234. The Tricyclooctanone Approach to the Total Synthesis of Steroids. The Cyclization of the A-CD Unit[1])

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Summary

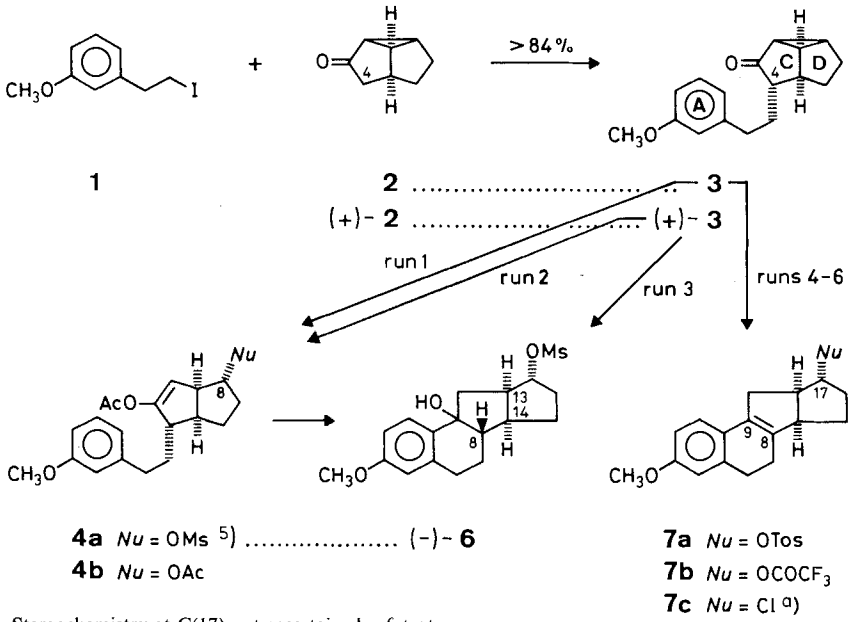
The first steps of a novel approach to the total synthesis of 9,11-dehydroestrone *via* tricyclo[3.3.0.$0^{2,8}$]octan-3-one (**2**) are described. One route involves a tandem-type transformation of the key intermediate **3** (A-CD unit) consisting of cyclopropane cleavage and ring B closure to afford C,18-bisnor-13α,17α-estradiol derivatives. *E.g.* the 3-methoxy-9ξ-hydroxy-17α-methanesulfonyloxy derivative (−)-**6** has been synthesized in 8 steps and 10% overall yield from 1,3-cyclohexadiene. As an alternative, the A-CD type intermediate **4b** has been prepared and could be used for a ring C enlargement prior to cyclization.

In a recent review we have presented a new polyvalent concept for the synthesis of cyclopentanoid natural products based on tricyclo[3.3.0.$0^{2,8}$]octan-3-one (**2**, *Scheme 1*) as a versatile building block [2]. The enantiomers of **2** are accessible in high chemical yields and in optical purities of > 98% [2] [3].

The basic requirements to be met for a competitive synthesis directed towards 9,11-dehydroestrone, estrone and functionalized derivatives, have been discussed in the context of recent literature [2]. Our tricyclooctanone route can also be adapted to the synthesis of potential precursors of ring C-functionalized steroids (*e.g.* 8- and 9,11-dehydroestrone) following the A-CD→ABCD build-up principle [2]: (−)-**6** (enantiomeric excess > 98%) is thus accessible in only 8 synthetic manipulations and in 10% yield starting from 1,3-cyclohexadiene. We now present experimental details of this and on a number of related transformations demonstrating further the versatility of the tricyclooctanone approach. The feature common to these transformations is that all involve a single operational step which includes the cleavage of the three-membered ring and the formation of ring B in a tandem-type process.

[1]) Presented in part at the 29th IUPAC Congress, Köln 1983 [1]; see also the recent review [2].

Scheme 1. *Alkylation of* **2** *and One-Step Transformations of the A-CD Unit* **3**[2])



[a]) Stereochemistry at C(17) not ascertained; *cf.* text.

