The Stereoselective $Ru_3(CO)_{12}$-Catalyzed Synthesis of Steroidal 1,3-Dihydropyrrol-2-one Derivatives from α,β-Unsaturated Imines, Carbon Monoxide and Ethylene

Wolfgang Imhof,[a,*] Daniel Berger,[a] M. Kötteritzsch,[b] M. Rost,[b] B. Schönecker[b]

[a] Institut für Anorganische und Analytische Chemie der Friedrich-Schiller-Universität Jena, August-Bebel-Str. 2, 07743 Jena, Germany
Fax: (+49) 3641–948–102, e-mail:cwi@rz.uni-jena.de
[b] Institut für Organische Chemie und Makromolekulare Chemie der Friedrich-Schiller-Universität Jena, Humboldtstr. 10, 07743 Jena, Germany

Received May 29, 2001; Accepted August 3, 2001

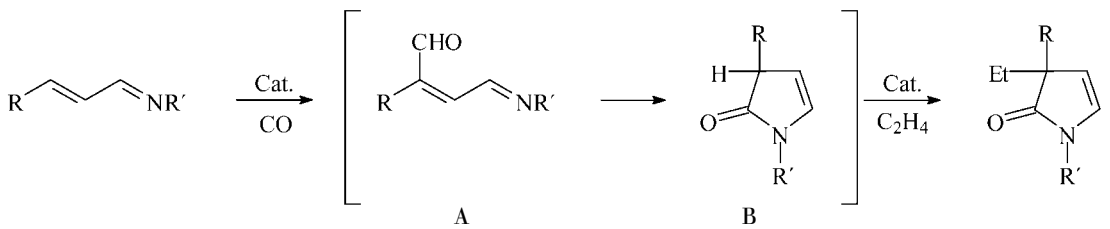
Dedicated to Prof. Dr. Ernst Anders on the occasion of his 60th birthday.

Abstract: The reaction of α,β-unsaturated imines, derived from steroidal amines and cinnamaldehyde, with carbon monoxide and ethylene leads to the formation of steroids with a 1,3-dihydropyrrol-2-one ring system attached to the D-ring of the steroid. In addition, a new stereogenic center at C-3 of the pyrrolone ring is produced during the reaction sequence. In the case of a 16-position of the imine moiety the yields are nearly quantitative but the diastereoselectivity is low whereas the sterically more hindered 17-position shows a decreased reactivity but quite good diastereoselectivities. Complete diastereoselectivity is achieved if the starting compound exhibits an additional silyl ether group in the 17β-position besides the imine subunit in the 16β-position. The compound bearing the pyrrolone substituent at 17β-position was characterized by means of X-ray crystallography showing that the rotation of the pyrrolone ring is hindered by a strong intramolecular hydrogen bond between the carbonyl oxygen of the pyrrolone moiety and the hydrogen at C-17. The question of whether this intramolecular hydrogen bond is also responsible for the observed diastereoselectivities is discussed.

Keywords: alkenes; C–H activation; diastereoselectivity; imines; ruthenium

Introduction

During the last years the catalytic formation of new carbon-carbon bonds by direct functionalization of C–H bonds has attracted considerable interest.[1] In this context, two ruthenium-catalyzed reactions leading to dihydropyrrol-2-one derivatives have recently been described. The reaction of α,β-unsaturated imines with CO was reported to yield 1,5-dihydropyrrol-2-ones[2] whereas a similar reaction published by some of us yielded the isomeric 1,3-dihydropyrrol-2-ones from the reaction of the corresponding unsaturated imines in a one-pot reaction with CO and ethylene.[3] The appearance of two different isomers in these reactions has been explained by proposing a mechanism (Scheme 1) in which, after an insertion of CO into the C–H bond in the β-position with respect of the imine double bond, an intramolecular cyclization leading to the observed pyrrolone system takes place. In a second step, ethylene is inserted into the C–H bond in an *ortho* position with respect to the pyrrolone carbonyl group. This reaction is very much



Scheme 1. Proposed reaction mechanism for the catalytic pyrrolone synthesis.

  1615-4150/01/34308-795–801 $ 17.50-.50/0

related to the insertion reactions of olefins into the *ortho* C–H bonds of aromatic ketones.[4]

