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Highly efficient Lewis acid catalyzed, one step conversions of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one to D-homosteroid and Δ^{13}-steroids

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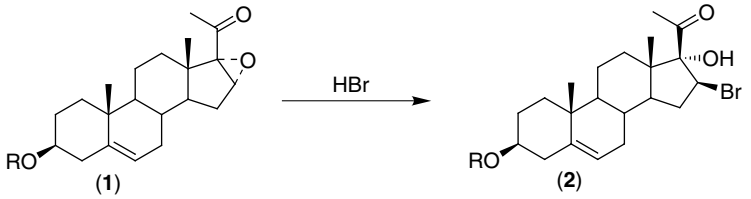
Abstract—Conversion of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (**1a**) to 16β-chloro-3β,17α-dihydroxy-17β-methyl-17a-homo-androst-5-en-17a-one (**3**) in very high yields (95%), in one step by treatment with 3 equiv. of anhyd. $AlCl_3$, has been achieved; use of two equiv. of $AlCl_3$ affords mixture of D-homosteroid **3** (70%) and chlorohydrin **4** (27%). On the other hand, treatment of **1a** with excess of acetic anhydride and anhydrous $ZnCl_2$ at room temperature leads to reversal of the direction of epoxide ring opening with concomitant methyl migration, leading to 3β,16α-diacetoxy-17-methyl-17α-pregna-5,13-diene-20-one (**6**) in high yield (92 %). The conversions are a remarkable improvement over related routes in terms of both yield and selectivity.

1. Introduction

17-Hydroxy-20-keto steroids have been extensively exploited[1] to obtain D-homosteroids, which continue to attract attention on account of their significant medicinal values.[2] 17-Hydroxy-steroids have also been converted to mixtures of 12-/13-dehydro steroids,[3] the latter are useful intermediates for a number of biologically active steroids.[3a,4] Though, facile one step epoxide ring opening—steroidal skeletal rearrangements, under milder conditions, are well known in the case of a number of steroidal ring A,B and C-epoxides,[5] the 16α,17α-epoxy-20-one system (**1**) has proven to be quite resistant to nucleophilic/Lewis acid catalyzed ring opening.[6] The only reported opening of the latter epoxide ring is the conversion by HBr–AcOH, of **1b** to bromohydrin **2b** (Scheme 1).[7] It was, therefore, desired to investigate possible one step transformations of 16α,17α-epoxy-3β-hydroxy/acetoxy-pregn-5-en-20-one (**1**) to both ring D-homosteroids and Δ^{13}-steroids.

2. Results and discussion

Treatment of 16α,17α-epoxy-3β-acetoxypregn-5-en-20-one (**1b**) with 1 equiv. of boron-trifluoride etherate in THF/Et_2O for 20 h failed to open the epoxide ring. Increasing the amount of BF_3OEt_2 (>4 equiv.) was also of no consequence; except for the hydrolysis of 3-acetate, no other transformation occurred. Refluxing **1a** in formic acid (96%, bp 101–102°C) for 7 h resulted only in formylation of C3–OH leading to **1c**; this only demonstrated the high stability of 16α,17α-epoxy-20-one system, because, refluxing in formic acid is reported to bring about skeletal rearrangements of ring-A streoidal epoxides.[5j] Subsequently, it was observed that treatment of epoxide **1a** with



(**1**)

a: R = H
b: R = CH_3CO
c: R = HCO

(**2**)

Scheme 1.

Keywords: epoxides; epoxy-steroids; Lewis acids; rearrangements; D-homosteriods; Δ^{13}-steroids.