Compounds (±)-**3** and (+)-**3** were prepared from the lithium enolate of (±)-**2** and (+)-**2**, respectively, by alkylation at −20° with *m*-methoxyphenylethyl iodide (**1**). A single product (**3**) was formed to which the 4-*exo*-configuration can be attributed in view of unequivocally established precedent [4].

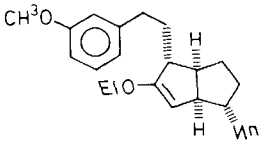
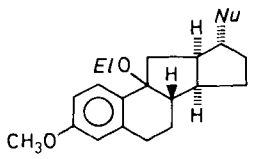
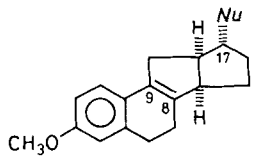
Substituting bromide and tosyloxy derivatives for the iodide **1**, and sodium for lithium in the enolate drastically reduced the yields of **3**. *m*-Methoxystyrene was formed instead as the result of a competing elimination process in accordance with earlier experience [5], possibly owing to a combination of the following factors. Elimination to form styrene may be preferred unless the bulky iodide bars the base from deprotonation. On the other hand, C(4), the reactive center of the lithium enolate of **2**, if acting as a base should be a sterically more hindered site, than the freely accessible negatively charged O-atom in the sodium enolate. Elimination is therefore favoured in the latter case.

(±)-**3** and (+)-**3** were treated with several reagents combining electrophilic (*El*) and nucleophilic (*Nu*) potential of various strength[3]). With acetyl methanesulfonate, (+)-**3** cyclized to form, after spontaneous partial hydrolysis, in > 70% yield the tetracyclic hydroxy-methanesulfonate (−)-**6** *(Scheme 1* and *Table)*. The two asymmetric centers of importance with respect to the target 9,11-dehydroestrone, C(8) and C(14), were already present after the alkylation step (+)-**2**→(+)-**3**. The mechanism of ring closure

[2]) All compounds in the *Schemes* and the *Table* are racemic, except for the transformations (+)-**3**→(−)-**6**.

[3]) For an account of the use and reactivity of such reagents on a more general level, see [6].

Table. *Products from the Reaction of* (±)-**3** *or* (+)-**3** *with ElNu-Type Reagents*[2])

Run	Reagent	Product[a])	Yield[b]) [%]	Reaction time [h]/ Reaction conditions
				
1	AcOMs	**4a** *El* = Ac, *Nu* = OMs[5])	75	1/$CHCl_3$, r.t.
2	Ac_2O	**4b** *El* = Ac, *Nu* = OAc	84	2/benzene, r.t. + $Cu(OAc)_2$; BF_3-etherate
				
3	AcOMs	(−)-**6** *El* = H, *Nu* = OMs	> 70[c])	10/$CHCl_3$, r.t.; H_2O workup
				
4	TsOH	**7a** *Nu* = OTos	67	3/benzene, r.t.
5	$(CF_3CO)_2O$	**7b** *Nu* = $OCOCF_3$	62	2/$CHCl_3$, r.t. + BF_3-etherate
6	$(CH_3)_3SiCl$ + CF_3CO_2Na	**7c** *Nu* = Cl[d])	85	1/$CHCl_3$, r.t.

[a]) The reactions have been carried out with (±)-**3**, except for the preparation of (−)-**6** (run 3), where (+)-**3** was used as a starting material (see *Scheme 1*).

[b]) The yields refer to purified materials and can be regarded as not yet fully optimized.

[c]) Yield refers to crystallized material only and does not account for residual product in the mother liquor.

[d]) Stereochemistry at C(17) not ascertained; *cf.* text.

