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TOTAL SYNTHESIS OF OPTICALLY ACTIVE 7α,18- AND 7β,18-DIMETHYL-19-NOR-TESTOSTERONE

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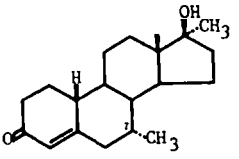
Abstract ——— A total synthesis of optically active 7α (β), 18-dimethyl-19-nor-testosterones **25** and **26** from the new common optically active synthon **5** obtained from acrolein **6** through the following sequence of reactions: 6→7→8→9→10→11→12→5, is described.

Introduction of 7-methyl group into the steroid molecule usually causes enhancemer and/or modification of parent hormonal activities[1]. For example, 7α,17α-dimethyl-19-nor-testosterone 1 has significant contragestative activity and is lack of estrogenicity. A great deal of papers on the partial syntheses of these compounds have been published in recent years[2] , but the paper concerned with the total synthesis of 7-methyl steroids seems dealing only with the syntheses of 7-methyl aromatic steroids 2 by using the optically active indanone derivative 3 as starting material.[3]



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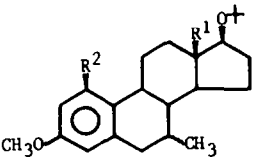
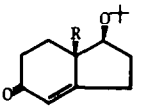
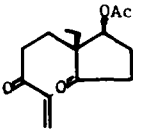


2 a. $R^1=CH_3$, $R^2=OCH_3$
b. $R^1=C_2H_5$, $R^2=H$



3 a. $R=CH_3$
b. $R=C_2H_5$



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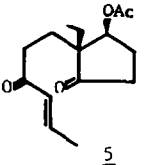

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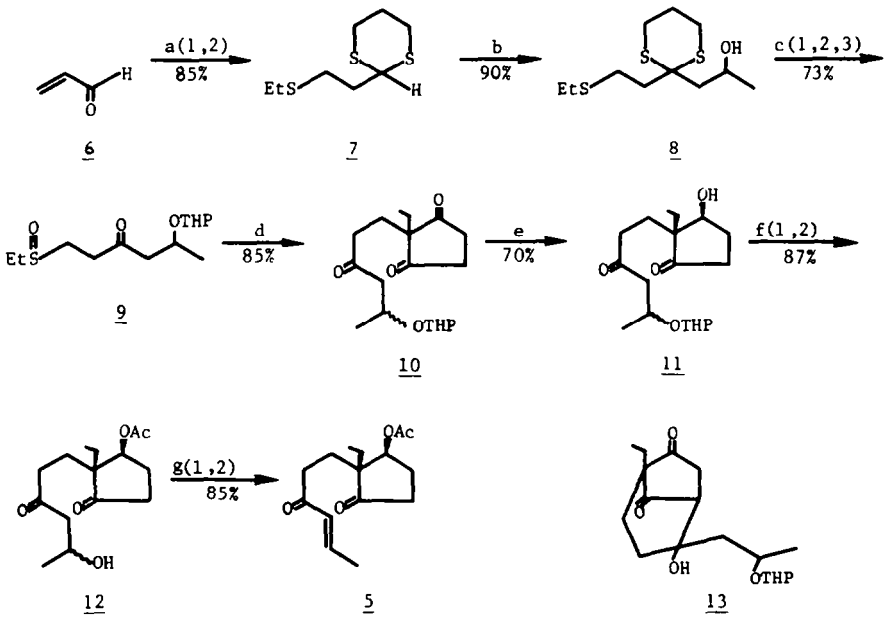
In our previous work, we have synthesized a new optically active synthon **4** for the total syntheses of steroids[4] starting from acrolein through γ-keto-sulfoxide and microbial asymmetric reduction. It occurred to us that this method could also be

used to synthesize the optically active synthon 5 containing an extra methyl group[5], which might be converted to the 7-methyl steroid molecule by introduction of the A,B ring through conjugate addition. We now report herein the synthesis of this new chiral synthon 5 and its application to the synthesis of 7α,18- and 7β,18-dimethyl-19-nor-testosterone.