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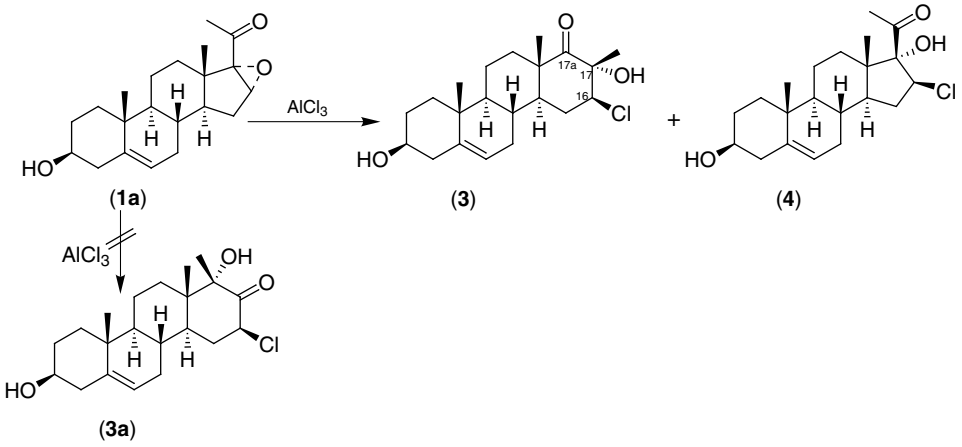


Scheme 2.

2 equiv. of anhyd. $AlCl_3$ in CH_3CN at ambient temperature affords a mixture of products characterized as 16β-chloro-3β,17α-dihydroxy-17β-methyl-17a-homoandrost-5-en-17a-one (**3**, 65%) and 16β-chloro-3β,17α-dihydroxypregn-5-en-20-one (**4**, 35%, Scheme 2). Reacting **1a** with 3 equiv. of anhyd. $AlCl_3$ in dry CH_3CN at 10°C for 6 h resulted in the formation of single product (**3**, 95%). Complete conversion of **1a** to **3** was also achieved in other solvents (Table 1). Interestingly, when the temperature is raised to 40°C (CH_3CN as solvent, 3 equiv. of $AlCl_3$) for 7 h, both products **3** (70%) and **4** (27%) are obtained, however, if after 7 h the reaction mixture is treated with one more equiv. of $AlCl_3$ or the contents are refluxed, only D-homosteroid **3** is obtained.

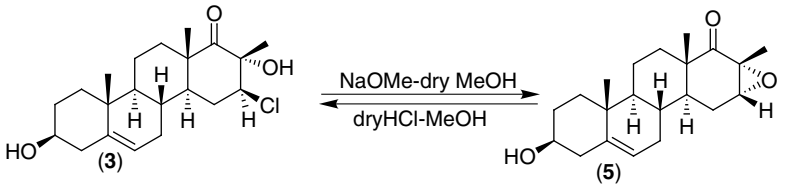
Compound (**3**) was isolated as white flakes (MeOH–$CHCl_3$) and was recrystallized from the same solvent mixture to obtain colorless flakes (mp 157°C). It has been characterized on the basis of spectroscopic data and microanalysis. The *m/z* peak at 368 (0.4%, M^++2) and 366 (0.9%, M^+) revealed the presence of Cl atom in the system, which was also supported by microanalytical data. A band in the IR spectrum at 1720 cm^{-1} was characteristic of saturated ketones. However, the presence of three methyl singlets in ^1H NMR at δ 1.25 (C17-Me), 1.15 (C19) and 1.01 (C18), indicated rearrangement to a D-homosteroid; otherwise the resonance for protons of the methyl group of C17-acetyl moiety was anticipated at ≥δ 2.0. In the ^{13}C NMR the carbonyl resonance (C17a) was located at δ 214.6 and its downfield shifted position as compared to the ^{13}C chemical shift of C20 in **1a** (δ 204.6) was corroboration of the assigned structure.[8] The resonances of the oxygen linked carbons were observed at δ 79.1 (quat. C17) and δ 71.3 (CH, C3); the resonances of Cl linked carbon (C16) was located at δ 67.7 (CH). The assigned stereochemistry at C16 is based on the coupling constant values for C16-H which appeared as a dd at δ 3.94 (J=12.6 and 4.4 Hz); the presence of 12.6 Hz coupling (axial–axial) corresponded to its axial orientations, thereby, confirming the β (equatorial) position of Cl. The structure of compound **4**, a colorless solid (mp 187°C), is also based on rigorous spectroscopic analysis and comparison of the spectral data with related systems.[9]