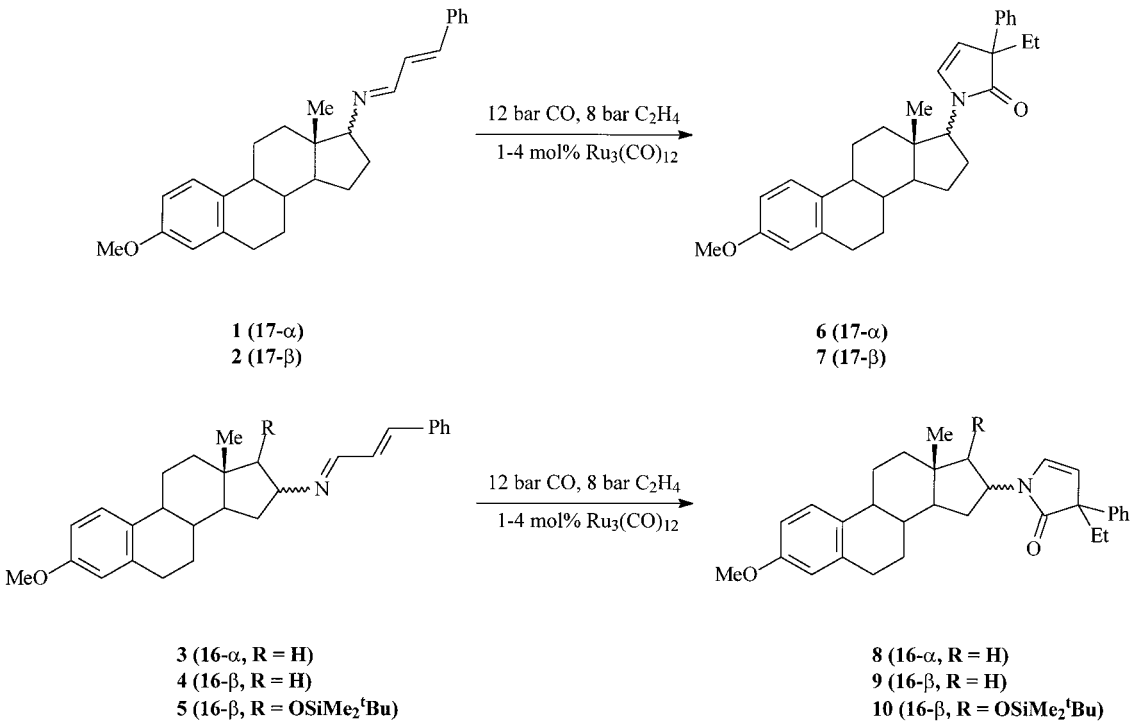
A similar reaction leading to the formation of 2,9b-dihydrobenzoisoindol-1-ones takes place under the same conditions if imines of β-naphthylcarbaldehydes are used as the starting material.[5]

Since the one-pot reaction of CO, ethylene and the corresponding imine also leads to the formation of a new stereogenic center at C-3 of the pyrrol-2-one system it is a straightforward goal to develop stereoselective reactions, especially because γ-lactams have found some interest as compounds exhibiting pharmaceutical potential.[6] In principle, the reaction may either be developed towards a diastereoselective pathway if starting compounds with a defined chirality are used or one could try to achieve an enantioselective catalysis by using chiral catalyst precursors. We chose the first approach because we have already found that the complexation of unsaturated imines derived from steroidal amines or amino alcohols, respectively, with $Fe_2(CO)_9$ may be tuned to complete diastereoselectivity by variation of the stereochemical environment of the imine chain.[7] These complexation reactions may well be considered as a model for a first substrate-catalyst interaction of the imine with the catalytically active organoruthenium species inducing the formation of the pyrrolone derivatives in the catalytic reactions described herein. In addition, steroids themselves may show a wide variety of properties which make them interesting compounds for pharmaceutical purposes such as, e. g., their antimicrobial activity.[8]

Results and Discussion

Scheme 2 shows the starting compounds as well as the products that we obtained in the reactions. The imines **1** – **5** may easily be prepared by condensation of cinnamaldehyde with the corresponding steroidal amines. Recently, we reported that the catalytic formation of 1,3-dihydropyrrol-2-one derivatives from unsaturated imines, CO and ethylene catalyzed by $Ru_3(CO)_{12}$ shows the best results concerning reactivity and selectivity if the organic substituents at the imine nitrogen atom are aliphatic groups.[3] So we considered the steroidal imines **1** – **5** to be suitable substrates for analogous catalytic reactions. In addition, we were able to show that the catalysis works with cinnamaldehyde imines as well as with crotonic aldehyde imines.[5] For the investigations described herein the cinnamaldehyde imines seemed to be more favorable to us since their preparation may be carried out with better yields and because they show much better properties in terms of crystallization compared to the crotonic aldehyde imines.

In Table 1 the results of the reactions depicted in Scheme 2 are summarized. It is obvious that the portion of substrate being converted into product compounds – and thus the turnover numbers – clearly depend on the substitution position of the imine moiety. The imines with the side-chain at C-16 of the steroid core and with no additional substituent in the 17-position (**3**, **4**) are nearly quantitatively converted into the pyrrolones **8** and **9**. In addition, the selectivity of



Scheme 2. Synthesis of steroidal cinnamaldehyde imines and pyrrolones.

Table 1. Portion of starting compound reacting under the given conditions (4 mol % cat., 140 °C, **6** – **9**: 15 h, **10**: 40 h) [%], selectivity of the formation of the pyrrolones **6** – **10** [%] and diastereomeric excess [%] for the reaction of **1** – **5**.

Substitution position	Starting compound	Product	Portion of substrate reacting	Selectivity [%]	de [%]
17α	**1**	**6**	55	91	50
17β	**2**	**7**	71	97	80
16α	**3**	**8**	95	95	0
16β	**4**	**9**	>98	>99	20
16β	**5**	**10**	80	>99	>96

the reaction is very good since the pyrrolones are the only products that may be identified from ^{1}H NMR spectra of the crude reaction mixtures.

On the other hand, the 17-imines **1** and **2** show smaller turnover numbers compared to **3** and **4**. The selectivity still is very good, meaning that nearly all of **1** and **2**, which reacted with CO and ethylene, ended up in the formation of **6** and **7**, whereas the remaining quantity of **1** and **2** did not react at all. This again is proven by the NMR spectra of the crude reaction mixtures still showing the resonance of the imine hydrogen atom at its characteristic position at about 8.2 ppm. If the reaction of **1** and **2** is performed for a prolonged period of time less of the starting compounds remains but the selectivity decreases and a lot of side products which we were not able to identify are observed.

