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Tetrahedron 63 (2007) 5622–5635
Tetrahedron

Stereoselective syntheses of 20-*epi* cholanic acid derivatives from 16-dehydropregnenolone acetate

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Received 5 December 2006; revised 14 March 2007; accepted 5 April 2007
Available online 14 April 2007

Abstract—A stereoselective total synthesis of naturally occurring 20-*epi* cholanic acid derivatives has been realized, starting from readily available 16-dehydropregnenolone acetate. The key step of these syntheses involves an ionic hydrogenation of a C-20,22-ketene dithioacetal and deoxygenation of steroidal C-20 *tert*-alcohols, to set up the unnatural C(20*R*) configuration with 100% stereoselectivity. The unnatural C-22 aldehydes with C(20*R*) stereocenters thus obtained were elaborated to 20-*epi* cholanic acid derivatives. Two derivatives of 20-*epi* cholanic acid were synthesized and their structures have been confirmed by single crystal X-ray analysis. Catalytic hydrogenation of 16-dehydropregnenolone acetate and 16-dehydropregnenolone in ethanol affords C-5,C-16 tetrahydro products. Crystal structure analysis of one of these products revealed C-5α and C-17α configurations of the hydrogen atoms.

1. Introduction

The isolation and synthesis of many biologically important steroids with modified side chains,[1] such as ecdysones,[2] metabolite of vitamin D_3,[3] brassinosteroids,[4] squalamine,[5] OSW-1,[6] contignasterol,[7] and marine sterols,[8] have stimulated much interest for the development of efficient methods to introduce such modified side chains into readily available steroids. Compounds with unnatural configuration at C-20 have attracted attention because of the interesting biological activities of these epimers[9] and hence methods for their stereoselective synthesis are highly desirable. Koreeda has pointed[10] that 20-isocholesterol **1** (Chart 1) with C(20*S*) stereochemistry showed significant in vitro inhibitory activity

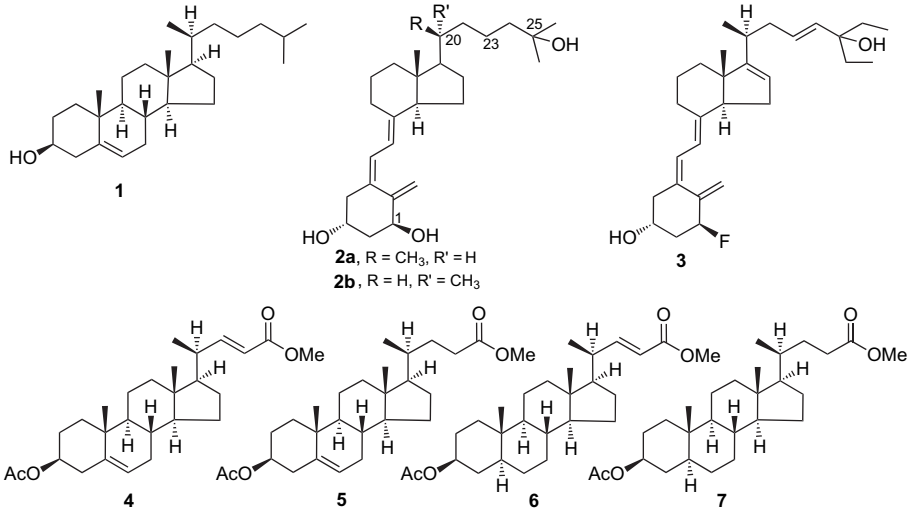

Chart 1. Isocholesterol **1**, vitamin D_3 **2**, deltanoid (Ro 26-9228) **3**, and 20(*S*) cholanic acid derivatives **4**–**7**.

Keywords: Ionic hydrogenation; Catalytic hydrogenation; Steroidal aldehydes; 20-*epi* Cholanic acid derivatives; Wittig reaction.
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0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.04.014

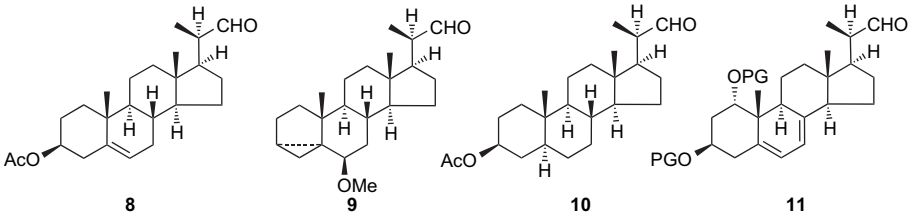
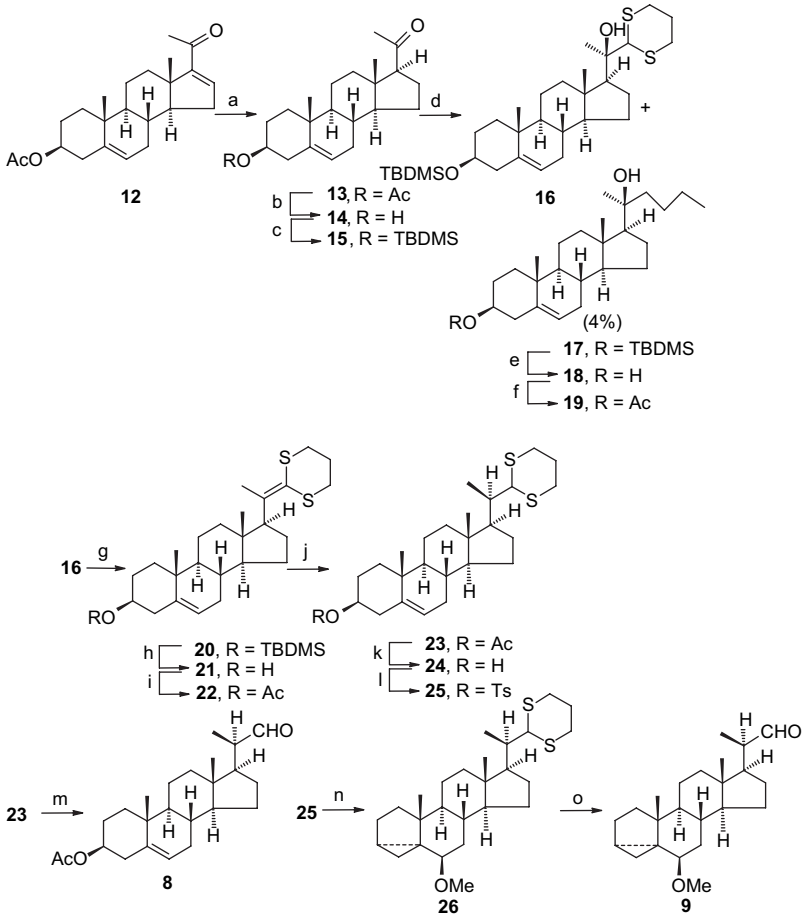