5 was easily obtained from pro-chiral compound 10 prepared from γ-keto-sulfoxide 9 and 2-ethyl-1, 3-cyclopentanedione by microbial asymmetric reduction followed by elimination of the hydroxyl group on the side chain. 9 was synthesized by a 5-step sequence of reactions: the dithian 7 obtained from acrolein[6] in 85% yield was treated with 1,2-epoxypropane to give hydroxyl compound 8 in 90% yield. 8 was hydrolysed with $HgCl_2$-HgO followed by protection with DHP and oxidation with $NaIO_4$ to afford γ-keto-sulfoxide 9 in 73% overall yield. Reaction of 9 with 2-ethyl-1, 3-cyclopentanedione under reflux in the presence of Et_3N in THF furnished pro-chiral trione 10 in 85%



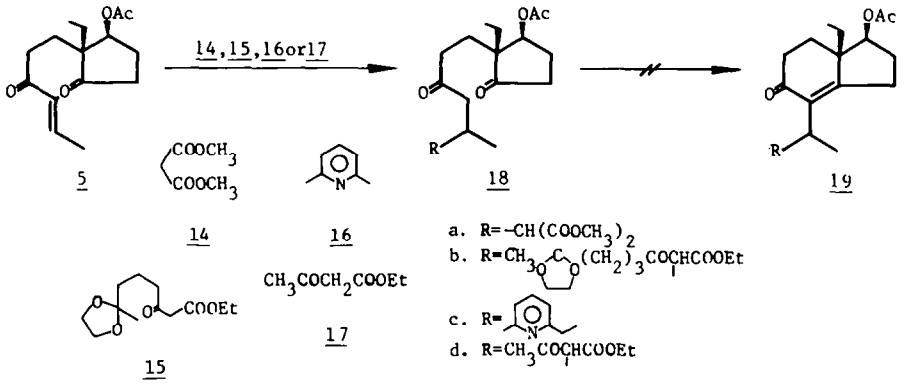
a. $^{1)}EtSH$, Et_3N $^{2)}$ SH, SH, $BF_3 \cdot Et_2O$; b. n-BuLi, ; c. $^{1)}HgCl_2$-HgO $^{2)}$DHP, p-TsOH $^{3)}NaIO_4$; d. . Et_3N-THF e. S.cerevisiae 2.346 f. $^{1)}Ac_2O$-py $^{2)}$THF-HAc-H_2O (1:2:1) g. $^{1)}MeSO_2Cl$-py. $^{2)}$ Et_3N-Et_2O

Scheeme 1

yield.[6] **10** was a mixture of diastereoisomers as shown by the ^{1}H NMR data which gave two sets of doublet at δ 1.16 and δ 1.26 corresponding to the protons in the termina CH_3 group of the side chain, respectively. Since the chiral center at this side chain will be destroyed finally, **10** was used directly for the following transformation Thus, **10** was asymmetrically reduced by incubation with Saccharomyces cerevisiae 2.346 under shaking continuously for 2 days at 28-30°C to furnish the optically active produ **11** in 70% yield together with the side product **13** in 4% yield which was deduced to be an endocyclic compound[4]. **11** was also a diastereomeric mixture as shown by its ^{1}H NMR spectrum.

Acetylation of **11** with Ac_2O-pyridine followed by removal of the THP protecting group afforded **12** in 87% overall yield. The new optically active synthon **5** was obtained finally by converting **12** to mesylate with methanesulfonyl chloride-pyridine at 0°C followed by elimination of mesylate with Et_3N in Et_2O at room temperature in 85% yield. The large coupling constant (16Hz) of two olefinic protons in ^{1}H NMR spectrum indicated that this two protons were in trans geometry and the compound **5** was thus established to be E isomer shown in scheme 1. The absolute configuration of **5** was tentatively assigned to be 2R, 3S ($[\alpha]_D^{16}$+55.6°)in comparison with the homologous 2R, 3S-**4** ($[\alpha]_D^{14}$+61.2). It is surprising that in contrast with **4**, the compound **5** is very stable and doesn't deteriorate after a long time storage, though it also contains an α,β-unsaturated ketone system. So it is an ideal synthon for syntheses of steroids.