The 16β-imine **5** bearing an additional bulky silyl ether group in the 17β-position needs a reaction time of 40 hours to be converted into **10** with a yield of 80%.

It is most reasonable that the differences in the reactivity of the starting compounds are due to the steric arrangements of the substituents neighboring the reactive center limiting the access of the catalyst as well as the substrate molecule to the imine group.

Since the imines **1** – **5** were prepared from enantiomerically pure steroidal amines, the formation of a new stereogenic center at C-3 of the pyrrol-2-one system under achiral conditions should lead to the formation of **6** – **10** each as mixtures of two diastereomers. The ratio of diastereomers can easily be determined from the resonances of the olefinic hydrogen atom next to the new stereogenic center which for all compounds **6** – **9** gives two doublets whereas in the spectrum of **10** only one doublet is observed. Carbon NMR spectra in this case seem to be less sensitive for the observation of the diastereomers of **6** – **9**. Some of the signals are broadened, the resonances of the carbon atoms of the A-, B- and C-rings of the steroid are not affected at all. Only in the case of **8** were separate resonances observed for the carbon atom directly attached to the new stereogenic center. In all other cases the carbon NMR spectra depicted in the experimental part represent the major component of the reaction mixture. The reactions of **3** and **4** show no or nearly no diastereoselectivity at all, whereas the reactions of **1** and **2** lead to the formation of one of the diastereomers to a significantly higher extent than the other one. In the case of **5** with all the substituents in β-positions, only one diastereomer of **10** is observed.

By recrystallization of crude **7**, which showed a diastereomeric ratio of 90 : 10, from toluene we were able to obtain crystals suitable for X-ray diffraction. The result of this structural analysis will also give us a hint to explain the differences in the diastereoselectivity in the reactions of **1** – **5**. A ^{1}H NMR spectrum from the crystalline material confirmed that it consisted only of one diastereomer and that it was the major component in the crude reaction mixture.

The most interesting bond lengths and angles are summarized in Table 2. The bond lengths and angles all show expected values with the bonds at the former imine nitrogen being in the range of single bonds with the exception of the bond with the carbonyl carbon atom which is shortened to 136.3(6) pm due to delocalization of the π-electron density between oxygen and nitrogen. This also leads to the planar arrangement around the nitrogen atom. The olefinic carbon-carbon bond in the pyrrolone ring shows a bond length of 132.6(7) pm whereas all bond lengths and angles at the new stereogenic center are indicative of a normal tetrahedrally surrounded sp^3 carbon

Table 2. Selected bond lengths [pm] and angles [°] for **7**.

N1–C17	147.1(6)	N1–C20	142.6(6)	N1–C23	136.3(6)
C20–C21	132.6(7)	C21–C22	149.8(7)	C22–C23	154.8(6)
C22–C30	155.3(6)	C22–C24	155.8(6)	O2–C17	290(1)
C23–N1–C20	110.3(4)	C23–N1–C17	123.3(4)	C20–N1–C17	126.2(4)
C21–C20–N1	110.4(4)	C20–C21–C22	109.8(4)	C21–C22–C23	102.1(4)
C21–C22–C30	113.3(4)	C23–C22–C30	110.5(4)	C21–C22–C24	112.8(4)
C23–C22–C24	109.1(4)	C30–C22–C24	108.8(4)	N1–C23–C22	106.8(4)

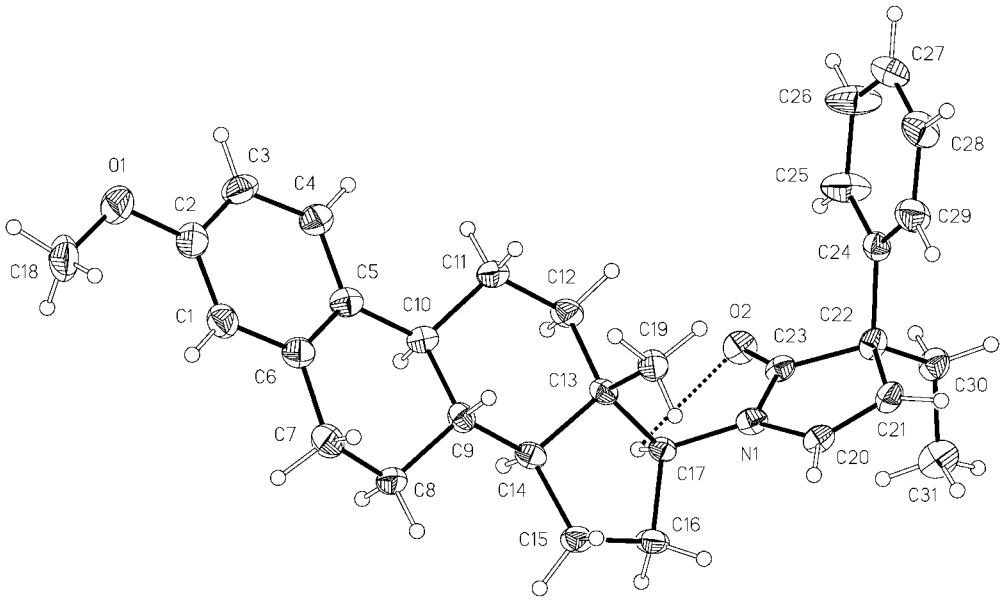


Figure 1. The molecular structure of **7**.