In order to exclude the alternative D-homosteroid structure **3a** for the obtained product, it was treated with NaOMe in MeOH when it was converted to epoxy-ketone **5**. Treatment of **5** with dry HCl–MeOH regenerated the compound **3**; the structure of epoxy ketone **5** has been established by rigorous spectroscopic analysis and it could not have been obtained from **3a** (Scheme 3).

Mechanistically, the ring opening of epoxide in **1a** and rearrangement to D-homosteroid can be thought of as following two distinct routes. For instance at low temperature and in presence of 3 equiv. of $AlCl_3$, in a polar solvent like CH_3CN, the reaction can be postulated to follow the path-a (involving intermediate **A**). This is corroborated by the absence of any other intermediate product (e.g. **4**) by TLC at any stage of the reaction. On the other hand, if the reactants are mixed at room temperature and the temperature is raised and maintained at ~40°C (everything else remaining the same) the reaction mixture develops a reddish color (in contrast to the colorless solution obtained at low temperature), and beside **3** (70%), chlorohydrin **4** (~27%) is also isolated; the amount of **4** increases to 35% if 2 equiv.

Table 1. Transformations of epoxy-steroid (**1a**) in presence of $AlCl_3$ under various conditions

S. No.	Solvent	Equiv. of $AlCl_3$	Reaction temp. (°C)	Reaction time (h)	Yield (%) of various products	
					3	**4**
1	CH_3CN	2	30	9	65	35
		3	10	6	95	–
		3	~40	7	70	27
		3	Reflux	2	92	–
2	THF	3	Reflux	10	88	–
3	CCl_4	3	Reflux	8	90	–



Scheme 3.

of $AlCl_3$ are employed. In the latter case, probably, the intermediate **B** is formed, which leads to **4** or on further addition of $AlCl_3$ yields **3** (through **A**); on refluxing **B** can lead directly to **3** (through **C**).[1f,i] In the case of non-polar solvents, the reaction follows path a or both path a and b, however, no other product is detected on TLC at any stage. Formation of **B** in CH_3CN (employing 3 equiv. of $AlCl_3$) at 40°C is, probably, a consequence of consumption of $AlCl_3$ by reaction with CH_3CN (Scheme 4).

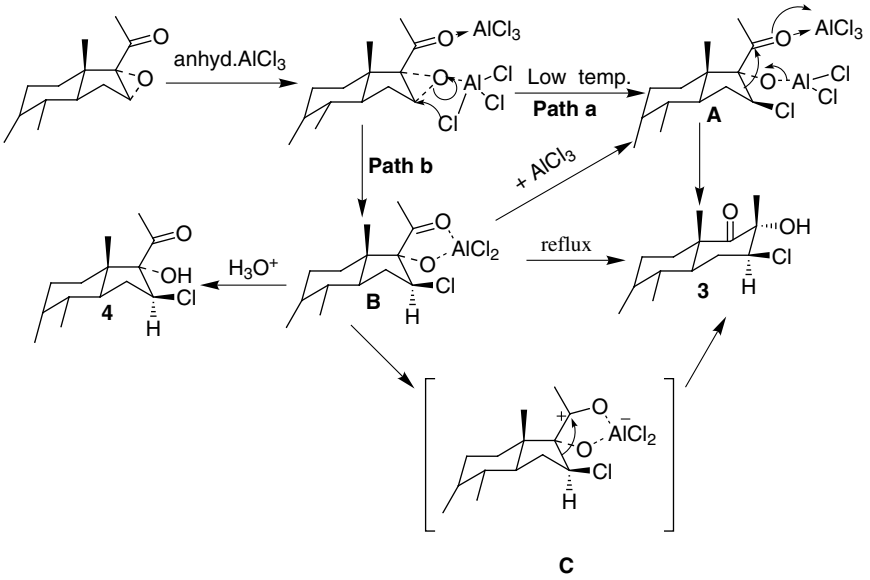
A further perusal of the literature revealed that refluxing of **1a** with excess of acetic anhydride in presence of *p*-toluene-sulphonic acid has been reported to afford Δ^{13}-steroid (**6**) in 54% yield[3e] (Scheme 5).