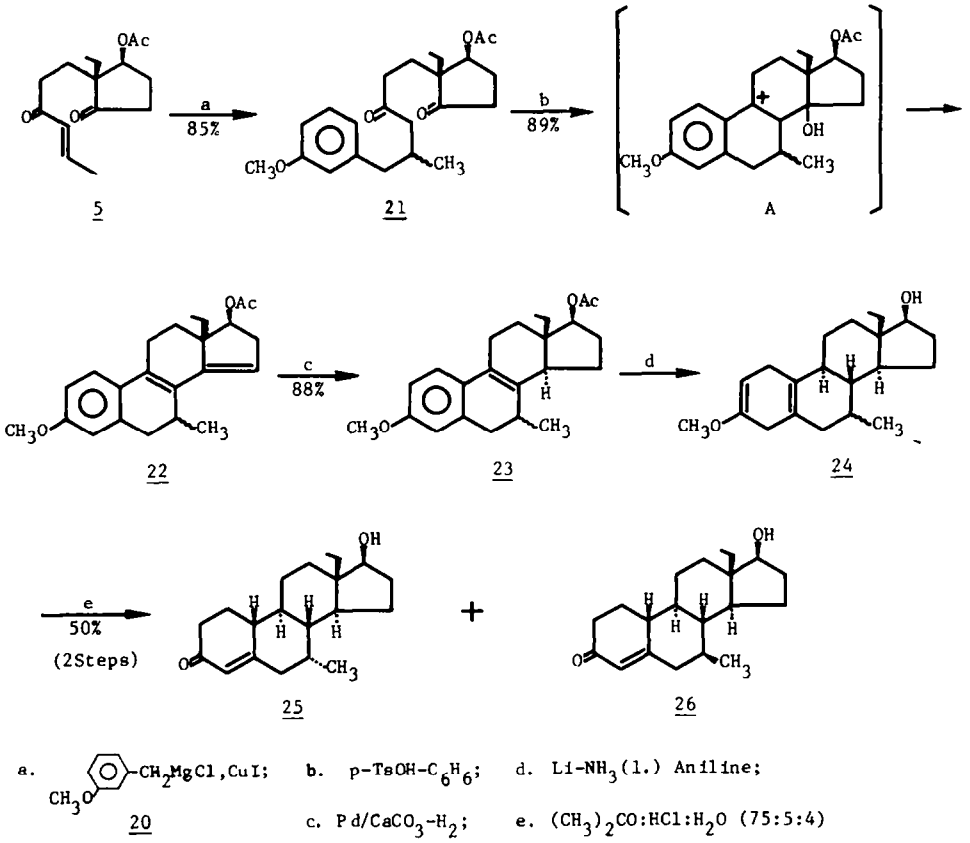
5 could react with a variety of Michael donors such as malonic ester **14**, β-ketoester **15**,[7] 2,6-lutidine **16** and acetoacetic ester **17** to form the corresponding Michael adducts **18** a,b,c,d, in good yields. Unfortunately, all our attempts at cyclization of **18** under various conditions failed.



Scheme 2

However,the cyclization of **21** was successful: reaction of α,β-unsaturated ketone **5** with m-methoxybenzylmagnesium chloride prepared from m-methoxybenzyl chloride and Mg turnings under reflux in THF in the presence of cuprous iodide afforded the regiospecific 1,4-adduct **21** in 85% yield. It was a mixture of 7-methyl epimers in ca. 54:46 ratio as shown in GC, which couldn't be easily separated in usual manner owing to their close retention time (7'40" and 7'45" respectively). Cyclization of **21** with methanolic hydrochloric acid at room temperature gave a complex mixture in which **22** was obtained only in about 10% yield separated by preparative TLC, while the reacion carried out with p-TsOH in benzene under reflux for 1.5 h, the yield of **22** was increased to 89%.