atom. The most important fact is the presence of a quite strong hydrogen bond (see Table 2) between the carbonyl oxygen atom and the hydrogen atom at C-17 of the steroid core. This kind of intramolecular hydrogen bonding was also observed for other pyrrolone and indolone derivatives in which the organic substituent attached to nitrogen exhibits at least one α-hydrogen atom.[3,5]

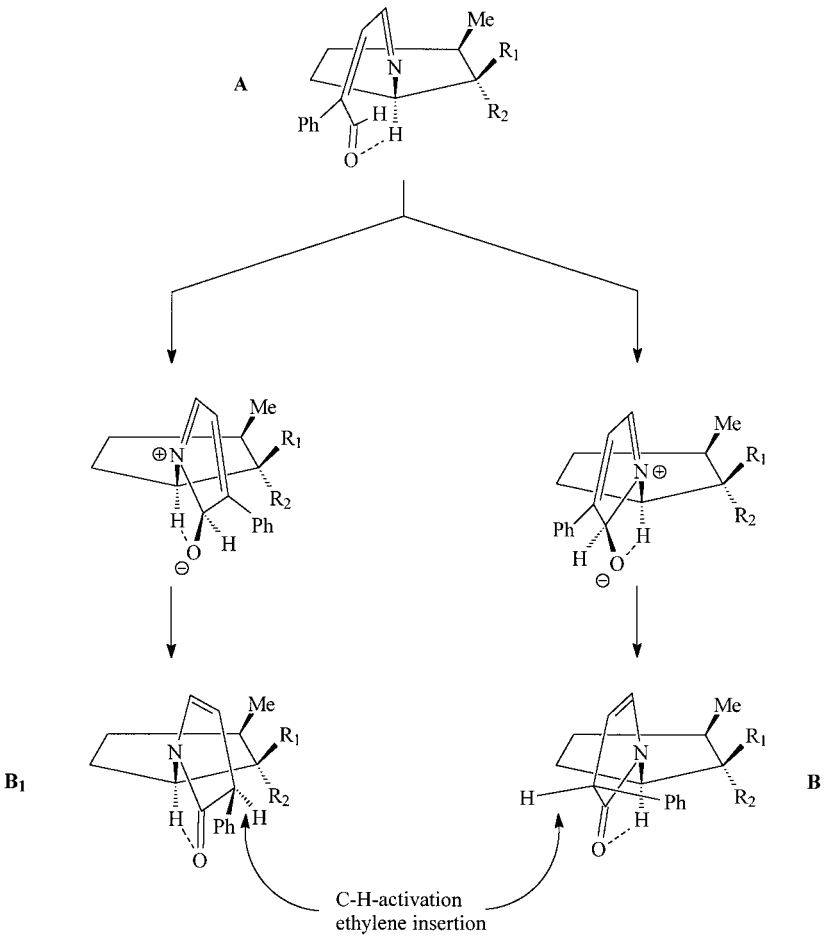
Figure 1 shows a view of **7**. The pyrrolone ring is fixed in a nearly perpendicular arrangement with respect to the D-ring of the steroid core by the intramolecular hydrogen bond. The angle between the plane of the pyrrolone ring and the plane defined by C-13, C-16 and C-17 measures 103°. Figure 1 also shows that ethylene is inserted into the molecule from the sterically less hindered side giving the *R*-configuration for the new stereogenic center. It is most reasonable that the ethylene insertion takes place following the reaction pathway that was described by Murai and coworkers for the related insertion of olefins into an aromatic C–H bond of acetophenone derivatives.[4] Thus, the catalytically active ruthenium species is pre-coordinated by the carbonyl oxygen atom. After activating the C–H bond by an intramolecular oxidative addition, the olefin component is inserted into the metal-hydrogen bond. Reductive elimination of the organometallic species produces the alkylated compounds.

Recently, we proposed that this kind of reaction proceeds via a stepwise mechanism in which first the CO is introduced (intermediate **A**), then the pyrrolone ring is built up (intermediate **B**) and as the last step ethylene is inserted (Scheme 1).[3,5] So it is most reasonable that the hydrogen bond between O-2 and H-17 is already fixed during the formation of intermediate **B**, in which the new stereogenic center is built up.

Scheme 3 shows the proposed mechanism leading to the formation of two different diastereomeric pyrrolone derivatives. The imine substituent in this example appears at C-16 in the β-position. The A-, B- and C-rings of the steroid as well as the catalytically active organometallic moiety have been omitted for the sake of clarity. Starting from intermediate **A** the formation of a hydrogen bond between the aldehyde function and the hydrogen at C-16 of the steroid leads to a pre-organization of **A** facilitating the formation of the pyrrolone ring by a nucleophilic attack of the imine nitrogen towards the carbonyl group. So two diastereomeric intermediates $\mathbf{B_1}$ and $\mathbf{B_2}$ may be formed, which by subsequent reaction steps may produce the compounds **6** – **10** by ethylene insertion.

A diastereoselective reaction may only occur if either $\mathbf{B_1}$ or $\mathbf{B_2}$ is the preferred intermediate. As can be seen from Scheme 3 this depends on the stereochemistry of the groups neighboring the imine function.

