yield 0.5 g (68%), m.p. 129−133°C. − IR (KBr): $\tilde{\nu}$ = 3060 cm^{-1} (w, =C−$H_{aromat.}$), 1662 (s, 3-C=O), 1615 (m, C=C). − ^1H NMR ($CDCl_3$): δ = 0.78 (s, 3 H; 18-CH_3), 1.19 (s, 3 H; 19-CH_3), 3.05 (t, ^3J = 7.3 Hz, 2 H; CH_2SBz), 3.64 (t, ^3J = 8.4 Hz, 1 H; 17-H), 5.71 (s, 1 H; 4-H), 7.41−7.97 (m, 5 H; $H_{aromat.}$). − ^{13}C NMR ($CDCl_3$): δ = 199.2, 192.0, 170.0, 137.1, 133.2, 128.5, 127.1, 125.8, 81.6, 47.1, 46.0, 42.8, 39.0, 38.6, 36.6, 36.3, 36.2, 35.9, 34.0, 30.3, 29.6, 29.0, 28.9, 26.9, 24.9, 22.8, 20.9, 18.0, 10.9. − $C_{31}H_{42}O_3S$ (494.74): calcd. C 75.26, H 8.56, S 6.48; found C 74.85, H 8.28, S 6.31.

17β-Hydroxy-7α-[5-mercaptopent-1-yl]androst-4-en-3-one (**8**): 70 mg (0.14 mmol) of the thiobenzoate **7** was dissolved in 4.5 ml of MeOH while stirring at room temperature under argon. To this solution 280 µl (0.28 mmol) of 1 N NaOMe was added. After 1.5 h, the pH was adjusted to 4−5 by 1 N HCl. Then, 5 ml of water was added and the solution was extracted with chloroform. Drying with $MgSO_4$ and evaporation of the solvent yielded a yellow residue which was purified by flash chromatography (EtOAc/*n*-hexane, 1:1). Yield 52 mg (95%), m.p. 150−153°C. − IR (KBr):$\tilde{\nu}$ = 3449 cm^{-1} (s, OH), 2551 (w, S−H), 1656 (s, 3-C=O), 1616 (m, C=C). − ^1H NMR ($CDCl_3$): δ = 0.79 (s, 3 H; 18-CH_3), 1.21 (s, 3 H; 19-CH_3), 1.59 (s-like, 1 H; SH), 3.76 (m, 1 H; 17-H), 5.72 (s, 1 H; 4-H). − ^{13}C NMR ($CDCl_3$): δ = 199.2, 170.0, 125.8, 81.7, 47.2, 46.0, 42.8, 39.0, 38.7, 36.7, 36.3, 36.2, 36.0, 34.0, 33.9, 30.3, 28.0, 26.9, 25.0, 24.6, 22.8, 20.9, 18.1, 10.9. − $C_{24}H_{38}O_2S$ (390.63): calcd. C 73.79, H 9.81, S 8.21; found C 73.54, H 10.06, S 7.86.

[5-(17β-Hydroxy-3-oxoandrost-4-en-7α-yl)pentan-1-thiolato]-oxo(3-thiapentane-1,5-dithiolato)rhenium(V)rhenium(V) (**12**): 78 mg (200 µmol) of chloro(3-thiapentane-1,5-dithiolato)oxorhenium(V) (**9**) was dissolved in 5 ml of hot acetonitrile while stirring. To this mixture a solution of the steroid **8** (117 mg, 300µmol) in 5 ml of acetonitrile was added . The mixture was refluxed for 2 h and then concentrated to dryness. The residue was purified by flash chromatography [*n*-hexane/ethylacetate, 1:1 and chloroform/methanol, 10:1]. After slow evaporation of the solvent, a brown glass was obtained. Yield 106 mg (71%). − IR (KBr): $\tilde{\nu}$ = 3437 cm^{-1} (s, OH), 1658 (s, C=O), 1613 (m, C=C), 961 (s, Re=O). − ^1H NMR ($CDCl_3$): δ = 0.79 (s, 3 H; 18-CH_3), 1.19 (s, 3 H; 19-CH_3), 3.12 (tt, 2 H, *J* = 14.3 Hz), 3.65−3.67 (m, 1 H; 17-H), 3.84 (t, 2 H, ^3J = 7.3 Hz; CH_2SReO"SSS"), 3.91 (br. d, 2 H, *J* = 10.2 Hz), 4.30 (br. d, 2 H, *J* = 13.2 Hz), 5.72 (s, 1 H; 4-H). − MS (FAB negative, tetraglyme); *m/z* (%): 741 (47.6), 742 (19.0), 743 (100) [M − 1], 744 (28.6), 745 (19.0), 746 (3.8). − $C_{28}H_{45}O_3S_4Re$ (744.13): calcd. C 45.20, H 6.10, S 17.24; found C 44.97, H 6.04, S 16.94.

[5-(17β-Hydroxy-3-oxoandrost-4-en-7α-yl)pentan-1-thiolato](3-oxapentane-1,5-dithiolato)oxorhenium(V) (**13**): 75 mg (128 µmol) of tetra-*n*-butylammonium tetrachlorooxorhenate(V) (**10**) was dissolved in 2 ml of EtOH and cooled to 0°C. At this temperature 50 mg (128 µmol) of the steroid **8** and 15 µl (128 µmol) of 3-oxapentane-1,5-dithiol (**11**) in 2 ml of chloroform was added while stirring. The color of the mixture immediately changed to red. The reaction mixture was stirred at 0°C for 2 h. The solution was then concentrated and the residue dissolved in chloroform yielding a red solution which was purified by flash chromatography [*n*-hexane/ethylacetate, 1:1 and chloroform/methanol, 10:1]. After slow evaporation of the solvent, a wine-red glass was obtained. Yield 13 mg (14%). − IR (KBr): $\tilde{\nu}$ = 3436 cm^{-1} (s, OH), 1659 (s, 3-C=O), 1613 (m, C=C), 969 (s, Re=O). − ^1H NMR ($CDCl_3$): δ = 0.79 (s, 3 H; 18-CH_3), 1.20 (s, 3 H; 19-CH_3), 2.87 (br. s, 1 H), 3.35 (br. s, 2 H), 3.52 (br. s, 2 H), 3.65−3.71 (m, 4 H), 3.94 (br. s, 1 H), 4.61 (br. s, 1 H), 4.70 (br. s, 1 H), 5.73 (s, 1 H, 4-H). − MS (FAB negative, tetraglyme); *m/z* (%): 725 (45.7), 726 (47.6), 727 (100) [M − 1], 728 (81.9), 729 (35.2), 730 (11.4). − $C_{28}H_{45}O_4S_3Re$ (728.05): calcd. C 46.19, H 6.23, S 13.21; found C 45.96, H 6.52, S 12.97.

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