At the same time fusion of estradiol methyl ether (**9**) with $ZnCl_2$ at 170–180°C has been reported to yield a mixture of products **10**, **11** and **12**.[3f] Also, it is reported that treatment of 11-deoxycorticosterone with sulphuric acid (97%) at room temperature resulted in a mixture of products including a Δ^{13}-steroid (32%).[10] Use has also been made of BF_3–Ac_2O for 16,17-epoxide ring opening (69% yield) in the synthesis of ring-C aromatic steroids[11] (Scheme 6).

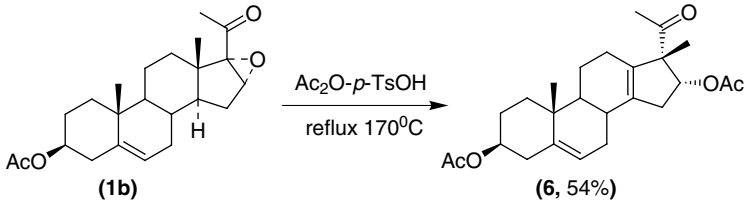
We have now carried out the reaction of 16α,17α-epoxy-3β-hydroxy-pregn-5-en-20-one (**1a**) with acetic anhydride in presence of anhyd. $ZnCl_2$ by stirring at room temperature and report the formation of 13,14-dehydrosteroids (**6**) as single product in 92% yield (Scheme 7).

Though the formation of compound **6** has been reported earlier, due to non-availability of its spectral data the same has been included under Section 3 and is in agreement with the assigned structure. Mechanistically, the reversed direction of epoxide ring opening requires it to be concerted with methyl migration and $ZnCl_2$ only activates the acetic anhydride.

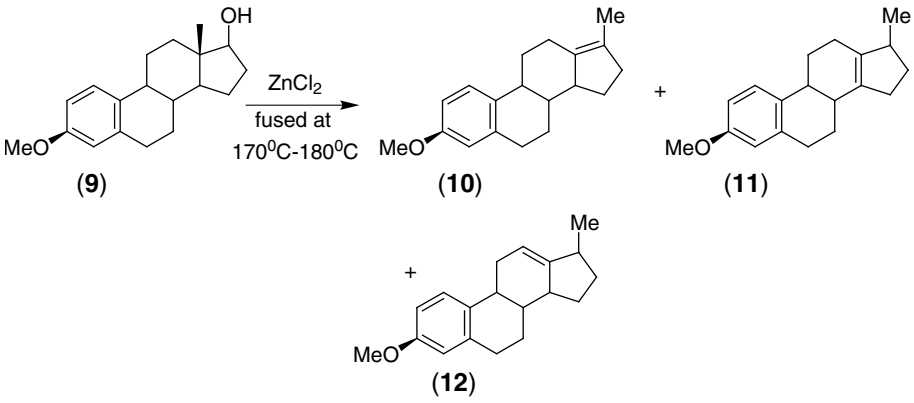
The present investigations have, thus, elaborated a simple low temperature conversion of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (**1b**) system to D-homosteroids in high yield by reacting with anhyd. $AlCl_3$. Alternatively,



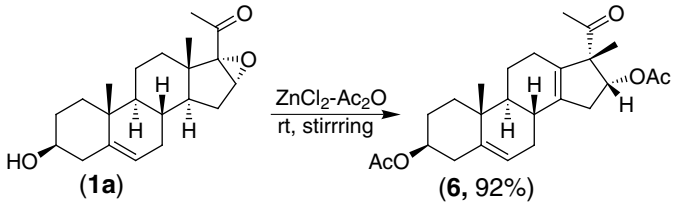
Scheme 4.