This gives us a possible explanation for the different stereoselectivities shown in Table 1. In the case of the 16-imines without an additional substituent at C-17 (**3**, **4**) the groups neighboring the imine moiety are methylene groups. Thus, the steric hindrance is low and so we do get a low or even no stereoselectivity at all. In the 17-substituted compounds **1** and **2** either the methyl group at C-13 or the connection to the C-ring of the steroid are in a *cis*-position with respect to the imine chain and may well have an influence on whether $\mathbf{B_1}$ or $\mathbf{B_2}$ is the preferred intermediate. Indeed, in both cases we do observe a quite promising diastereoselectivity. In the case of **5** as the



Scheme 3. The formation of two diastereomeric pyrrolone derivatives. A-, B- and C-rings of the steroid core as well as the catalytically active organometallic moiety have been omitted for the sake of clarity.

starting compound, both the bulky silyl ether group in the 17-position and the methyl group at C-13 are in a *cis*-position with respect to the imine moiety. This obviously leads to a preferential formation of an intermediate of type $\mathbf{B_2}$, because the organometallic residue which has to be fixed to the carbonyl oxygen atom and which most reasonably also performs the hydrogen transfer reaction building up the new stereogenic center shows the higher steric demand compared to the phenyl substituent. Thus, after the ethylene insertion into the C–H bond *ortho* to the pyrrolone oxygen only one diastereomer of **10** is observed.

The fact that hydrogen bonds may have a decisive influence on the reaction pathway and the stereochemistry of stoichiometric as well as catalytic reactions, of course, is a principle not only being used by synthetic chemists but also to a great extent by nature itself in chemical transformations in biological systems.[9]

Further investigations are ongoing in order to improve the range of substrates towards ketimines, substituted olefins and heterocumulenes.

Conclusions

We were able to show that the catalytic formation of 2-pyrrolone derivatives from α,β-unsaturated imines, carbon monoxide and ethylene may be tuned to complete diastereoselectivity starting from chiral imines with steroid substituents at the imine nitrogen atom. The observed diastereoselectivities depend on the stereochemical properties of the substituents neighboring the imine function of the starting compounds. The reaction most reasonably takes place stepwise by first inserting one carbon monoxide into the C–H bond of the imine chain in the β-position with respect to the imine double bond followed by the formation of the pyrrolone ring. The observed diastereoselectivities may be rationalized by the assumption of an intramolecular hydrogen bond leading to a stereoselective formation of the new stereogenic center at C-3 of the pyrrolone system. The corresponding hydrogen bond is still preserved in the products after ethylene insertion at the C–H bond at C-3 of the pyrrolone as shown by the result of a X-ray structure analysis of one of the products.

Experimental Section

General Remarks

All procedures were carried out under an argon atmosphere in anhydrous, freshly distilled solvents. 16α- and 16β-amino-3-methoxyestra-1,3,5(10)-triene[8] as well as 17α- and 17β-amino-3-methoxyestra-1,3,5(10)-triene[10] were prepared by literature procedures. The synthesis of **1** – **5** from the reaction of the steroidal amines with cinnamaldehyde was already reported by some of us.[7] Infrared spectra were recorded on a Perkin Elmer FT-IR System 2000 using 0.2 mm KBr cuvettes. NMR spectra were recorded on a Bruker AC 200 spectrometer (^{1}H: 200 MHz, ^{13}C: 50.32 MHz, $CDCl_3$ as internal standard). Mass spectra were recorded on a Finnigan MAT SSQ 710 instrument. High resolution mass spectra were recorded on a Finnigan MAT 95 XL using ESI techniques and methanol as the solvent.

X-Ray Crystallographic Study

The structure determination of **7** was carried out on an Enraf Nonius Kappa CCD diffractometer, crystal detector distance 25 mm, 180 frames, using graphite monochromated Mo-Kα radiation. The crystal was mounted in a stream of cold nitrogen. Data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods and refined by full-matrix least squares techniques against F^2 using the programs SHELXS86 and SHELXL93.[11] Computation of the structure was done with the program XPMA[12] and the molecular illustrations were drawn using the program XP.[13] The crystal and intensity data are given in ref. [14] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-164107. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.) +44 1223/336–033; e-mail: deposit@ccdc.cam.ac.uk].

Synthesis of the Compounds 6 – 10

The reactions were carried out in 75-mL stainless steel autoclaves. 1 mmol of the starting compounds (399 mg) and 0.04 mmol of $Ru_3(CO)_{12}$ (25 mg) together with 3 mL of toluene were put into the autoclave. Then the autoclave was evacuated and pressurized with 12 bar CO and 8 bar C_2H_4 and the reaction mixture was heated to 140 °C for 15 hours (**6** – **9**) or 40 hours (**10**), respectively. After cooling down the autoclave to room temperature the pressure was released and the product mixture was transferred to a Schlenk tube. Evaporation of toluene yielded a brown oil which was used for the determination of the diastereomeric ratios by NMR without further purification. Compounds **7** – **10** were purified by recrystallization from toluene or hexane/toluene mixtures and were obtained as a mixture of diastereomers. In the case of **7** it was possible to obtain crystals of only one diastereomer by fractional crystallization from toluene.