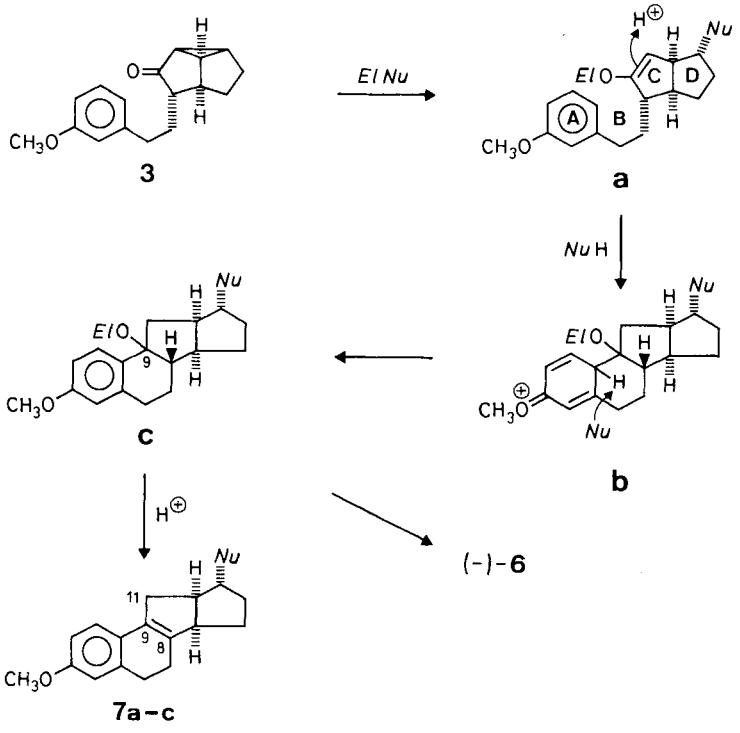
must involve a two-step process *(Scheme 2)*. The nucleophilic mesyloxy group should be incorporated in the primary step of the cyclopropane cleavage in an overall S_N2 mechanism accompanied by enolacetate formation (→**a**, *El* = $COCH_3$, *Nu* = CH_3SO_3) [6]. The subsequent closure of ring B (→**b**) and rearomatization of ring A (→**c**) is probably catalyzed by traces of acid[4]) which are very difficult to remove during the

[4]) Strong acids are known to catalyze ring-B-closure with the parent 6-membered ring-C-ketone; for a survey see [7].

preparation of the reagent. Thus, when the reaction was run for 1 h only, the enol acetate **4a**[5]) was isolated as the major product. Further treatment of **4a** with either acetyl methanesulfonate or methanesulfonic acid afforded cleanly (−)-**6** after workup with water. The cyclization was suppressed, however, when the acid traces in acetyl methanesulfonate were neutralized by the addition of excess Et_3N. Furthermore, we found the acid strength to be an important factor in the cyclization process: **4a** in the presence of AcOH remained unchanged. Guided by this result, low-acidity conditions were found to cleanly stop the transformation of **3** at the intermediate enol acetate stage and offer the option to expand ring C prior to closure of ring B. Thus racemic **3** in Ac_2O, with BF_3-etherate and $Cu(OAc)_2$ as catalysts, afforded **4b** in good yield (*Table:* run 2). The stereochemistry at C(8) of **4b** can safely be assigned on the basis of close precedent [2] [6].

In a further set of reactions, three elimination products **7a–c** (*Scheme 1* and *Table,* runs 4–6) were obtained directly. They have in common the C(8), C(9)-double bond but possess various substituents at C(17). We may assume that the three reactions (runs 4–6) proceed similarly in mechanistic terms, and that they are initiated as indi-

Scheme 2. *Mechanism of Ring-B-Closure*[2])



[5]) The contamination of product **4a** (80% purity by ^{1}H-NMR) with starting material, (+)-**3**, and with the cyclized product (−)-**6** did not allow to determine the optical rotation.

cated in *Scheme 2*. The elimination step (**c**→**7a–c**) is undoubtedly due to the presence of strong acids, in runs 5 and 6 trifluoroacetic acid and HCl[6]), respectively. All conditions exclusively afforded the C(8), C(9)-double bond isomers **7a–c**. Judging from NMR, the presence of 9,11-isomers could be ruled out, in contrast to comparable reactions leading to the 6-membered ring-C-homologue 9,11-dehydroestrone [7].