In comparison with **18**, the cyclization of **21** was



Scheme 3

much easier and might be considered as a result of the formation of the low energetic cation A, in which the positive charge created in the reaction might be delocalized to the benzene ring.

Catalytic hydrogenation of **22** over palladium on calcium carbonate at room temperature in THF gave stereoselectively the C,D ring trans compound **23** in 88% yield. Birch reduction of **23** at -50°C for 5 h followed by acidic hydrolysis of the resulting diene compound **24** gave a 1:1 mixture of 7α,18-dimethyl-19-nor-testosterone **25** and 7β, 18-dimethyl-19-nor-testosterone **26** in 50% yield (from Birch reduction), which was separated by repeated preparative thin layer chromatography to the pure components.

Comparison of the chemical shifts of CH_3 group at C-7 in **25** (δ 0.78) and **26** (δ 1.04)with the corresponding ^1H NMR data of 7-methyl steroid reported in the literature[1b] suggested that **25** and **26** have the 7α-CH_3 and 7β-CH_3 configuration, respectively.

Thus, a new synthesis of optically active 7α(β), 18-dimethyl-19-nor-testosterone was accomplished starting from acrolein **6** through 16 steps in 8% overall yield (14% overall yield based on 2-ethyl-1,3-cyclopentanedione).

EXPERIMENTAL

The silica gel used for the chromatography was 100-200 or 200-300 mesh in size and GF_{254}, silica gel H, respectively. Iodine vapour and vanilin were used for colour developing. The m.p. and b.p. were uncorrected. The optical rotation was measured on WZZ autopolarimeter and Autopol® III polarimeter. IR spectra were measured as thin films or Nujol mulls on polished NaCl plates using UR-10, 751 and Shimadzu 440 infrared spectrophotometers. UV spectra were obtained from 730 UV spectrometer. ^1H NMR spectra were obtained on Varian EM-360 (60 MHz) and XL-200 (200 MHz) spectrometers using TMS or HMDS as an internal standard. The unit of δ was ppm. Mass spectra were obtained with JMS-01U and Finnigan 4021 GC-MS instruments. Elemental analyses were performed by Analytical Department of this Institute.

2-(2'-ethylthio)-ethyl-1,3-dithian 7

To a stirred solution of freshly distilled acrolein (11.2g) and triethylamine (5ml) in chloroform (90 ml), 15g of EtSH was added dropwise at room temperature, to which, after being stirred for 3 h, 14g of BF_3 Et_2O and 25g of 1,3-propanedithiol were added and the mixture was stirred continuously for 3 h. The reaction mixture was poured into water. The organic layer was washed successively with water, 7% KOH solution and water and dried over anhydrous Na_2SO_4. Removal of the solvent in vacuum followed by distillation afforded 36g of colourless oil of 7 (85%) b.p. 102-114°C/9x10^{-3}mm. NMR (CCl_4, HMDS): 1.19(3H,t,J=7Hz), 1.60-2.16(4H,m),2.10-2.80 (8H,m), 3.99(1H,t,J=7Hz); MS(m/e): 208(M^+); Found: C,46.22, H,7.69, S,45.82; Calcd. for $C_8H_{16}S_3$: C,46.15, H,7.69, S.46.15.

2-(2'-ethylthio)-ethyl-2-(2'-hydroxy)-propyl-1,3-dithian 8

A stirred solution of 7 (19g) in THF (180 ml) was cooled to -70°C in a dry ice-bath and 75ml of BuLi(1.48M) was added dropwise under N_2. The temperature was not allowed to exceed -50°C during addition and then warmed to -20°C within 2 h. To the cold reaction mixture (-70°C), was added 8ml of 1,2-epoxypropane and the

temperature was raised to -20°C within 3 h. Most of the solvent was removed in vacuum and 50ml of saturated NH_4Cl solution was added and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were washed successively with 5% KOH solution, water, and dried. Removal of solvent followed by distillation gave 21.84g of the pale yellow oil **8** (90%) b.p. 130-150°C/ $8x10^{-3}$mm. IR(ν_{max}): 3420 cm^{-1}(-OH); NMR (100 MHz,CCl_4,TMS): 1.14(3H,d.J=7Hz), 1.25 (3H,t,J=7Hz), 4.07(1H,m); Found: S, 36.19; Calcd. for $C_{11}H_{22}OS_3$: 36.09.