*1′-[3-Methoxyestra-1,3,5(10)trien-17α-yl]-(1′,3′-dihydro-3′-ethyl-3′-phenyl-2*H*-pyrrol-2′-one)* **6**: $C_{31}H_{37}NO_2$ (M = 455.64); MS (DCI, H_2O): *m/z* [%]: = 456 (MH^+, 48), 426 ($M^+ - C_2H_5$, 6), 229 ($C_{15}H_{15}NO^+$, 100); ^{1}H NMR ($CDCl_3$, 293 K): δ = 0.76 – 0.86 (m, 6H, CH_3), 1.10 – 2.30 (m, 13H, CH_2, CH), 2.72 – 2.75 (m, 2H, CH_2), 3.75 (s, 3H, CH_3), 4.21 – 4.26 (m, 1H, CH), 5.62 (d, 0.9H, $^3J_{H,H}$ = 5.0 Hz, CH), 5.65 (d, 0.1H, $^3J_{H,H}$ = 5.0 Hz, CH), 6.61 – 6.68 (m, 3H, C_{ar}H, CH), 7.14 – 7.33 (m, 4H, C_{ar}H), 7.48 – 7.52 (m, 2H, C_{ar}H); ^{13}C NMR ($CDCl_3$, 293 K): δ = 9.1 (CH_3), 17.9 (CH_3), 26.2 (CH_2), 28.0 (CH_2), 29.7 (CH_2), 31.3 (CH_2), 31.9 (CH_2), 32.3 (CH_2), 38.3 (CH_2), 38.8 (CH_2), 41.7 (CH), 43.9 (CH), 47.0 (CH), 48.9 (C), 55.2 (CH_3), 58.8 (CH), 111.5 (CH), 113.8 (CH), 114.1 (CH), 126.7 (CH), 126.9 (CH), 128.4 (CH), 129.0 (CH), 132.5 (C), 137.7 (C), 140.1 (C), 157.5 (C), 180.6 (C=O).

*1′-[3-Methoxyestra-1,3,5(10)trien-17β-yl]-1′,3′-dihydro-3′-ethyl-3′-phenyl-2*H*-pyrrol-2′-one)* **7**: $C_{31}H_{37}NO_2$ (M = 455.64); elemental analysis [% found (calculated)]: C 81.38 (81.72), H 8.25 (8.19), N 2.79 (3.07); HRMS (ESI) M^+ 455.28326 (Δ = −0.830 mmu); MS (EI): *m/z* [%] = 455 (M^+, 100), 426 ($M^+ - X_2H_5$, 36); ^{1}H NMP ($CDCl_3$, 293 K): δ = 0.69 (s, 3H, CH_3), 0.78 (t, 3H, $^3J_{H,H}$ = 7.4 Hz, CH_3), 1.25 – 1.45 (m, 6H, CH_2, CH), 1.80 – 2.00 (m, 7H, CH_2, CH), 2.15 – 2.18 (m, 2H, CH_2), 3.74 (s, 3H, CH_3), 4.15 (m, 1H, CH), 5.54 (d, 0.8H, $^3J_{H,H}$ = 5.1 Hz, CH), 5.56 (d, 0.2H, $^3J_{H,H}$ = 5.1 Hz, CH), 6.59 – 6.67 (m, 2H, C_{ar}H), 6.73 (d, 0.8H, $^3J_{H,H}$ = 5.1 Hz, CH), 7.12 – 7.45 (m, 6H, C_{ar}H, CH); ^{13}C NMR ($CDCl_3$, 293 K): d = 9.0 (CH_3), 12.8 (CH_3), 23.2 (CH_2), 24.4 (CH_2), 26.0 (CH_2), 27.2 (CH_2), 29.7 (CH_2), 30.6 (CH_2), 36.7 (CH_2), 38.5 (CH), 43.7 (CH), 44.8 (CH), 51.7 (C), 55.1 (CH_3), 58.7 (CH), 111.3 (CH), 112.2 (CH), 113.7 (CH), 126.2 (CH), 126.5 (CH), 126.8 (CH), 128.4 (CH), 130.4 (C), 132.5 (C), 137.7 (C), 140.1 (C), 157.3 (C), 180.6 (C=O).

*1′-[3-Methoxyestra-1,3,5(10)trien-16α-yl]-1′,3′-dihydro-3′-ethyl-3′-phenyl-2*H*-pyrrol-2′-one)* **8**: $C_{31}H_{37}NO_2$ (M = 455.64); HRMS (ESI) $C_{31}H_{37}NO_2Na$ 478.27339 (Δ = −1.191 mmu); MS (DCI, H_2O): *m/z* [%] = 456 (MH^+, 61), 229 ($C_{15}H_{19}NO^+$, 100), 201 ($C_{13}H_{15}NO^+$, 63); ^{1}H NMR ($CDCl_3$, 293 K): δ = 0.83 – 0.92 (m, 6H, CH_3), 1.37 – 2.10 (m, 13H, CH_2, CH), 2.27 – 2.33 (m, 2H, CH_2), 2.83 – 2.86 (m, 2H, CH_2), 3.77 (s, 3H, CH_3), 4.72 – 4.81 (m, 1H, CH), 5.67 (d, 1H, $^3J_{H,H}$ = 5.0 Hz, CH), 6.64 – 6.74 (m, 3H, C_{ar}H, CH), 7.15 – 7.35 (m, 4H, C_{ar}H), 7.44 – 7.49 (m, 2H, C_{ar}H); ^{13}C NMR ($CDCl_3$, 293 K): δ = 9.0 (CH_3), 17.8 (CH_3), 26.2 (CH_2), 26.7 (CH_2), 28.0 (CH_2), 29.7 (CH_2), 31.2 (CH_2), 38.2 (CH_2), 38.8 (CH), 40.6/40.7 (C), 43.8 (CH), 46.9/47.1 (CH), 48.9/49.0 (CH_2), 50.1 (C), 52.0 (CH), 53.2 (CH), 55.1 (CH_3), 58.7 (C), 68.2 (CH), 111.4 (CH), 113.7 (CH), 126.1 (CH), 126.7 (CH), 126.8 (CH), 128.3 (CH), 132.4 (C), 137.7 (C), 140.1 (C), 178.8 (C=O).