The stereochemistry at C(17) of (−)-**6**, **7a** and **7b** has been assigned on the basis of ample precedent concerning the *ElNu*-initiated cyclopropyl ketone opening of tricyclooctanone **2** [2] [6]. The C(17)-assignment for **7c** is much less certain. We have found no close precedent for the reaction conditions of run 6. It appears plausible to expect that trimethylsilyl trifluoroacetate, which is formed *in situ*[7]), is responsible for the opening of the 3-membered ring, leading to the *exo*-trifluoroacetate in the primary step (*i.e.*, →**a**, *El* = $(CH_3)_3Si$, *Nu* = CF_3CO_2). The exchange of the trifluoroacetoxy group with chloride, which is the less efficient leaving group, (→**c**, *El* = $(CH_3)_3Si$, *Nu* = Cl) is possibly assisted by homoallylic charge delocalization [6]. The 17α-configuration of **7c**, *i.e.* retention of configuration, would result from such an exchange mechanism.

In summary, a short synthetic approach to novel optically active 18,C-dinor steroids (**6**, **7a–c**) has been elaborated, which, furthermore, promises to eventually be developed into a total synthesis of 9,11-dehydroestrone either *via* compounds of type **6** or **7**, or by ring-C-enlargement of **4** and subsequent formation of ring B.

We thank Mr. *W. Wisniewski* (*Max-Planck*-Institut für Kohlenforschung) for collaborative help and access to the ^{13}C-NMR data bank[8]).

Experimental Part

General. Melting points (m.p.) were determined on a *Kofler* block and are uncorrected. Specific optical rotations, $[\alpha]_D$, were measured at 23° in $CHCl_3$, *c* in parantheses, exptl error ±5%. The UV spectra (EtOH unless stated otherwise) were measured on a *Cary 17* spectrophotometer; maxima are given in nm, with ε_{max} values in parantheses. IR spectra were run in $CHCl_3$, unless stated otherwise, on *Perkin-Elmer 137* and *700* instruments. ^1H- and ^{13}C-NMR spectra were measured in $CDCl_3$, unless stated otherwise, on *Bruker WP-80* (80 MHz for ^1H and 20.1 MHz for ^{13}C) and *WH-270* (270 MHz for ^1H and 67.9 MHz for ^{13}C) FT-instruments. Chemical shifts are reported in ppm downfield from internal TMS. Mass spectra (MS; in *m/e*) were recorded on a *Varian MAT CH5* instrument at 70 eV. Elemental analyses were performed by *Dornis* and *Kolbe*, Mülheim a.d. Ruhr. GLC analyses were performed with a *Varian Aerograph 1700* instrument equipped with a flame ionization detector coupled to a *Spectra Physics Autolab System I* computing integrator. *OV 101* glass capillary columns of 20 and 35 m length were used, with N_2 as the carrier gas. The solvents were purified using standard procedures. All reactions were run under Ar-atmosphere. In the routine workup procedure the solvent was removed *in vacuo* and the residue taken up in Et_2O/H_2O; after shaking, the organic layer was separated and dried over $MgSO_4$.

*2-(*m*-Methoxyphenyl)ethyl Iodide* (**1**). 2-(*m*-Methoxyphenyl)ethanol (25 g, 164 mmol) was dissolved in CCl_4 (150 ml) and the solution was warmed to 60°. After addition of PBr_3 (19 g, 70 mmol), the mixture was heated under reflux for 3 h. The completion of the reaction was monitored by GLC. After cooling to r.t., H_2O was added in small portions and the mixture shaken. The org. layer was separated and dried over $MgSO_4$. After evaporation of the solvent, the crude residue was directly redissolved in dimethoxyethane (DME) (150 ml), NaI (32 g, 213 mmol) was added and the mixture was stirred at reflux temp. for 5 h. The routine workup and distillation (60°, 8×10^{-2} Torr) afforded **1** [5] [8] (37.7 g, 87.5% yield) in 99% purity (by GLC).