Ethyl,3-oxo-5-tetrahydropyranoxy-hexyl sulfoxide 9

To a stirred solution of $HgCl_2$(50g) and red HgO(18g) in 800ml of 80% aqueous solution of acetonitrile was added a solution of **8** (21.84g) in 100ml of 80% aqueous solution of acetonitrile. The mixture was refluxed under N_2 for 4.5 h. After cooling, the mixture was filtered through celite. The residue was washed with CH_2Cl_2 and the organic layer was separated. After extraction of the aqueous layer with methylene chloride the combined organic extracts were washed with 5M NH_4OAc solution and saturated NaCl solution, then dried. The solvent was removed in vacuum to give 12.3g of crude product. The analytic specimen was obtained by preparative TLC developed by acetone-petroleum ether (3:7). IR(ν_{max}). 3450 (-OH), 1700 cm^{-1}(-CO), NMR (60 MHz,CCl_4,TMS): 1.17 (3H,d,J=7Hz), 1.26 (3H,t,J=7Hz), 2.74(4H,S), 4.20(1H,m).

To a stirred solution of above crude product (12.3g) in THF (30ml) was added 120mg of p-TsOH. The mixture was cooled on an ice-water bath and 15ml of DHP was added dropwise. The mixture was stirred for 2 h at room temperature and poured into 20ml of ice water. After extraction with ethyl acetate, the organic layer was washed successively with saturated $NaHCO_3$ and NaCl solution and then dried over anhydrous Na_2SO_4. Removal of solvent gave 18.94g of crude oil, which was purified by chromatography on 200g of silica gel (gradient elution, acetone-petroleum ether) to give 15.67g of light yellow oil IR(ν_{max}), 1700 cm^{-1}(-CO); NMR(60 MHz,CCl_4,TMS): 1.10(1.5H,d,J=7Hz), 1.15(1.5H,d,J=7Hz), 1.22(3H,t,J=7Hz), 2.70(4H,s), 4.56(1H,s).

To a solution of 3.9g of $NaIO_4$ in 30ml of water was added dropwise a solution of 3.70g of above product in 30ml of methanol below 30°C. The mixture was stirred for 30 min and then filtered. The residue was washed with CH_2Cl_2. After extraction with CH_2Cl_2, the organic layer was dried over anhydrous Na_2SO_4. Evaporation of solvent gave 3.90g of semisolid of **9** in 73% overall yield (from **8**). IR(ν_{max}): 1710(-CO), 1020 cm^{-1}(-SO); NMR (60 MHz,CCl_4,TMS): 1.17(3H,t,J=7Hz), 1.36(3H,d,J=7Hz), 4.58(1H,s), MS(m/e): 277(M^++1).

2-ethyl-2-(3'-oxo-5'-tetrahydropyranoxy-)-hexyl-1,3-cyclopentanedione 10

A solution of **9**(16.6g), 2-ethyl-1,3-cyclopentanedione(9.5g) and Et_3N (5ml) in 130ml of THF was refluxed under N_2 for 24 h. After cooling, the solvent was removed and the residue was chromatographed over 200g of silica gel (gradient elution; acetone-petroleum ether) to afford 16.15g yellow oil **10** in 83% yield IR(ν_{max}): 1770, 1730 cm^{-1}(β-diketone of 5 member ring); NMR (60 MHz,CCl_4,TMS):0.75(3H,t,J=7Hz), 1.16 (1.5H,d,J=7Hz), 1.26(1.5H,d,J=7Hz), 2.75(4H,s),4.62(1H,t,J=4Hz); MS(m/e):325(M^++1); Found: C, 66.62, H, 8.72; Calcd. for $C_{18}H_{28}O_5$: C, 66.64, H, 8.70.