Scheme 5.



Scheme 6.



Scheme 7.

on treatment of **1b** with acetic anhydride in presence of anhyd. $ZnCl_2$ at room temperature, the direction of epoxide ring opening is reversed with concomitant methyl migration, leading to Δ^{13}-steroid (**6**) in very high yield.

3. Experimental

3.1. General

NMR spectra were recorded on Bruker AC-200FT NMR spectrometer, using TMS as internal standard and $CDCl_3$ as solvent. IR spectra ware recorded on Shimadzu DR 2001 FT-IR spectrometer in $CHCl_3$, unless otherwise mentioned and mass spectra were recorded on Shimadzu GCMS-QP-2000A spectrometer. Column chromatography was conducted using Silica Gel 60–120 mesh. The microanalytical data was collected on a Perkin–Elmer 240C elemental analyser. All solvents were purified and dried. 16α,17α-Epoxy-3β-hydroxy/acetoxypregn-5-en-20-ones (**1a**,**b**) were prepared by the literature method.[7] Optical rotation were taken with a JASCO DIP-360. All melting points are uncorrected and have been measured in open glass capillaries.

3.1.1. Reaction of 16α,17α-epoxy-3β-acetoxypregn-5-en-20-one (1b) with $BF_3{\cdot}Et_2O$ in dry THF/diethyl ether. Epoxide **1a** (110 mg, ~0.3 mmol) was taken up in dry THF or dry diethyl ether (25 ml) under nitrogen atmosphere and $BF_3{\cdot}Et_2O$ (1.2 ml of 32% etheral solution, 1 equiv.). The contents were stirred at room temperature; regular monitoring by TLC for 20 h did not indicate any reaction. Subsequent increasing of the $BF_3{\cdot}Et_2O$ up to 4 equiv. also failed to bring about epoxide ring opening. Work up of the reaction afforded starting material (**1b**) besides some acetate hydrolysis product (**1a**, mp, ^1H NMR), which were separated by column chromatography over silica gel.

3.1.2. Reaction of 16α, 17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) with formic acid. Epoxide **1b** (100 mg, 0.3 mol) was taken in 96% formic acid (15 ml) and was refluxed for 7 h. The reaction was worked up by adding diethyl ether (50 ml) and washing the solution with water, $NaHCO_3$ solution, brine and again with water. The ethereal layer was dried over anhyd. Na_2SO_4, filtered and solvent was distilled off. Removal of traces of solvent under vacuum afforded a solid, which was crystallized from MeOH–$CHCl_3$ (3:1), to obtain 16α,17α-epoxy-3β-formyloxypregn-5-en-20-one (**1c**) as colorless needles, mp 187°C; $[\alpha]_D^{32}=-30.22$ (*c* 0.23; $CHCl_3$);[found C, 73.88; H, 8.56, $C_{22}H_{30}O_4$ requires C, 73.71; H, 8.44%]; ν_{max} ($CHCl_3$): 1724 (formate C=O), 1695 (C=O) cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.99 (s, 1H, *H*CO–), 5.37 (br d, 1H, *J*=4.8 Hz, C6–H), 4.72 (m, 1H, C3–H), 3.64 (s, 1H, C16–H), 2.36 (d, 1H, *J*=7.7 Hz, C7–H), 2.07–0.98 (br m, 24H, having singlets at δ 2.01 and 1.04, 2×CH_3); δ_C (50 MHz, $CDCl_3$): 204.5 (q, C20), 160.3 (q, H*C*O–), 139.6 (q, C5), 122.1 (CH, C6), 73.6 (C3), 70.8 (C17), 60.2 (CH, C16), 50.3, 50.3, 45.4, 41.4, 37.9, 36.7, 31.3, 31.2, 29.6, 27.6, 27.4, 25.8, 20.3, 19.1, 15.1; *m/z*: 330 (4%, M^+-39), 313 (17%), 312 (67%).