*1′-[3-Methoxyestra-1,3,5(10)trien-16β-yl]-1′,3′-dihydro-3′-ethyl-3′-phenyl-2*H*-pyrrol-2′-one)* **9**: $C_{31}H_{37}NO_2$ (M = 455.64); elemental analysis [% found (calculated)]: C 81.56 (81.72), H 8.39 (8.19), N 2.84 (3.07); MS (DCI, H_2O): *m/z* [%] = 456 (MH^+, 100), 426 ($M^+ - C_2H_5$, 8); ^{1}H NMR ($CDCl_3$, 293 K): δ = 0.80 (t, 3H, $^3J_{H,H}$ = 7.4 Hz, CH_3), 0.97 (s, 3H, CH_3), 1.40 – 1.49 (m, 7H, CH_2, CH), 1.86 – 2.03 (m, 6H, CH_2, CH), 2.26 – 2.28 (m, 2H, CH_2), 2.81 – 2.85 (m, 2H, CH_2), 3.76 (s, 3H, CH_3), 4.57 – 4.65 (m, 1H, CH), 5.64 (d, 1H, $^3J_{H,H}$ = 5.1 Hz, CH), 6.60 – 6.61 (m, 1H, C_{ar}H), 6.68 – 6.71 (m, 1H, C_{ar}H), 6.74 (d, 1H, $^3J_{H,H}$ = 5.1 Hz, CH), 7.13 – 7.32 (m, 4H, C_{ar}H), 7.45 – 7.47 (m, 2H, C_{ar}H); ^{13}C NMR ($CDCl_3$, 293 K): δ = 9.1 (CH_3), 20.3 (CH_3), 26.5 (CH_2), 28.0 (CH_2), 29.7 (CH_2), 31.2 (CH_2), 31.8 (CH_2), 37.8 (CH), 38.9 (CH_2), 40.3 (C), 43.6 (CH), 45.6 (CH_2),

49.5 (CH), 52.3 (C), 52.4 (CH), 55.1 (CH_3), 58.7 (C), 111.4 (CH), 113.6 (CH), 113.7 (CH), 126.1 (CH), 126.7 (CH), 126.8 (CH), 128.9 (CH), 132.5 (C), 137.7 (C), 140.1 (C), 179.4 (C=O).

1′-[3-Methoxyestra-1,3,5(10)trien-16β-yl-17β-(dimethyl-tert.-*butylsilyloxy)]-1′,3′-dihydro-3′-ethyl-3′-phenyl-2*H-*pyrrol-2′-one)* **10**: $C_{37}H_{51}NO_3Si$ (M = 585.90); HRMS (ESI) $C_{37}H_{52}NO_3Si$ 586.37210 (Δ = −0.452 mmu); MS (EI): *m/z* [%] = 584 ($M - H^+$, 1), 556 ($C_{36}H_{50}NO_2Si^+$, 2), 528 ($C_{34}H_{46}NO_2Si^+$, 100), 500 ($C_{32}H_{42}NO_2Si^+$, 8), 472 ($C_{30}H_{38}NO_2Si^+$, 7), 414 ($C_{26}H_{28}NO_2Si^+$, 13), 357 ($C_{24}H_{25}NO_2^+$, 21), 264 ($C_{17}H_{14}NO_2^+$, 9), 227 ($C_{14}H_{13}NO_2^+$, 13), 171 ($C_{11}H_9NO^+$, 14), 158 ($C_{10}H_8NO^+$, 12), 129 ($C_6H_{13}OSi^+$, 47), 104 ($C_8H_8^+$, 10), 91 ($C_7H_7^+$, 11), 75 ($C_2H_7OSi^+$, 41), 73 ($C_3H_9Si^+$, 34), 57 ($C_4H_9^+$, 9), 41 ($C_3H_7^+$, 6); ^{1}H NMR ($CDCl_3$, 293 K): δ = −0.46 (s, 3H, CH_3), −0.19 (s, 3H, CH_3), 0.63 (s, 9H, CH_3), 0.69 (t, 3H, $^3J_{H,H}$ = 6.9 Hz, CH_3), 0.81 (s, 3H, CH_3), 1.12 – 1.60 (m, 6H, CH_2, CH), 1.68 – 1.88 (m, 4H, CH_2), 1.92–2.29 (m, 3H, CH_2, CH), 2.64 – 2.88 (m, 2H, CH_2), 3.68 (s, 3H, CH_3), 3.73 (d, 1H, $^3J_{H,H}$ = 9.8 Hz, CH), 4.62 (q, 1H, $^3J_{H,H}$ = 9.8 Hz, CH), 5.54 (d, 1H, $^3J_{H,H}$ = 4.9 Hz, CH), 6.55 (d, 1H, $^3J_{H,H}$ = 2.5 Hz, $C_{ar}H$), 6.63 (dd, 1H, $^3J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 2.5 Hz, $C_{ar}H$), 6.69 (d, 1H, $^3J_{H,H}$ = 4.9 Hz, CH), 7.13 – 7.30 (m, 5H, $C_{ar}H$), 7.42 – 7.51 (m, 2H, $C_{ar}H$); ^{13}C NMR ($CDCl_3$, 293 K): δ = −5.2 (CH_3), −5.1 (CH_3), 9.2 (CH_3), 12.9 (CH_3), 17.9 (C), 25.9 (CH_3), 26.5 (CH_2), 27.6 (CH_2), 29.7 (CH_2), 31.6 (CH_2), 33.4 (CH_2), 37.4 (CH_2), 38.0 (CH), 43.8 (C), 44.2 (CH), 47.1 (CH), 51.2 (C), 55.2 (CH_3), 57.6 (CH), 80.4 (CH), 111.1 (CH), 111.6 (CH), 113.9 (CH), 125.3 (CH), 126.7 (CH), 128.0 (CH), 128.2 (CH), 129.0 (CH), 132.4 (C), 137.8 (C), 140.2 (C), 157.6 (C), 180.0 (C=O).