(2R,3S)-(-)-2-ethyl-2-(3'-oxo-5'-tetrahydropyranoxy)-hexyl-3-hydroxy-cyclopentanone 11

To a solution of 1000ml of culture medium containing 3% glycose, 2% corn starch,0.2% K_2HPO_4, 0.2% $NaNO_3$, 0.1% K_2HPO_4, 0.05% $MgSO_4$,0.02% KCl and 0.02% $FeSO_4$

in 5L of Erlenmeyer flask was added 25ml of Saccharomyces cerevisiae 2.346 medium which had been cultured for 24 h. After shaking at 28-30°C for 24 h, the pH of the mixture was adjusted with 6N NaOH solution to 6.7-7.0, and a solution of 2g of **10** in 8ml of 95% EtOH was added. The mixture was shaken continuously for 48 h. The mycelia were removed and the solution was extracted with ethyl acetate. The organic layer was washed with water and dried. Removal of solvent gave crude proudt which was separated by flash chromatography [acetone-petroleum ether (2:8) as eluant] gave 1.58g of **11** in 78% yield. $[\alpha]_D^8$-5.2°(C 1.97, C_6H_6); IR(ν_{max}): 3420 (-OH), 1730, 1710 cm^{-1}(-C=O); NMR(60 MHz,CCl_4,TMS): 0.80 (3H, t,J=7Hz), 1.12(1.5H,d,J=7Hz), 1.20(1.5H,d,J=7Hz), 4.54(1H,s); MS(m/e): 327(M^++1); Found: C, 66.28, H, 9.07; Calcd. for $C_{18}H_{30}O_5$: C, 66.23, H, 9.20 and 0.15g of endocyclic compound **13**. IR(ν_{max}): 3460(-OH), 1760, 1730 cm^{-1}(β-diketone of 5 member ring); NMR (60 MHz,CCl_4,TMS): 0.73(3H,t,J=7Hz), 1.13(1.5H,d,J=7Hz), 1.17(1.5H,d,J=7Hz), 4.52(1H,s).

(2R,3S)-(+)-2-ethyl-2-(3'-oxo-5'-hydroxy)-hexyl-3-acetoxy-cyclopentanone 12

A solution of **11** (0.84g) and acetic anhydride (1.2ml) in pyridine (8ml) was heated on a steam bath for 1 h and then cooled. The reaction mixture was poured into 50ml of ice water and extracted with ethyl acetate. The organic extracts were washed successively with 20% HCl solution, saturated $NaHCO_3$ solution and saturated NaCl solution. Removal of solvent gave 0.97g of crude acetylated product which was used without further purification for the next experiment. 0.97g of this acetylated product was dissolved in 25ml of mixed solvent (HAc:THF:H_2O=2:1:1) and stirred at 55°C for 6 h. The solution was neutralized with KOH solution and extracted with ethyl acetate. The organic extracts were washed with saturated $NaHCO_3$ and NaCl solution successively and dried. Removal of solution gave 0.88g of crude product, which was purified by chromatography over 45g of silica gel (gradient elution, acetone-petroleum ether) to afford 0.64g of colourless oil **12** in 87% overall yield (2 steps). $[\alpha]_D^{12}$+49.4° (C 1.25,$CHCl_3$); IR(ν_{max}): 3450(-OH) 1730, 1240 cm^{-1} (CH_3-CO-O-); NMR (60 MHz, CCl_4,TMS): 0.78(3H,t,J=7Hz), 1.10(3H,d,J=7Hz), 2.00(3H,s), 2.83(1H,br), 4.00(1H,m), 5.08(1H,t,J=4Hz), MS(m/e): 285(M^++1).

(2R,3S)-(+)-2-ethyl-2-(3'-oxo-4'E-ene)-hexyl-3-acetoxy-cyclopentanone 5

A solution of **12** (100mg) in pyridine(1.5ml) was stirred at 0°C on an ice bath, to which was added 0.12ml of methanesulfonyl chloride. The resulting mixture was stirred at 0°C for 2 h and poured into 10ml of ice water. The solution was extracted with ethyl acetate. The organic layer was washed successively with 20% HCl, saturated $NaHCO_3$ and NaCl solution and dried. Removal of solvent gave 140mg of yellowish oil. The analytic specimen was obtained by preparative TLC. IR (ν_{max}): 1730, 1250 (CH_3COO-), 1360, 1170 cm^{-1}(CH_3SO_3-); NMR (60 MHz,CCl_4, TMS): 0.78(3H,t,J=7Hz), 1.40(3H,d,J=7Hz), 2.00(3H,s), 2.90(3H,s), 5.10(1H,t,J=6Hz).