3.1.3. Reaction of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) with anhyd. $AlCl_3$ in CH_3CN. Epoxide **1a** (100 mg, 0.3 mmol) was taken up in dry CH_3CN (25 ml) and powdered anhyd. $AlCl_3$ (80.8 mg, 0.60 mmol, 2 equiv.) was added in one portion. The contents were stirred at ambient temperature (25–30°C) for 9 h, when TLC monitoring indicated the consumption of starting material. The solvent was removed under vacuum and treating the residue with water followed by extraction with diethyl ether (3×25 ml). The ethereal extract was washed with

aqueous $NaHCO_3$, brine solution and again with water. It was dried over anhyd. Na_2SO_4, filtered and the solvent was evaporated. The residue was separated on a silica gel (60–120 mesh, 20 g) column using hexane–chloroform (4:1) as eluent to afford: 16β-chloro-3β,17α-dihydroxy-17β-methyl-17a-homoandrost-5-en-17a-one (**3**,72 mg, 65%), colorless flakes, mp 157°C ($CHCl_3$–MeOH,1:2); [found C, 68.73; H, 8.55. $C_{21}H_{31}O_3Cl$ requires C, 68.85; H, 8.46%]; $[\alpha]_D^{25}=-68.99$ (*c* 0.70; EtOH); ν_{max} ($CHCl_3$): 1720 (C=O), 1379.3 cm^{-1}; δ_H (200 MHz; $CDCl_3$): 5.34 (bd, 1H *J*=4.4 Hz, C6–H), 4.18 (bs, 1H, suppressed on shaking with D_2O, –OH), 3.94 (dd, *J*=4.4 and 12.6 Hz, C16–H), 3.54 (m, 1H, C3–H), 2.40–0.99 (br m, 27H, having singlets at δ 1.25, 1.15 and 1.01, 3×CH_3); δ_C (50 MHz, $CDCl_3$): 214.6 (C17a), 140.64(C5), 120.4 (C6), 79.1 (C17), 71.3 (C3), 67.7 (C16), 49.4, 48.9, 48.3, 46.5, 41.8, 36.7, 32.7, 32.1, 31.5, 31.4, 30.8, 30.7, 23.6, 19.2, 15.76; *m/z* 368 (0.4%, M^++2), 367 (2.1%, M^++1), 366 (0.9, M^+), 363 (1.1), 362 (1.3), 335 (1.6), 334 (0.8), 333 (3.5), 332 (2.5), 331 (10.3). 16β-chloro-3β,17α-dihydroxy-pregn-5-en-20-one (4, 39 mg, 35%), colorless flakes, mp 187°C ($CHCl_3$–MeOH, 1:2); [found: C, 68.79; H, 8.51. $C_{21}H_{31}O_3Cl$ requires C, 68.85; H, 8.46%]; $[\alpha]_D^{32}=-19.50$ (*c*0.4, $CHCl_3$); ν_{max} ($CHCl_3$): 1709(C=O) cm^{-1}; δ_H (200 MHz, $CDCl_3$): 5.33 (br d, IH, *J*=4.8 Hz, C6–H), 4.09 (dd, 1H, *J*=4.2 and 5.5 Hz, C16–H), 3.49 (m, IH, C3–H), 3.31 (s, 1H, suppressed by shaking with D_2O, –OH), 2.52–1.00 (br m, 27H, having singlets at δ 2.31, 1.21 and 1.00, 3×CH_3); δ_C (50 MHz; $CDCl_3$): 205.00 (C=O), 140.47 (C5), 120.63 (C6), 95.75 (C17), 71.16 (C3), 62.71 (C16), 49.17, 46.21, 41.79, 37.77, 36. 62, 36.17, 31.36, 31.16, 30.83, 30.56, 29.31, 29.04, 19.54, 18.99, 15.36; *m/z*: 366 (1.1%, M^+), 348 (1.2%).