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[6]) It is difficult to eliminate traces of HCl from trimethylsilyl chloride, and no such attempt was made in run 6.

[7]) Upon mixing of the components, $(CH_3)_3SiCl$ and sodium trifluoroacetate, at room temperature, trimethylsilyl trifluoroacetate was found in the supernatant solution.

[8]) Fully assigned ^{13}C-NMR spectra are part of the thesis of *G. Mikhail*.

(+)-*4*-exo-*[2-(*m-*Methoxyphenyl)ethyl]tricyclo[3.3.0.0^{2,8}]octan-3-one* (**3**). BuLi (16 mmol) in hexane was concentrated under a stream of Ar, then a solution of diisopropyl amine (1.19 g, 19 mmol) in DME (5 ml) was added dropwise during 30 min at −78° and under vigorous stirring. A crystal of 2,2-bipyridine was added as indicator (red color of the solution [9]) followed by the dropwise addition of a solution of ketone (+)-**2** (1,1 g, 9.02 mmol) in DME (3 ml) within 15 min. The mixture was warmed to r.t. with stirring and finally heated to 40° for another hour. The mixture was subsequently cooled to −78° and a solution of the iodide **1** (2.5 g, 9.54 mmol) in DME (3 ml) was added dropwise. The reddish color of the mixture still remained. The temp. was then raised to −20° and kept constant for 16 h. Workup afforded 2.5 g of an oily residue (77% **3** by GLC, 7% unreacted (+)-**2**, 8% iodide **1** and 8% *m*-methoxystyrene). The mixture was chromatographed on a silica ready-made column *(Lobar C, Merck)* using toluene and toluene 2% Et_2O; 2.1 g of (+)-**3** were obtained (> 90% purity by GLC, > 84% yield); $[\alpha]_D = +56.5°$ (0.75). IR: 3020*w*, 2920*s*, 3940*w*, 1710*s*, 1600*m*, 1580*m*, 1485*m*, 1450*m*, 1435*w*, 1310*m*, 1260*s*, 1190*w*, 1155*m*, 1045*m*, 945*w*, 870*w*, 785*w*. ^{1}H-NMR (400 MHz): 7.11 (*dd*, *J* = 2.5 and 8.5, 1 H); 7.09 (*d*, *J* = 8.5, 1 H); 6.7 (*m*, 2 H); 3.7 (*s*, 3 H); 2.6 (*m*, 4 H); 2.1–1.9 (*m*, 3 H); 1.9 (*m*, 1 H); 1.8 (*m*, 1 H); 1.8–1.6 (*m*, 2 H); 1.6 (*m*, 1 H); 1.5 (*m*, 1 H). ^{13}C-NMR: 218.33 (*s*); 159.69 (*s*); 143.17 (*s*); 129.28 (*d*); 120.87 (*d*); 114.22 (*d*); 111.29 (*d*); 56.88 (*d*); 55.07 (*q*); 44.10 (*d*); 40.22 (*t*); 38.32 (*d*); 35.32 (*d*); 34.74 (*d*); 32.98 (*t*); 31.67 (*t*); 25.16 (*t*). MS: 256 (M^+), 176, 135, 122 (100), 107, 94, 79.