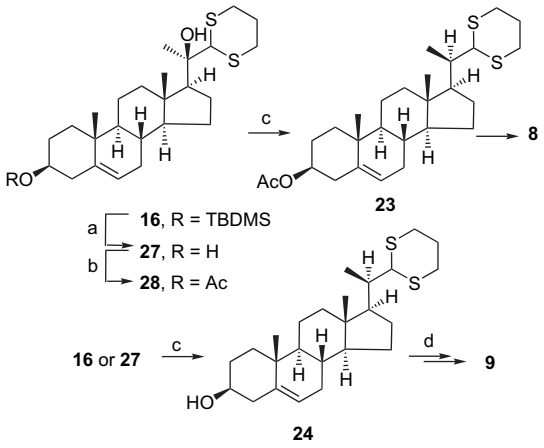
Chart 2. Steroidal C(20*R*) aldehydes **8**–**11**.

for the conversion of cholesterol to pregnenolone. Recently, it has been reported[9f,11] that in the 20-*epi* analog of the metabolite of vitamin D_3, **2a** is more potent in regulating cell growth and cell differentiation than the corresponding compound with natural C-20 stereoisomer **2b**. It is also interesting to mention that the 20-*epi* analog **2a** exhibits immunosuppressive properties[12] and that of 1α-fluoro-16,23-diene-20-*epi* hybrid deltanoid (Ro 26-9228) **3** is in human clinical trials for the treatment of osteoporosis[13] (Chart 1). Djerassi et al.[9a,b] have isolated four 20-*epi* cholanic acid derivatives **4**–**7** (Chart 1) with unnatural configuration at C-20 from a sea pen, *Ptilosarcus guerneyi* and also devised methods for their synthesis. The key intermediate for the synthesis of these sterols **4**–**7** is the unnatural C(20*R*) aldehyde **9**, which was obtained by epimerization of the corresponding (20*S*) aldehyde in poor yield (Chart 2). Again, synthesis of the 20-*epi* cholanic acid derivatives **4**, **5**, and **7** has been carried out by Takano et al.[14a] and by Dauben and Brookhart.[14b] The aldehyde **8** has been prepared by base catalyzed epimerization[15] of natural C(20*S*) aldehyde and Lewis acid catalyzed rearrangement of a C-20,22-oxido steroid[16] in poor yield. The unnatural C(20*R*) aldehyde **11** was prepared by epimerization of the corresponding 20(*S*) aldehyde, is the key intermediate for the synthesis of the 20-*epi* vitamin D_3 analogs.[17]

Construction of the steroidal side chain with unnatural configuration at C-20 by using various organometallic reagents,[18] specific reactions,[19] and rearrangements[20] has been documented. However, much attention has not been given for the synthesis of unnatural configuration at C-20 starting from readily available[21] 16-dehydropregnenolone acetate (16-DPA) **12**. We have reported[22] the synthesis of



Scheme 1. Reagents and conditions: (a) 10% Pd–C, H_2, EtOAc, 45 psi, 30 °C, 12 h, 98%; (b) KOH, MeOH, H_2O, 30 °C, 2 h, 97%; (c) TBDMSCl, imidazole, DMF, 30 °C, 10 h, 92%; (d) 1,3-dithiane, *n*-BuLi, THF, −30 °C for 2 h and 0 °C for 12 h, 82%; (e) *n*-Bu_4NF, THF, 30 °C, 18 h, 93%; (f) Ac_2O, pyridine, DMAP, 25 °C, 2 h, 96%; (g) $SOCl_2$, pyridine, CH_2Cl_2, −5 °C, 5 min, 84%; (h) *n*-Bu_4NF, THF, 25 °C, 12 h, 93%; (i) Ac_2O, pyridine, DMAP, 30 °C, 3 h 98%; (j) Et_3SiH, CF_3COOH, CH_2Cl_2, 25 °C, 18 h, 89%; (k) KOH, MeOH, THF, 30 °C, 4 h, 92%; (l) *p*-toluenesulfonyl chloride, pyridine, 30 °C, 12 h, 94%; (m) HgO, $HgCl_2$, CH_3CN, H_2O, reflux, 3 h, 96%; (n) MeOH, CH_3COONa, reflux, 4 h, 83%; (o) Dess–Martin periodinane, CH_3CN, CH_2Cl_2–H_2O, 30 °C, 5 h, 55%.



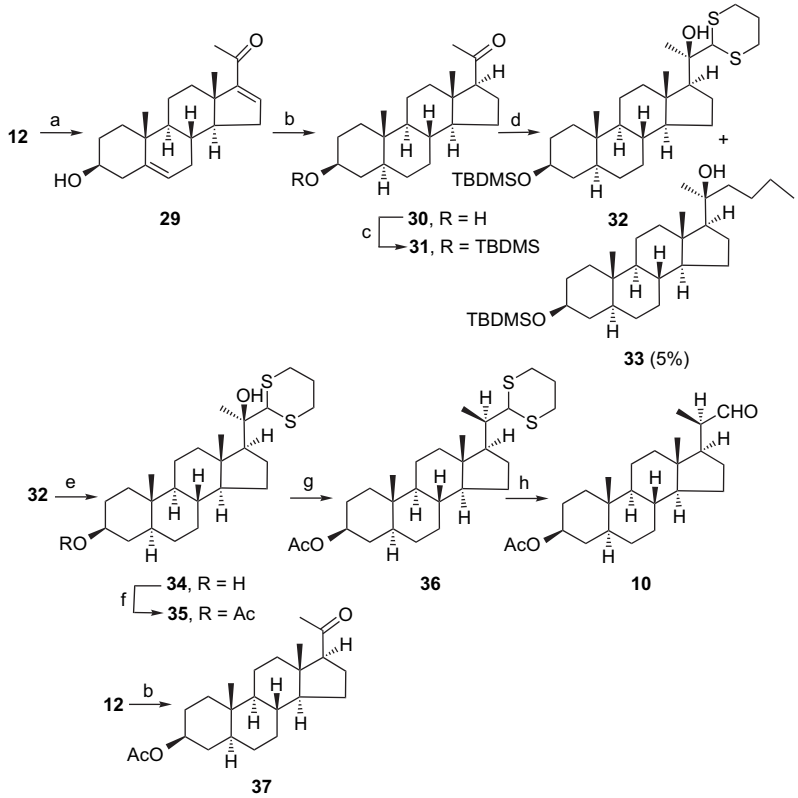
Scheme 2. Reagents and conditions: (a) *n*-Bu_4NF, THF, 30 °C, 18 h, 93%; (b) Ac_2O, pyridine, DMAP, 25 °C, 2 h, 96%; (c) Et_3SiH, $BF_3{\cdot}OEt_2$, DCM, 0 °C, 10 min, 90–94%; (d) see Scheme 1, reagents and conditions: (l), (n), and (o).