3.1.4. Reaction of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) with anhyd. $AlCl_3$ (3 equiv.) in CH_3CN at 10°C. Epoxide **1a** (110 mg) was taken in dry CH_3CN (25 ml) and 3 equiv. of powdered anhyd. $AlCl_3$ was added in one portion; the contents were stirred at 10°C for 6 h and then worked up as described earlier. The residue obtained on evaporation of solvent was recrystallized from $CHCl_3$–MeOH (1:2) to obtain **3** (116 mg, ~95%).

3.1.5. Reaction of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) with anhyd. $AlCl_3$ (3 equiv.) in CH_3CN at 35–40°C. Epoxide **1a** (110 mg) was taken in dry CH_3CN (25 ml) and 3 equiv. of powdered anhyd. $AlCl_3$ was added in one portion; the reaction mixture was stirred at ~40°C for 7 h and then worked up accordingly. The obtained mixture of products when resolved column chromatographically, as described earlier, afforded **3** (70%) and **4** (27%); Alternatively, if after 7 h 1 equiv. of $AlCl_3$ was added to the reaction mixture or the mixture was refluxed for 1 h, in both cases it led to the formation of **3** as the only product (>90%).

3.1.6. Reaction of 16α,17α-epoxy-3β-hydroxy-pregn-5-en-20-one (1a) with anhyd. $AlCl_3$ (3 equiv.) in CH_3CN under refluxing. To epoxide **1a** (100 mg) in dry CH_3CN (25 ml), 3 equiv. of powdered anhyd. $AlCl_3$ was added in single lot and the reaction mixture was refluxed with stirring for 2 h and then worked up accordingly. The residue obtained on removal of solvent was dried and crystallized, as described earlier, to give product **3** (~102 mg, 92%).

3.1.7. Reaction of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) with anhyd. $AlCl_3$ in dry THF. Epoxide **1a** (110 mg) was taken in dry THF (25 ml) and powdered anhyd. $AlCl_3$ (3 equiv.) was added in one portion. The contents were refluxed, with stirring, for 10 h and the reaction worked up in a manner as described earlier by evaporating the solvent and extracting with ether. The solvent from the dried ethereal extract was removed under vacuum to obtain a solid residue which was recrystallized from $CHCl_3$–MeOH to obtain **3** (107 mg, 88%).

3.1.8. Reaction of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) with anhyd. $AlCl_3$ in dry CCl_4. Epoxide **1a** (110 mg) was taken in dry CCl_4 (35 ml) and 3 equiv. of anhyd. $AlCl_3$ was added in one portion. The contents were refluxed, with stirring for 8 h and the reaction was worked up by removal of solvent under vacuum and treating the residue with water followed by extraction with chloroform (3×25 ml). The chloroform layer was washed with aqueous $NaHCO_3$, brine solution and again with water. It was dried over anhyd. Na_2SO_4, filtered and the solvent was evaporated. The residue was crystallized to obtain compound **3** (109 mg, 90%).