$C_{17}H_{20}O_2$ (256.34) Calc. C 79.69 H 7.81% Found C 80.00 H 7.56%

(−)-9 ξ-Hydroxy-17α-mesyloxy-3-methoxy-18,C-dinor-13α-estra-1,3,5(10)triene (**6**) via **4a**. A solution of (+)-**3** (1.28 g, 5 mmol) in $CHCl_3$ (20 ml, passed over *Alox*) was treated with acetyl methanesulfonate (0.5 ml, 0.76 g, 5.5 mmol), which had been carefully distilled prior to use (for the preparation and purification of this reagent see [10]). The color of the mixture turned brown while stirring at r.t. After 1 h, one tenth of the mixture was worked up by dilution with $CHCl_3$ and shaking with H_2O. Drying of the org. layer over $MgSO_4$ and evaporation of the solvent afforded a brownish oil (190 mg, 80% purity by ^{1}H-NMR), of which the analytical data indicated **4a** to be the major component[5]). IR: 2940*m*, 1750*s*, 1665*w*, 1645*w*, 1600*m*, 1580*m*, 1460*w*, 1360*s*, 1335*s*, 1170*s*, 1015*m*, 905*s*. ^{1}H-NMR (60 MHz): 7.35 (*m*, 1 H); 6.8 (*m*, 3 H); 5.5 (*m*, 1 H); 4.9 (*m*, 1 H); 3.8 (*s*, 3 H); 3.4 (*m*, 1 H); 3.0 (*s*, 3 H); 2.9–1.3 (*m*, 10 H); 2.1 (*s*, 3 H). MS: 394 (M^+), 352, 334, 298, 273, 256, 134, 122 (100), 91, 43.

The remaining portion of the reaction mixture was stirred for a total of 10 h and then worked up in the same way. A solid brown residue (1.24 g) was isolated and crystallized by dissolving in a minimum quantity of $CHCl_3$, followed by the addition of a 1:1 benzene/pentane mixture (20 ml) and keeping the solution at −30° for 24 h. 1.112 g of (−)-**6** (> 95% purity by GLC, > 70% yield) were obtained. $[\alpha]_D = -29°$ (0.8), m.p. 117°. IR: 3000*m*, 2900*w*, 1600*m*, 1570*w*, 1500*w*, 1350*s*, 1320*s*, 1130*m*, 880*w*. ^{1}H-NMR (400 MHz): 6.89 (*d*, *J* = 8.5, 1 H); 6.72 (*d*, *J* = 2.7, 1 H); 6.68 (*dd*, *J* = 8.5 and 2.7, 1 H); 4.92 (*m*, fine coupling, 1 H); 3.79 (*s*, 3 H); 3.37 (*t*, *J* = 8, 1 H); 3.1–2.95 (*m*, 3 H); 3.03 (*s*, 3 H); 2.95–2.75 (*m*, 3 H); 2.39 (*dt*, J_d = 14.9, J_t = 1.6, 1 H); 2.3 (*m*, 2 H); 2.0 (*m*, 2 H); 1.7 (*m*, 2 H); 1.6 (1 H, exchangeable with D_2O). MS: 352 (M^+), 334 (100), 255, 239, 223, 210, 198, 165, 153, 115, 79.

3,8-exo-*Diacetoxy-4*-exo-*(*m-*methoxyphenylethyl)bicyclo[3.3.0]oct-2-ene* (**4b**). Ac_2O (2.55 g, 25 mmol), $Cu(OAc)_2$ (1.82 g, 10 mmol) and two drops of BF_3-etherate were added to a solution of (±)-**3** (2.56 g, 10 mmol) in dry benzene (20 ml). The mixture was stirred at r.t. for 8 h. The reaction mixture was worked up by extracting twice with aq. $NaHCO_3$. The org. layer was then shaken with brine and dried over $MgSO_4$. The crude material, which was obtained after evaporation of the solvent, was purified on a *Florisil* column (60–100 mesh, 25-fold) with toluene and toluene/1% Et_2O affording (±)-**4b** as a nearly colorless oil (3.2 g, 94% purity on GLC, 84% yield). IR: 2975*w*, 2820*w*, 2830*w*, 1750*m*, 1725*s*, 1600*m*, 1580*w*, 1490*w*, 1455*w*, 1370*m*, 1260*s*, 1220*m*, 1160*m*, 1020*m*, 915*s*, 870*w*. ^{1}H-NMR: 7.16 (*dd*, *J* = 7.5, 1 H); 6.74 (*dd*, *J* = 7.5 and 1, 1 H); 6.7 (*m*, 2 H); 5.4 (*m*, 1 H); 4.87 (*m*, 1 H); 3.75 (*s*, 3 H); 3.1 (*m*, 1 H); 2.75–2.42 (*t*, *J* = 2, 4 H); 2.08 (*s*, 3 H); 1.99 (*s*, 3 H); 2.13–1.75 (*m*, 3 H); 1.7 (*m*, 1 H); 1.6–1.45 (*m*, 2 H). ^{13}C-NMR: 170.66 (*s*); 168.21 (*s*); 159.63 (*s*); 152.72 (*s*); 143.77 (*s*); 129.31 (*d*); 120.73 (*d*); 114.19 (*d*); 113.13 (*d*); 110.69 (*d*); 79.86 (*d*); 55.10 (*q*); 52.81 (*d*); 51.13 (*d*); 43.82 (*d*); 35.03 (*t*); 33.11 (*t*); 31.68 (*t*); 30.54 (*t*); 21.26 (*q*); 21.06 (*q*). MS: 298 (M^+ − HOAc), 256, 238, 135, 122, 91, 57, 43 (100).