steroidal unnatural C(20*R*) aldehydes **8** and **9** by the ionic hydrogenation of the C-20,22-ketene dithioacetal **22** with excellent unnatural C(20*R*) stereoselectivity (Scheme 1). Very recently, we have reported[23] the synthesis of the same aldehydes **8** and **9** by the deoxygenation of tertiary alcohols **16**, **27**, and **28** (Scheme 2). Synthesis of the C-5(6)-saturated unnatural C(20*R*) aldehyde **10** by deoxygenation of alcohol **35** has also been reported[23] (Scheme 3). Now we wish to report here: (i) details of the ionic hydrogenation of the C-20,22-ketene dithioacetal and deoxygenation of steroidal C-20 *tert*-alcohols, (ii) study of the effects of solvents on catalytic hydrogenation of 16-DPA **12** and 16-dehydropregnenolone **29** and confirmation of the stereochemistry of tetrahydro product by crystal structure analysis, (iii) the elaboration of the unnatural C(20*R*) aldehyde **8** to naturally occurring 20-*epi* cholanic acid derivatives **4** and **5**, also (iv) conversion of C-5(6)-saturated unnatural C(20*R*) aldehyde **10** to cholanic acid derivatives **6** and **7** (Scheme 4). The structures of naturally occurring 20-*epi* cholanic acid derivatives **4** and **6** were confirmed unambiguously by single crystal X-ray analysis.

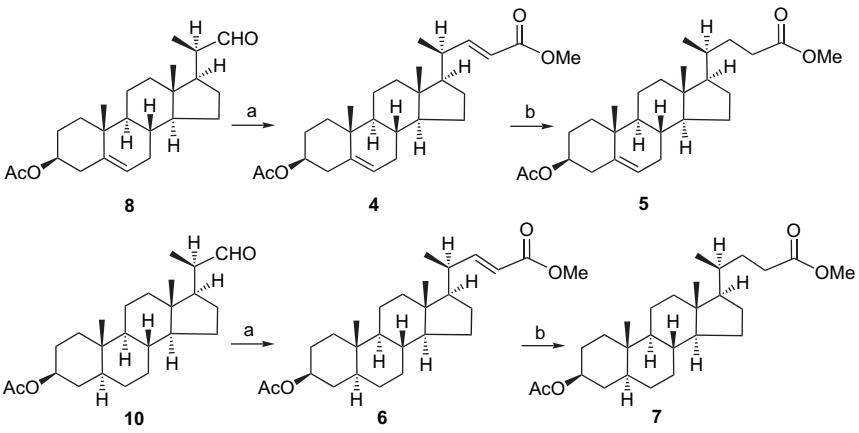
2. Results and discussion

2.1. Synthesis of steroidal unnatural C(20*R*) aldehydes 8 and 9 by ionic hydrogenation of the C-20,22-ketene dithioacetal

Commercially available 16-dehydropregnenolone acetate **12** on chemoselective catalytic hydrogenation with 10% palladium on charcoal in ethyl acetate, hydrolysis of the acetate **13** with potassium hydroxide in aqueous methanol, followed by protection of 3β-hydroxy group in *N*,*N*-dimethylformamide (DMF) afforded compound **15**[24] with an overall yield of 87% in three steps (Scheme 1). Compound **15** on reaction with 2-lithio-1,3-dithiane in THF at −30 °C furnished stereoselectively the C-20-hydroxydithiane **16** in 82% yield. Addition of 2-lithio-1,3-dithiane to 20-keto pregna derivatives is known[25] to generate stereoselectively the C(20*R*) configuration at this center. When the addition of compound



Scheme 3. Reagents and conditions: (a) KOH, *t*-BuOH, H_2O, 30 °C, 10 h, 96%; (b) 10% Pd–C, H_2, EtOH, 55 psi, 30 °C, 12 h, 99%; (c) TBDMSCl, imidazole, DMF, 30 °C, 10 h, 97%; (d) 1,3-dithiane, *n*-BuLi, THF, −30 °C for 2 h and 0 °C for 12 h, 82%; (e) *n*-Bu_4NF, THF, 30 °C, 18 h, 93%; (f) Ac_2O, pyridine, DMAP, 25 °C, 2 h, 97%; (g) Et_3SiH, $BF_3{\cdot}OEt_2$, DCM, 0 °C, 10 min, 94%; (h) HgO, $HgCl_2$, CH_3CN, H_2O, reflux, 3 h, 96%.



Scheme 4. Reagents and conditions: (a) $Ph_3P{=}CHCO_2Me$, THF, reflux, 48 h, **4** (95%), **6** (93%); (b) H_2, 10% Pd–C, EtOAc, 45 psi, 10 h, **5** (99%), **6** (97%).

15 to 2-lithio-1,3-dithiane was done at −45 °C, C-20-hydroxydithiane **16** was isolated in 77% yield, along with the side product **17** (4%). This compound **17** was then prepared in 91% yield by the reaction of **15** with *n*-BuLi. The C(20*S*) configuration of compound **17** was confirmed by X-ray analysis of the 3β-acetate **19** (obtained by deprotection of TBDMS group in compound **17** and acetylation of the hydroxy product **18**) (Fig. 1).

Dehydration of the C(20*R*)-*tert*-alcohol **16** following a literature procedure[27] afforded ketene dithioacetal **20** in 69% yield (Scheme 1). Use of $SOCl_2$–pyridine in CH_2Cl_2 at −5 °C for 5 min gave C-20,22-ketene dithioacetal **20** in 84% yield. The attempted reduction of the C-20,22-double bond of compounds **20**–**22** by catalytic hydrogenation with Pd–C, with Mg in methanol, and with Zn in acetic acid[28] resulted in recovery of the starting materials. Ionic hydrogenation[29] of compound **20** with triethylsilane and trifluoroacetic acid in dichloromethane at varying temperatures (0–30 °C) led to a mixture of products, in which deprotection of the TBDMS group takes place and 3β-hydroxy compound **21** was isolated in 58% yield. Compound **21** was then obtained by deprotection of the TBDMS group of **20** with *n*-tetrabutylammonium fluoride (*n*-Bu_4NF). Acetylation of the 3β-OH group of compound **21** with acetic anhydride and catalytic *N*,*N*-dimethylaminopyridine (DMAP) in pyridine furnished the 3β-acetate **22** in 86% yield over two steps. Ionic hydrogenation of the C-20,22-ketene dithioacetal **22** using triethylsilane and trifluoroacetic acid afforded the C(20*R*) saturated compound **23** in 89% yield.