A solution of 130mg of above mesylate and 0.1ml of Et_3N in 2ml of ethyl ether was stirred at room temperature over night. After removing solvent the residue was purified by preparative TLC to give 80mg of pale yellowish oil, which became crystal on standing at room temperature, in 85% overall yield (from **12**). m.p. 59-59.5°C (petroleum ether - isopropyl ether) $[\alpha]_D^{16}$+55.6°(C 1.08, $CHCl_3$); IR(ν_{max}): 1730, 1240(CH_3COO-), 1670, 1630 cm^{-1}(α,β-unsaturated ketone); UV(λ_{max}^{EtOH}): 222nm (ε 12,400); NMR (60 MHz, CCl_4,TMS): 0.78(3H,t,J=7Hz), 1.87(3H,d-d,J=7,1Hz), 2.00(3H,s), 5.12(1H,t,J=4Hz), 5.97(1H,d-q,J=16,1Hz), 6.72(1H,d-q,J=16,7Hz);

MS(m/e): 267(M^++1); Found: C, 67.67, H, 8.37; Calcd. for $C_{15}H_{22}O_4$: C, 67.67, H, 8.27.

(2R,3S)-(+)-2-ethyl-2-(3'-oxo-5'-methyl-6'-m-methoxyphenyl)-hexyl-3-acetoxy-cyclopentanone 21

A solution of 1.56g of m-methoxybenzyl chloride[8,9] in 8.6ml of anhydrous THF was added dropwise to a stirred suspension of 500mg of magnesium turnings in 2ml of anhydrous THF at reflux temperature. The mixture was then stirred for an additional 1.5 h under reflux. After cooling to room temperature, 25ml of anhydrous THF and 600mg of cuprous iodide were added and the mixture was stirred for 15 min. A solution of 530mg of α,β-unsaturated ketone **5** in 4ml of anhydrous THF was added dropwise and the mixture was stirred at room temperature for 10 min. The reaction solution was then poured into a cooled solution of 1N aqueous H_2SO_4. After stirring for 5 min. the mixture was extracted with ethyl acetate. The organic layer was washed successively with saturated $NaHCO_3$ and NaCl solution and dried. After removing solvent the crude product was purified by flash chromatography [ethyl acetate-petroleum ether (2:8) as eluant] to afford 650mg of 1.4-adduct **21** in 85% yield. $[\alpha]_D^{17}$+46.8°(C 1.64, $CHCl_3$); IR(ν_{max}): 1740, 1710(-C=O), 1610, 1595 cm^{-1} (aromatic ring); UV(λ_{max}^{EtOH}): 217(ε 7800), 273(ε 2015), 280 (ε 1900)nm; NMR (200 MHz, CCl_4,TMS): 0.72(3H,t,J=7Hz), 0.80(3H,m), 1.94(3H,s), 3.69(3H,s), 5.06(1H,t,J=4Hz), 6.50-6.60(3H,m), 6.98-7.07(1H,m); Found: C, 71.20, H, 8.35; Calcd. for $C_{23}H_{32}O_5$: C, 71.13, H. 8.25.