3.1.9. Reaction of D-homosteroid (3) with NaOMe in dry MeOH. D-Homosteroid (**3**, 100 mg) was dissolved in dry MeOH (25 ml) and NaOMe (32.7 mg, 2 equiv.) was added to it in one portion. The contents were refluxed for 4 h with stirring and the reaction was quenched with 5% HCl (15 ml), diluted with ice cold water (100 ml) and cooled. The separated solid was filtered, dried and crystallized from ether–ethanol (1:3) to obtain: epoxy-D-homosteroid (5 mg), colorless needles, mp 214°C; $[\alpha]_D^{30}=-82.70$ (*c* 0.27; $CHCl_3$); [found: C, 75.84; H, 9.68. $C_{21}H_{30}O_3$ requires C, 76.13; H, 9.36]; ν_{max} ($CHCl_3$): 1713.6 (C=O), 1448.6, 1277.6, 1247.7, 1051.10 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 5.31 (br d, 1H, *J*=4.6 Hz, C6–H), 3.53 (m, 1H, C3–H), 3.29 (s, 1H, C16–H), 2.36–0.98 (br m, 27H, having singlets at δ 1.41, 1.05 and 0.98, 3×CH_3); δ_C (50 MHz, $CDCl_3$): 207.5 (C=O), 140.5 (C5), 120.9 (C6), 71.6 (C3), 59.5 (C16), 56.1 (C17), 48.9, 45.0, 42.0, 38.6, 36.9, 36.7, 31.8, 31.6, 31.2, 29.7, 24.9, 19.9, 19.4, 16.6, 15.6;*m/z*: 331 (20%, M^++1), 330 (66%, M^+), 329, 328, 316, 315.

3.1.10. Conversion of 5 to 3 by treatment with dry HCl in dry MeOH. The epoxy-D-homosteroid (**5**, 100 mg) was dissolved in dry MeOH (50 ml), cooled in ice bath and dry HCl was bubbled for 15 min. The reaction was quenched by neutralizing with aqueous $NaHCO_3$, further diluted with ice cold water (50 ml) and chilled. The separated solid was filtered crystallized from MeOH–$CHCl_3$ and recrystallized from MeOH–$CHCl_3$ to obtain **3** (102 mg, mp 157°C, undepressed mixed mp and spectral data).

3.1.11. Conversion of 16α,17α-epoxy-3β-hydroxypregn-5-en-20-one (1a) to β,16α-diacetoxy-17-methyl-17α-pregna-5,13-dien-20-one (6). The epoxide (**1a**, 100 mg, 0.3 mmol) was dissolved in Ac_2O (20 ml) and anhydrous $ZnCl_2$ (124 mg, 3 equiv.) was added. The contents were stirred for 6 h at room temperature until TLC monitoring

indicated the completion of the reaction. The reaction was quenched with 40% $NaHCO_3$ solution when a solid separated out. The contents were extracted with ether (2×25 ml), washed with brine, water and dried over anhydrous sodium sulfate and filtered. Evaporation of solvent followed by drying under vacuum afforded 3β,16α-diacetoxy-17-methyl-17α-pregna-5,13-dien-20-one(6), hexagonal colorless crystals, mp 201–202°C (EtOH–$CHCl_3$, 1:1), Lit.[3e] mp 213–214.5°C; [found: C, 72.42; H, 8.26. $C_{25}H_{34}O_5$ requires C, 72.46; H, 8.21]; $[\alpha]_D^{25}=-11.99$ (*c* 0.6; $CHCl_3$); $\nu_{max}(CHCl_3)$: 1733.7, 1731.6, 1705.0, 1474.2, 1457.1, 1440.0, 1375.9, 1367.4, 1363.1, 1256.2, 1200.7, 1042.50 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 5.44 (br d, 1H, C6–H), 5.17 (dd, *J*=6.9 and 8.1 Hz, 1H, C16–H), 4.62 (m, 1H, C3–H), 2.87–0.99 (brm, 31H, having sharp singlet at δ 2.09, 2.01, 1.99, 1.18 and 0.99; 5×CH_3); δ_C (50 MHz, $CDCl_3$): 207.3 (C=O), 169.6 (ester C=O), 140.5 (C5), 138.8 and 137.0 (C13 and C14), 121.9 (C6), 81.4 (C16), 73.5 (C3), 64.9 (C17), 48.6, 38.4, 37.9, 36.9, 36.6, 32.8, 30.5, 27.4, 27.2, 23.0, 22.4, 21.1, 20.8, 19.9, 18.5; *m/z*: 373 (4%, M^++1−43), 372 (61%, M^+−43), 371 (60%), 355, 354, 353, 311, 252, 251.

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