In the present ionic hydrogenation, there is formation of carbocation at C-22 to give the sulfur-stabilized intermediate[29b] **22A** (Chart 3). Concomitant protonation (from F_3CCOOH) at C-20 in compound **22** from the less hindered α-face of the steroid backbone led to the formation of carbocation at C-22, followed by simultaneous transfer of hydride (from Et_3SiH) at C-22 resulted in the exclusive formation of the C(20*R*)-methyl product **23**. Ionic hydrogenation of compound **22** is chemoselective as the 5,6-double bond is unaffected.

Exclusive formation of the unnatural C(20*R*)-methyl compound **23** by ionic hydrogenation of the C-20,22-ketene dithioacetal **22** is confirmed by a single C-21 methyl at δ 1.05 ppm (d, J=6 Hz) in the ^{1}H NMR spectrum and by a single methyl signal at δ 15.8 ppm in the ^{13}C NMR spectrum. This was further confirmed unequivocally by crystal structure analysis (Fig. 2).

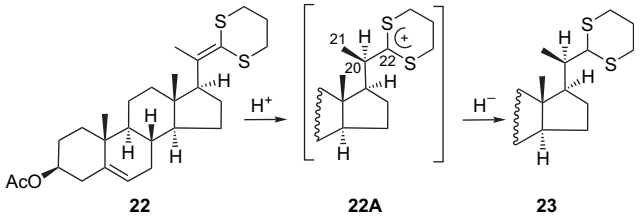


Chart 3. Mechanism of ionic hydrogenation of the C-20,22-ketene dithioacetal **22**.

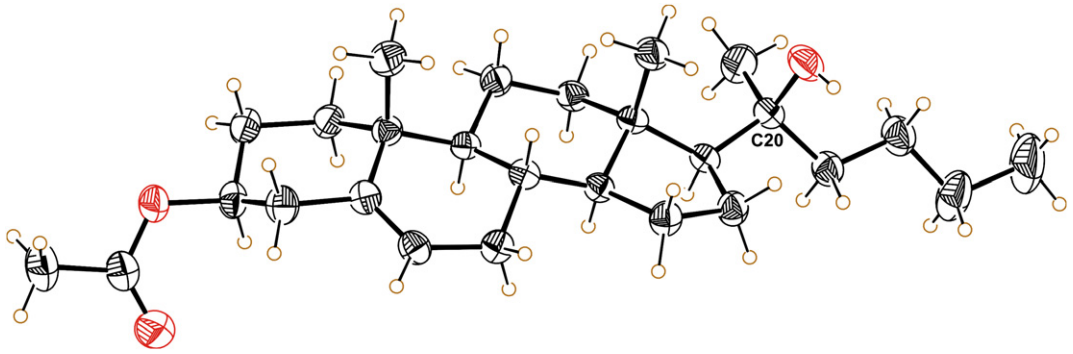


Figure 1. ORTEP[26] view of 3β-acetoxy-20(*S*)-hydroxy-20-butyl-pregna-5-ene **19**.

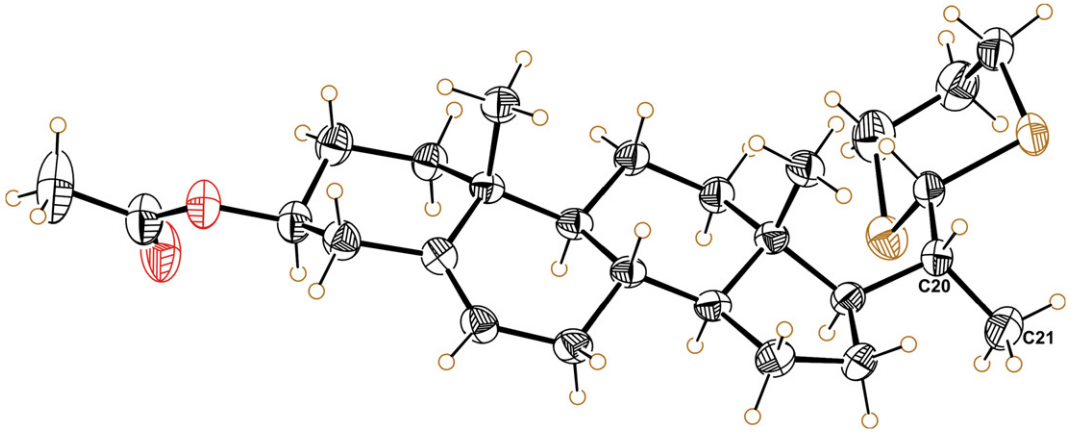


Figure 2. ORTEP view of 3β-acetoxy-pregna-5-en-(20*R*)-20-dithiane **23**.

The crystal structure shows that the C-20 dithiane moiety is to the left side of 17(20)-bond. It is known[30] from crystal structure data of sterols with the C-20 natural configuration that the conformation about 17(20)-bond in the usual view of the molecule C-22 is to the right. The preference of this 'right handed' rotational isomer probably derives from its having the smallest of the groups on C-20 (the H-atom) in front and, therefore, adjacent to C-18 in a pseudo 1,3-diaxial fashion. On the other hand, in the C-20 unnatural configuration, it should be the left-handed conformer, which is skew, and which possesses the least steric compression, i.e., an opposite conformational preference compared to the natural one.

Removal of the C-20 dithiane moiety of compound **23** by oxidative hydrolysis afforded the known aldehyde[9c,15] **8** in 96% yield (Scheme 1). Hydrolysis of the 3β-acetate **23**, tosylation of the 3β-hydroxy compound **24**, and treatment of the tosylate **25** with CH_3COONa in dry CH_3OH gave the *iso*-methyl ether **26** in three steps with an overall 72% yield. Oxidative hydrolysis of the C-20 dithiane moiety of compound **26** results in the opening of the *iso*-methyl ether, deprotection of the dithiane moiety, and formation of other products, which were not characterized. Therefore, the cleavage of the C-20 dithiane moiety of the acid-sensitive *iso*-methyl ether **26** was carried out[31] using Dess–Martin periodinane reagent under mild conditions to afford the known[9b] aldehyde **9** in 55% yield.