(-)-3-methoxyestra-7,18-dimethyl-17-acetoxy-1,3,5(10), 8(9), 14(15)-pentanene 22

A solution of 370mg of **21** and 150mg p-TsOH in 7ml of benzene was refluxed under N_2 for 1.5 h. After cooling, the reaction solution was diluted with benzene and washed successively with saturated $NaHCO_3$ and NaCl solution. After removing the solvent, the crude product was purified by flash chromatography [ethyl acetate-petroleum ether (0.5:9.5) as eluant] to give 300mg of **22** in 89% yield $[\alpha]_D^{15}$ -190° (C 1.18, $CHCl_3$); IR(ν_{max}): 1740, 1240(CH_3COO-),1600, 1500 cm^{-1}(benzene ring); UV(λ_{max}^{EtOH}): 313nm (ε 25100); NMR(200 MHz,CCl_4,TMS): 0.79-0.93(6H,m), 204(3H,s), 3.74(3H,s), 5.05(1H,t,J=7Hz), 5.10(1H,br), 6.54(2H,m), 7.0-7.20(1H,m); MS(m/e): 352(M^+).

(-)-3-methoxyestra-7,18-dimethyl-17-acetoxy-1,3,5(10),8(9)-tetraene 23

100mg of 5% $PdCl_2/CaCO_3$ in 1ml of THF were treated with H_2 at room temperature under stirring to form black Pd-$CaCO_3$. A solution of 85mg of **22** in 2ml of THF was added and the mixture was stirred under H_2 until no hydrogen was taken up. Filtration and evaporation followed by preparative TLC gave 75mg of **23** in 88% yield. $[\alpha]_D^{20}$-36.8°(C 0.63, $CHCl_3$); IR(ν_{max}): 1740, 1240(CH_3COO-), 1600, 1500 cm^{-1}(benzene ring); UV(λ_{max}^{EtOH}): 278 nm(ε 17,500); NMR (200 MHz, $CDCl_3$. TMS): 0.80(3H,t,J=7Hz), 0.93(1.5H,d,J=7Hz), 0.98(1.5H,d,J=7Hz), 2.04(3H,s); 3.78(3H,s), 6.57(2H,m), 7.0-7.20(1H,m); MS(m/e): 354(M^+).

(+)-7α,18-dimethyl-19-nor-testosterone 25 and (+)7β,18-dimethyl-19-nor-testosterone 26

To a solution of 100mg of metal Li in 10ml dried liquid NH_3 was added a solution of 0.3ml of aniline in 1ml of THF and then a solution of 50mg of **23** in 3ml THF. The mixture was stirred at -40--60°C for 5 h. 2ml of methanol were added carefully and the mixture was stirred for additional 1 h. 2ml of 10% aqueous HOAc were added dropwise and the temperature was raised to room temperature gradually for removal of

NH_3. The residue was diluted with H_2O followed by extration with ethyl acetate. The organic layer was washed with saturated NaCl solution and dried. Removal of solvent gave 45mg of crude diene **24** which was dissolved in 2ml of mixed solvent (CH_3COCH_3:HCl:H_2O=75:5:4) and stirred at room temperature for 1 h. The resulting solution was extracted with ethyl acetate and the organic layer was washed successively with saturated $NaHCO_3$ and NaCl solution. After removal of solvent, the crude product was separated by preparative TLC to give 20mg of **25** and **26** which was further separated by preparative TLC, developing successively for 3-4 times in ethyl acetate-petroleum ether (3:7) to give 1:1 ratio of 7α-methyl steroid **25** $[\alpha]_D^{25}$+43.2° (C 0.426, EtOH); IR(ν_{max}): 3400(-OH), 1660 cm^{-1}(α,β -unsaturated ketone); UV(λ_{max}^{EtOH}): 242nm (ε 14,200) NMR (200 MHz, $CDCl_3$,TMS): 0.76(3H,d,J=7Hz), 1.02(3H,t,J=7Hz), 3.76(1H,t,J=7Hz), 5.83(1H,s); MS(m/e): 302(M^+) and 7β-methyl steroid **26** $[\alpha]_D^{25}$+46.4° (C 0.112, EtOH); IR(ν_{max}): 3400(-OH), 1600 cm^{-1} (α,β -unsaturated ketone), UV(λ_{max}^{EtOH}): 242nm (ε 13,700); NMR(200MHz,$CDCl_3$,TMS): 0.97(3H,t,J=7Hz), 1.04(3H,d,J=7Hz), 3.83(1H,m), 5.93(1H,s); MS(m/e): 302(M^+).

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