Acknowledgements

The authors gratefully thank the Deutsche Forschungsgemeinschaft (SFB 436) for financial support.

References and Notes

[1] (a) G. Dyker, *Angew. Chem.* **1999**, 111, 1808; (b) Y. Guari, S. Sabo-Etienne, B. Chaudret, *Eur. J. Inorg. Chem.* **1999**, 1047.

[2] T. Morimoto, N. Chatani, S. Murai, *J. Am. Chem. Soc.* **1999**, *121*, 1758.

[3] D. Berger, W. Imhof, *J. Chem. Soc., Chem. Commun.* **1999**, 1457.

[4] (a) S. Murai, F. Kakiuchi, S. Seine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Pure Appl. Chem.* **1994**, *66*, 1527; (b) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Nature* **1993**, *366*, 529; (c) F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, S. Murai, *Bull. Chem. Soc. Jpn.* **1995**, *66*, 62; (d) F. Kakiuchi, Y. Yamamoto, N. Chatani, S. Murai, *Chem. Lett.* **1995**, 681; (e) M. Sonoda, F. Kakiuchi, A. Kamatani, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 109; (f) F. Kakiuchi, M. Yamauchi, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 111; (g) M. Sonoda, F. Kakiuchi, N. Chatani, S. Murai, *J. Organomet. Chem.* **1995**, *504*, 151; (h) S. Murai, N. Chatani, F. Kakiuchi, *Bull. Chem. Soc. Jpn.* **1997**, *69*, 589, (i) M. Sonoda, F. Kakiuchi, N. Chatani, S. Murai, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117.

[5] D. Berger, W. Imhof, *Tetrahedron* **2000**, *56*, 2015.

[6] (a) E. R. Gamzu, T. M. Hoover, S. I. Gracon, *Drug. Dev. Rev.* **1989**, *18*, 177; (b) S. Bertozzi, P. Salvadori, *Synth. Commun.* **1996**, *26*, 2659.

[7] D. Berger, M. Dubs, A. Göbel, W. Imhof, M. Kötteritzsch, M. Rost, B. Schönecker, *Tetrahedron: Asymmetry* **1999**, *10*, 2983.

[8] R. Krieg, R. Wyrwa, U. Möllmann, B. Schönecker, *Steroids* **1992**, *63*, 28.

[9] See, e. g.: (a) G. R. Desiraju, *Crystal Engineering: The Design of Organic Solids*, Elsevier, Amsterdam, **1989**; (b) J.-M. Lehn, *Supramolecular Chemistry*, VCH, Weinheim, **1995**; (c) C. B. Aakeröy, K. R. Seddon, *Chem. Soc. Rev.* **1993**, 397; (d) R. Taylor, O. Kennard, *Acc. Chem. Res.* **1984**, *17*, 320; (e) G. A. Jeffrey, W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer, **1991**; (f) Y. Gu, T. Kar, S. Scheiner, *J. Am. Chem. Soc.* **1999**, *121*, 9411; (g) G. R. Desiraju, T. Steiner, *The Weak Hydrogen Bond*, Oxford University Press, **1999**.

[10] M. Gonschior, M. Kötteritzsch, M. Rost, B. Schönecker, R. Wyrwa, *Tetrahedron: Asymmetry* **2000**, *11*, 2159.

[11] (a) G. Sheldrick, SHELXS-86, Universität Göttingen **1986**; (b) G. Sheldrick, SHELXL-93, Universität Göttingen **1993**.

[12] L. Zsolnai, G. Huttner, XPMA, Universität Heidelberg **1996**.

[13] Siemens Analytical Xray Inst. Inc., XP – Interactive Molecular Graphics, Vers. 4.2, **1990**.

[14] Crystal and intensity data for **7**: 183 K, crystal color: pale yellow, crystal size: 0.8 × 0.3 × 0.02 mm, monoclinic, a = 8.9796(6), b = 6.5244(7), c = 21.681(2) Å, β = 94.643(6)°, V = 1266.1(2) Å^3, Z = 2, F(000) = 492, ρ_{calc} = 1.195 g cm^{-3}, space group $P2_1$, abs. coeff. 0.073 mm^{-1}, θ limit 3.48 – 27.48°, φ- and ω-scan, 7011 refl. measured, 4766 independent refl., 2985 obs. refl. $F_o^2 > 2\sigma(F_o^2)$, 318 parameter, GOOF = 1.104, R1 = 0.1048, wR2 = 0.1485, final diff. map electron density [e Å^{-3}] 0.189.