2.2. Stereoselective deoxygenation of steroidal C-20 *tert*-alcohols by ionic hydrogenation

2.2.1. Synthesis of steroidal unnatural C(20*R*) aldehydes 8 and 9 by deoxygenation of C-20 *tert*-alcohols 16, 27, and 28. Ionic hydrogenation is an effective method to reduce tertiary alcohols.[32] Very recently, stereoselective deoxygenation of the steroidal tertiary alcohols with triethylsilane and $BF_3 \cdot OEt_2$ has been reported.[33] Deoxygenative reduction of anomeric tertiary hydroxy group of lactols, bearing 1,3-dithianyl moiety at the same position, to cyclic ethers has been documented.[34] On the basis of these findings, we have carried out[23] deoxygenation of the C-20 tertiary alcohols possessing α-hydroxy-1,3-dithianyl moiety in compounds **16**, **27**, and **28** with triethylsilane–borontrifluoride diethyl etherate to get the products **23** and **24** having unnatural C(20*R*) configuration with 100% stereoselectivity (Scheme 2). Compound **24** has been converted to its *iso*-methyl ether **26**. Intermediates **23** and **24** have been elaborated to unnatural C(20*R*) aldehydes **8** and **9**, respectively.[22,23]

2.2.2. Synthesis of C-5(6)-saturated unnatural C(20*R*) aldehyde 10 by deoxygenation of C-20 *tert*-alcohol 35. After the successful synthesis of steroidal C(20*R*) aldehydes **8** and **9**, our next goal was to synthesize C-5(6)-saturated aldehyde **10**. Starting from 16-dehydropregnenolone acetate **12**, preparation of the C-5(6)-saturated C(20*R*) aldehyde **10** was carried out, following the procedure adopted for the synthesis of aldehydes **8** and **9**, which involved ionic hydrogenation of the C-20 tertiary alcohol as a key step. 16-Dehydropregnenolone acetate **12** was converted to 3β-hydroxy compound **29** in 96% yield (Scheme 3). There are very recent reports on the catalytic hydrogenation of pregnenolone **14** with 10% Pd–C in tetrahydrofuran–glacial acetic acid[35a] and in ethanol[35b] to get compound **30** in 90% and 100% yield, respectively. Marker has reported[21] the hydrogenation of compound **29** in the presence of 3% palladium–barium sulfate in neutral solvents, such as ethanol and ether, to give 16,17-dihydro product **14**, in which 5,6-olefinic bond remains unchanged.

3β-Hydroxy compound **29** on catalytic hydrogenation in ethanol with 10% Pd–C afforded 5α-pregnane-3β-ol-20-one **30** in 99% yield (Scheme 3). Similarly, hydrogenation of 16-dehydropregnenolone acetate **12** in ethanol has no chemoselectivity, the tetrahydro compound **37** was isolated in 98% yield. It is worth mentioning here that catalytic hydrogenation of **12** and **29** with 10% Pd–C in ethyl acetate is chemoselective and reduces only the 16(17)-double bond to afford[36a] compounds **13** and **14**, respectively, in almost quantitative yields. Similar chemoselective reduction of 16(17)-double bond is also reported by Marino and Abe.[36b] A general trend, which could be termed 'solvent effect', is emerging from these hydrogenation experiments. However, detail study of selective hydrogenation of 5(6) and 16(17)-double bonds in compounds **12** and **29** in ethyl acetate and ethanol has not been explored earlier and reported here for the first time. The 3β-hydroxy group of **30** was transformed to its TBDMS derivative **31** in excellent yield (97%). Compound **31** is an useful intermediate[37] for

the synthesis of azasterols, which are the inhibitors of sterol 24-methyltransferase in *Leishmania* species and *Trypanosoma cruzi*. Crystal structure analysis of compound **31** unambiguously reveals α-orientation of two hydrogens at C-5 and C-17 (Fig. 3).

The compound **31** on reaction with 2-lithio-1,3-dithiane gave **32** as a major product in 82% yield along with minor amount of **33** (5%). Compound **32** on deprotection of the TBDMS group with *n*-Bu_4NF yielded 3,20-diol **34** in 93% yield. The stereochemistry at C-20 of the 3β-hydroxy compound **34** was assigned by spectroscopic data and unambiguously confirmed by single crystal X-ray structure analysis (Fig. 4).

Selective acetylation of the 3β-hydroxy group of compound **34** furnished the 3β-acetate **35**, which on deoxygenation of the C-20 tertiary alcohol by ionic hydrogenation afforded compound **36** exclusively with unnatural C(20*R*) configuration over two steps in 95% yield (Scheme 3). The synthesis of the C(20*R*) aldehyde **10** in 96% yield by oxidative hydrolysis of C-20 dithiane moiety of compound **36** with HgO–$HgCl_2$ has been reported by us.[23]

2.3. Elaboration of steroidal unnatural C(20*R*) aldehydes to 20-*epi* cholanic acid derivatives 4–7

Djerassi and Vanderah obtained[9b] the crucial unnatural C(20*R*) aldehyde **9** from stigmasterol in very poor yield (≈6%) over six steps. These authors have reported the synthesis of the 20-*epi* cholanic acid derivatives **4** and **5** from aldehyde **9** in three and four steps, respectively, in moderate yield. Again, these authors have synthesized 20-*epi* cholanic acid derivatives **6** with poor overall yield (≈2%) and compound **7** from **5** by catalytic hydrogenation in excellent yield.

Elaboration of steroidal aldehyde **8** to methyl (20*S*,22*E*)-3β-acetoxychola-5,22-dienoate **4** and methyl (20*S*)-3β-acetoxychol-5-enoate **5** and also synthesis of methyl (20*S*,22*E*)-3β-acetoxy-5α-chol-22-enate **6** and methyl (20*S*)-3β-acetoxy-5α-cholanate **7** from the saturated aldehyde **10** is reported here. Wittig reaction on aldehydes **8** and **10** with carbomethoxymethylenetriphenylphosphorane[38] ($Ph_3P{=}CHCO_2Me$) in refluxing tetrahydrofuran for 48 h afforded methyl (20*S*,22*E*)-3β-acetoxychola-5,22-dienoate **4** and methyl (20*S*,22*E*)-3β-acetoxy-5α-chol-22-enate **6** in 95 and 93% yields, respectively (Scheme 4). Catalytic hydrogenation of compounds **4** and **6** on 10% Pd–C in ethyl acetate yielded methyl (20*S*)-3β-acetoxychol-5-enoate **5** and methyl (20*S*)-3β-acetoxy-5α-cholanate **7** in 99 and 97% yields, respectively.