$C_{21}H_{26}O_5$ (358.43) Calc. C 70.39 H 7.26% Found C 70.06 H 7.02%

(±)-*3-Methoxy-17α-tosyloxy-18,C-dinor-13α-8-estra-1,3,5(10),8(9)-tetraene* (**7a**). TsOH (1.29 g, 7.5 mmol) and methyl orthoformate (0.5 ml) were added to a solution of (±)-**3** (1.58 g, 6.2 mmol) in benzene (20 ml). The mixture was stirred at r.t. for 5 h and then worked up by shaking twice with H_2O. The crude material (1.85 g), which was obtained after drying the org. layer ($MgSO_4$) and evaporation of the solvent, was

passed over a short silica gel column (10-fold, toluene) to afford 1.68 g of (±)-**7a** (67% yield). IR: 3000*m*, 1600*m*, 1565*w*, 1495*m*, 1430*w*, 1350*s*, 1245*s*, 1175*s*. ^{1}H-NMR: 7.8 (*d*, *J* = 8, 2 H); 7.32 (*d*, *J* = 8, 2 H); 6.83 (*d*, *J* = 8, 1 H); 6.7 (*d*, *J* = 2, 1 H); 6.65 (*dd*, *J* = 8 and 2, 1 H); 4.71 (*s*, 1 H); 3.76 (*s*, 3 H); 3.3 (*t*, *J* = 5.3, 1 H); 4.0–3.7 (*m*, 4 H); 2.45 (*s*, 3 H); 2.3–2.1 (*m*, 3 H); 2.0–1.7 (*m*, 2 H); 1.7–1.5 (*m*, 2 H). MS: 410 (100, M^+), 255, 238, 223, 210, 198, 165, 155, 91.

$C_{24}H_{26}O_4S$ (410.51) Calc. C 70.24 H 6.34 S 7.80% Found C 70.05 H 6.30 S 8.14