Thus, the 20-*epi* cholanic acid derivatives **4–7** have been synthesized from readily available 16-dehydropregnenolone acetate **12** in 9 and 10 steps with an excellent overall yield of 55%. The physical and spectral properties of compounds **4–7** are identical in all respects with the compounds **4–7** reported earlier.[9b] (20*S*)-Stereochemistry and C(22*E*)-configuration in compounds **4** and **6** have been unequivocally

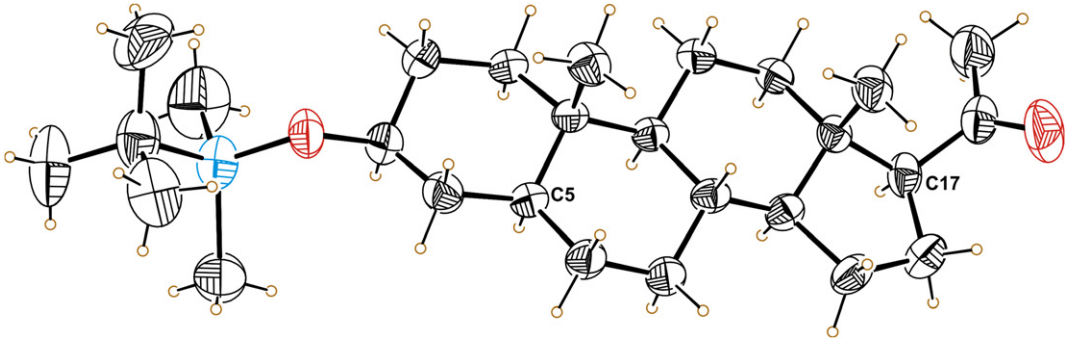


Figure 3. ORTEP view of 3β-*tert*-butyldimethylsilyloxy-5α-pregna-20-one **31**.

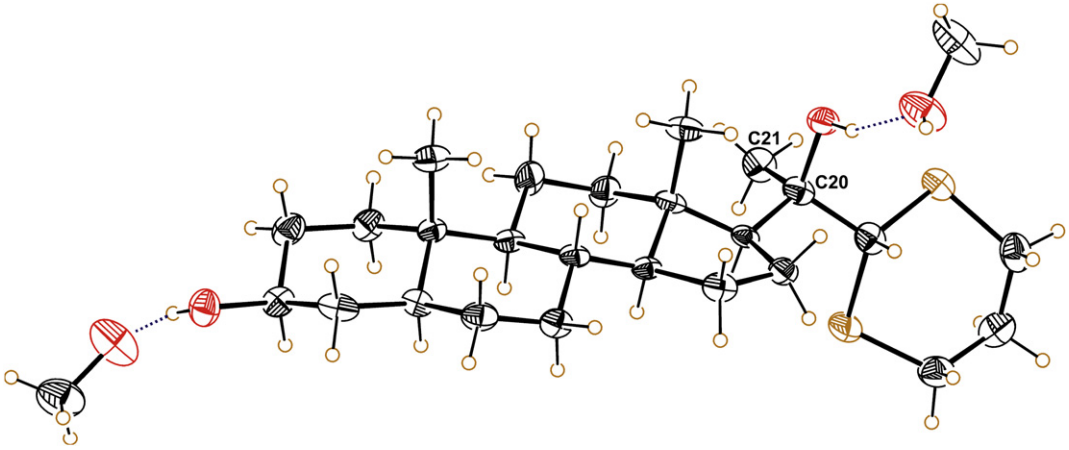


Figure 4. ORTEP view of 3β,20(*R*)-dihydroxy-5α-pregna-20-dithiane **34** with methanol solvate.

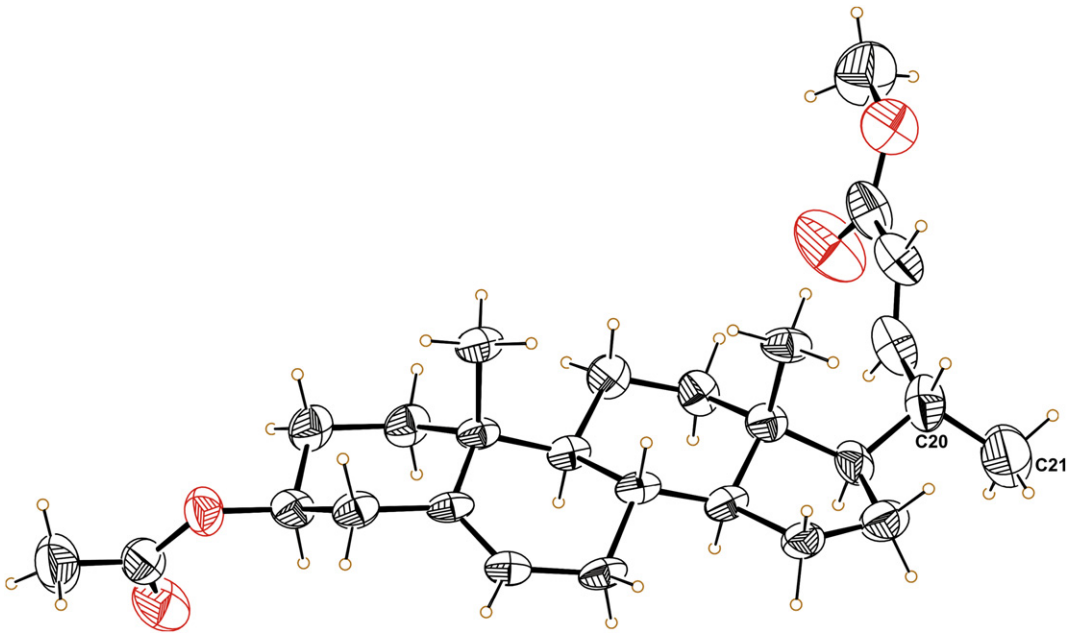


Figure 5. ORTEP view of methyl (20*S*,22*E*)-3β-acetoxychola-5,22-dienoate **4**.

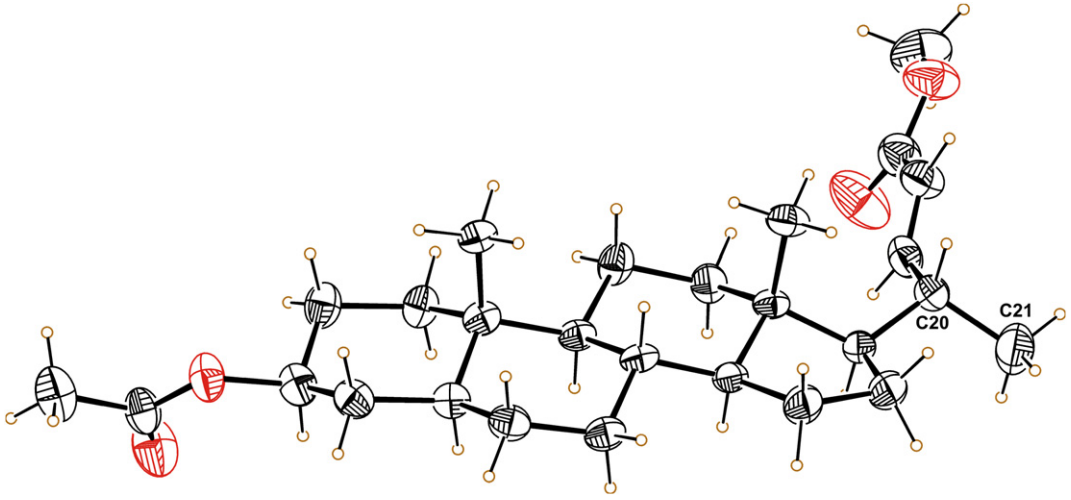


Figure 6. ORTEP view of methyl (20*S*,22*E*)-3β-acetoxy-5α-chol-22-enate **6**.

confirmed by single crystal X-ray structure analysis (Figs. 5 and 6).

3. Conclusions

A highly stereoselective total syntheses of naturally occurring 20-*epi* cholanic acid derivatives have been achieved via unnatural C(20*R*) aldehydes, starting from readily available 16-dehydropregnenolone acetate. Ionic hydrogenation of the C-20,22-ketene dithioacetal or deoxygenation of steroidal C-20 *tert*-alcohols is the key step to set the unnatural C(20*R*) configuration with 100% stereoselectivity. The solvent effect on the catalytic hydrogenation of 16-dehydropregnenolone acetate and 16-dehydropregnenolone has been thoroughly studied. The stereochemistries of the two cholanic acid derivatives **4** and **6** at C-5,C-17,C-20, and also C-22(*E*) configuration have been explicitly confirmed by single crystal X-rays.

The methodology used for the synthesis of 20-*epi* cholanic acid derivatives may be useful for the synthesis of a variety of other 20-*epi* steroids such as 20-*epi* vitamin D_3 (which is more active than the natural one), *epi*-cholesterol (which shows totally different activity than natural cholesterol), and other 20-*epi* steroids, whose biological activity has not been explored yet.

4. Experimental section

4.1. General methods

All melting points were determined on Yanco Micro melting point apparatus and are uncorrected. Optical rotations were obtained on Bellingham and Stanly ADP-220 Polarimeter. Yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer

chromatography (TLC) using TLC aluminum sheets, silica gel 60-F_{254} precoated, Merck, Germany and locating the spots using UV light as the visualizing agent or spraying with ethanolic phosphomolybdic acid (PMA) solution followed by heating. Flash column chromatography was carried out with silica gel (300–400 mesh). Preparative thin-layer chromatography separations were carried out on 0.25 mm E. Merck silica gel plates (60-F_{254}). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200 (200 MHz) at 200.13 and 50.32, or on a Bruker MSL-300 (300 MHz) at 300.13 and 75.47 or on a Bruker DRX-500 (500 MHz) spectrophotometer at 500.13 and 125.78, respectively. Chemical shifts are given in δ values relative to TMS (tetramethylsilane) as internal standard. IR spectra were recorded on Shimadzu 8400 series FTIR instrument and values are reported in cm^{-1} units. Specific rotations ($[\alpha]_D$) are reported in deg/dm and the concentration (c) is given in g/100 ml in the specific solvent. Mass spectra were recorded by either LC–MS or MS-TOF API QSTAR PULSAR spectrophotometer, samples introduced by infusion method using Electrospray Ionization Technique. Elemental analyses were performed by CHNS-O EA 1108-Elemental analyzer, Carloerba Instrument (Italy) or Elementor Vario EL (Germany) and were within ±0.4% of calculated values.

4.1.1. 3β-*tert*-Butyldimethylsilyloxy-(20*R*)-20-hydroxy-pregna-5-en-20-dithiane (16) and 3β-*tert*-butyl-dimethylsilyloxy-(20*S*)-20-hydroxy-20-butyl-pregna-5-ene (17). In a two-necked round bottom flask equipped with a magnetic stirring bar and a septum, 1,3-dithiane (1.362 g, 11.34 mmol) was placed in dry tetrahydrofuran (15 mL). The solution was cooled to −30 °C and *n*-BuLi in hexane (1.7 M, 8 mL, 13.6 mmol) was added to it dropwise under nitrogen atmosphere. The reaction mixture became pale yellow and it was stirred at that temperature for a period of 2 h. To it 3β-*tert*-butyldimethylsilyloxy-pregna-5-en-20-one **15**[39] (3.256 g, 7.56 mmol) in anhydrous tetrahydrofuran (20 mL) was added dropwise at −30 °C under nitrogen atmosphere. The reaction mixture slowly brought to 0 °C and was stirred at that temperature for an additional 12 h. After the completion of the reaction, it was quenched with cold saturated ammonium chloride solution and THF was removed under reduced pressure. The residue was extracted with ethyl acetate (4×100 mL). The organic layer was washed with water (2×50 mL), brine (2×50 mL), and dried over Na_2SO_4. Solvent was removed under reduced pressure to afford crude compound (3.923 g). Flash column chromatographic purification over silica gel using ethyl acetate–petroleum ether (1:99, R_f 0.4 10% EA–PE) as eluant afforded pure 3β-*tert*-butyldimethylsilyloxy-(20*S*)-20-hydroxy-20-butyl-pregna-5-ene **17** (0.148 g, 4%) as a white solid. Mp: 128–130 °C (ethyl acetate–petroleum ether). IR (Nujol, cm^{-1}): 3315 (–OH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.32 (d, 1H, J=6 Hz, 6-H), 3.49 (m, 1H, 3-H), 1.28 (s, 3H, 21-H_3), 1.01 (s, 3H, 19-H_3), 0.89 (s, 9H, $SiCMe_3$), 0.87 (s, 3H, 18-H_3), 0.06 (s, 6H, $SiMe_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 141.6 (C), 121.0 (CH), 75.1 (C), 72.6 (CH), 57.8 (CH), 57.0 (CH), 50.2 (CH), 43.7 (CH_2), 42.8 (CH_2), 42.7 (C), 40.2 (CH_2), 37.4 (CH_2), 36.6 (C), 32.1 (CH_2), 31.8 (CH_2), 31.4 (CH_2), 26.4 (CH_3), 25.9 (3×CH_3), 23.7 (CH_2), 23.3 (CH_2), 22.4 (CH_2), 20.9 (CH_2), 19.4 (CH_3), 18.2 (C), 14.0 (CH_3), 13.6 (CH_3), −4.6 (2×CH_3).