(±)-*3-Methoxy-17α-trifluoroacetoxy-18,C-dinor-13α-estra-1,3,5(10),8(9)-tetraene* (**7b**). Trifluoroacetic anhydride (0.5 ml) and two drops of BF_3-etherate were added to a stirred $CHCl_3$-solution (3 ml) of (±)-**3** (100 mg, 0.4 mmol). The reaction was run for 36 h at r.t., then cooled to 0° and Et_3N (1 ml) added dropwise. Shaking the mixture with H_2O, drying the org. layer ($MgSO_4$) and evaporation of the solvent afforded a crude oil (80% purity by GLC). Chromatography on a silica gel column (10-fold, benzene) gave 85 mg of oily (±)-**7b** (62% yield). IR: 2970*m*, 2840*w*, 1775*s*, 1605*m*, 1570*w*, 1500*m*, 1465*s*, 1430*w*, 1380*s*, 1345*m*, 1320*w*, 1300*w*, 1280*m*, 1250*s*, 1225*s*, 1170*s*, 1130*m*, 1100*w*, 1075*w*, 1035*w*, 1005*w*, 990*w*. ^{1}H-NMR: 6.92 (*d*, *J* = 8.5, 1 H); 6.74 (*d*, *J* = 2.5, 1 H); 6.7 (*dd*, *J* = 8.5 and 2.5, 1 H); 5.17 (*s*, 1 H); 3.8 (*s*, 3 H); 3.4 (*t*, *J* = 8, 1 H); 3.1–2.7 (*m*, 4 H); 2.46 (*dt*, J_d = 16 and J_t = 2.5, 1 H); 2.3 (*m*, 2 H); 2.1–1.8 (*m*, 2 H); 1.8–1.6 (*m*, 2 H). ^{13}C-NMR: 158.53 (*s*); 157.20 (*q*, $^2J_{CF}$ = 41.6); 137.85 (*s*); 137.07 (*s*); 131.96 (*s*); 126.41 (*s*); 123.59 (*d*); 114.58 (*q*, $^1J_{CF}$ = 285.8); 114.07 (*d*); 110.71 (*d*); 88.32 (*d*); 55.26 (*q*); 52.07 (*d*); 46.80 (*d*); 36.01 (*t*); 30.33 (*t*); 29.19 (*t*); 27.19 (*t*); 22.85 (*t*). MS: 352 (100, M^+), 239, 223, 197, 173, 165, 153, 128, 115, 69, 28.

(±)-*17ξ-Chloro-3-methoxy-18,C-dinor-13α-estra-1,3,5(10),8(9)-tetraene* (**7c**). Trimethylchlorosilane (10 ml) and sodium trifluoroacetate (2 g, 14.7 mmol) were mixed and stirred at r.t. for 0.5 h. Ketone (±)-**3** (2.56 g, 10 mmol) was then added. After 0.5 h at r.t. the mixture was worked up. The solid residue obtained after evaporation of the solvent was crystallized from $CHCl_3$/pentane at −30°, to give 2.33 g of (±)-**7c** (98% purity by GLC, 85% yield); m.p. 115°. IR: 3055*s*, 3040*s*, 2990*m*, 2830*s*, 1605*s*, 1570*s*, 1500*s*, 1460*m*, 1425*s*, 1370*w*, 1330*m*, 1310*m*, 1300*s*, 1275*s*, 1245*s*, 1190*w*, 1150*m*, 1125*s*, 1070*m*, 1055*s*, 815*m*, 805*m*. ^{1}H-NMR: 6.89 (*d*, *J* = 8.5, 1 H); 6.72 (*d*, *J* = 2.6, 1 H); 6.68 (*dd*, *J* = 8.5 and 2.6, 1 H); 4.1 (*m*, 1 H); 3,79 (*s*, 3 H); 3.37 (*t*, *J* = 8, 1 H); 3.1–2.7 (*m*, 4 H); 2.39 (*dt*, J_d = 16 and J_t = 2.1, 1 H); 2.3–2.1 (*m*, 3 H); 2.0–1.8 (*m*, 2 H); 1.6 (*m*, 1 H). ^{13}C-NMR: 158.37 (*s*); 138.46 (*s*); 137.0 (*s*); 131.36 (*s*); 126.58 (*s*); 123.41 (*d*); 113.93 (*d*); 110.59 (*d*); 68.11 (*d*); 55.20 (*q*); 51.7 (*d*); 51.44 (*d*); 36.91 (*t*); 35.03 (*t*); 29.14 (*t*); 27.51 (*t*); 22.81 (*t*). MS: 274 (M^+), 239 (100), 222, 210, 198, 165, 152, 127, 115, 28.

$C_{17}H_{19}OCl$ (274.78) Calc. C 74.45 H 6.93 Cl 12.77% Found C 74.74 H 6.84 Cl 13.16%

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