Elution with the same solvent system afforded 3β-*tert*-butyldimethylsilyloxy-(20*R*)-20-hydroxy-pregna-5-en-20-dithiane **16** (3.415 g, 82%) as a colorless solid, from which, 75 mg was crystallized from 5 mL of solvent (dichloromethane–hexane 2:8). Mp: 229–230 °C. $[\alpha]_D^{30}$ −56.6 (c 2.4, $CHCl_3$). IR (Nujol, cm^{-1}): 3450 (–OH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.32 (d, 1H, J=6 Hz, 6-H), 4.15 (s, 1H, 22-H), 3.49 (m, 1H, 3-H), 2.88 (m, 4H, dithiane-CH_2), 1.44 (s, 3H, 21-H_3), 1.00 (s, 3H, 19-H_3), 0.89 (s, 9H, $SiCMe_3$), 0.88 (s, 3H, 18-H_3), 0.06 (s, 6H, $SiMe_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 141.6 (C), 121.0 (CH), 76.8 (C), 72.6 (CH), 61.2 (CH), 56.9 (CH), 55.2 (CH), 50.1 (CH), 43.0 (C), 42.8 (CH_2), 40.2 (CH_2), 37.4 (CH_2), 36.6 (C), 32.1 (CH_2), 31.8 (CH_2), 31.5 (CH_2), 31.3 (CH), 30.8 (CH_2), 26.0 (CH_2), 25.9 (3×CH_3), 24.2 (CH_3), 23.7 (CH_2), 21.7 (CH_2), 21.0 (CH_2), 19.4 (CH_3), 13.4 (CH_3), −4.6 (2×CH_3). Anal. Calcd for $C_{31}H_{54}O_2SiS_2$: C, 67.63; H, 9.68. Found: C, 67.91; H, 9.35.

4.1.2. 3β,20(*R*)-Dihydroxy-pregna-5-en-20-dithiane (27). To the solution of 3β-*tert*-butyldimethylsilyloxy-(20*R*)-20-hydroxy-5-en-20-dithiane **16** (0.55 g, 1 mmol) in dry tetrahydrofuran (7 mL), 1 M of *n*-tetrabutylammonium fluoride in tetrahydrofuran (2 mL, 2 mmol) was added. The reaction mixture was stirred at 30 °C for 12 h and then quenched with aqueous ammonium chloride. Tetrahydrofuran was removed under vacuo and the reaction mixture was extracted with ethyl acetate (2×100 mL). The combined organic extracts were washed with brine (2×25 mL) and dried over Na_2SO_4. Solvent was removed under reduced pressure to afford the crude compound (0.523 g). Column chromatographic purification over silica gel using ethyl acetate–petroleum ether (20:80, R_f 0.4, 25% EA–PE) as eluant gave **27** (0.405 g, 93%) as a colorless solid, out of which 58 mg was crystallized from 4 mL of solvent (ethyl acetate–hexane 6:4). Mp: 204 °C. $[\alpha]_D^{26.8}$ −50.70 (c 0.35, $CHCl_3$). IR (Nujol, cm^{-1}): 3506 (–OH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.35 (d, 1H, J=6 Hz, 6-H), 4.15 (s, 1H, 22-H), 3.52 (m, 1H, 3-H), 2.88 (m, 4H, dithiane-CH_2), 2.27 (d, 2H, J=6 Hz, 4-H), 1.44 (s, 3H, 21-H_3), 1.01 (s, 3H, 19-H_3), 0.88 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.9 (C), 121.6 (CH), 76.8 (C), 71.8 (CH), 61.3 (CH), 56.9 (CH), 55.2 (CH), 50.1 (CH), 43.0 (C), 42.3 (CH_2), 40.2 (CH_2), 37.3 (CH_2), 36.5 (C), 31.8 (CH_2), 31.7 (CH_2), 31.5 (CH_2), 31.4 (CH_2), 30.8 (CH_2), 26.0 (CH_2), 24.2 (CH_3), 23.8 (CH_2), 21.7 (CH_2), 21.0 (CH_2), 19.4 (CH_3), 13.4 (CH_3). MS (LC–MS) m/z: 454.99 (M+H_2O), 435.99, 419.99, 339.99. Anal. Calcd for $C_{25}H_{40}O_2S_2$: C, 68.75; H, 9.23; S, 14.68. Found: C, 68.69; H, 9.40; S, 14.55.

4.1.3. 3β-Acetoxy-20(*R*)-hydroxy-pregna-5-en-20-dithiane (28). To the solution of 3β,20(*R*)-dihydroxy-pregna-5-en-20-dithiane **27** (0.436 g, 1 mmol) in dry pyridine (2 mL) were added acetic anhydride (0.19 mL, 2 mmol) and catalytic amount of *N*,*N*-dimethylaminopyridine (0.024 g, 0.2 mmol). The reaction mixture was stirred at 25 °C for 2 h, quenched with crushed ice, and extracted with ethyl acetate (2×100 mL). The combined organic extracts were washed with brine (2×25 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to give crude compound **28** (0.465 g). Column chromatographic purification over silica gel using ethyl acetate–petroleum ether (6:94, R_f 0.5, 10% EA–PE) as an eluant afforded

pure product **28** (0.46 g, 96%) as a colorless solid. From this 41 mg was crystallized in 3.5 mL of solvent (ethyl acetate–hexane 3:7). Mp: 212–213 °C. $[\alpha]_D^{26.5}$ −57.83 (*c* 0.4, $CHCl_3$). IR (Nujol, cm^{-1}): 3506 (–OH), 1728 (–$OCOCH_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.37 (d, 1H, *J*=6 Hz, 6-H), 4.60 (m, 1H, 3-H), 4.14 (s, 1H, 22-H), 2.88 (m, 4H, dithiane-CH_2), 2.33 (d, 2H, *J*=6 Hz, 4-H), 2.03 (s, 3H, –$OCOCH_3$), 1.44 (s, 3H, 21-H_3), 1.02 (s, 3H, 19-H_3), 0.88 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.4 (C), 139.8 (C), 122.5 (CH), 76.8 (C), 74.0 (CH), 61.3 (CH), 56.8 (CH), 55.2 (CH), 50.0 (CH), 43.0 (C), 40.1 (CH_2), 38.1 (CH_2), 37.0 (CH_2), 36.5 (C), 31.7 (CH_2), 31.5 (CH), 31.4 (CH_2), 30.8 (CH_2), 27.8 (CH_2), 26.0 (CH_2), 24.2 (CH_3), 23.7 (CH_2), 21.7 (CH_2), 21.4 (CH_3), 20.9 (CH_2), 19.3 (CH_3), 13.4 (CH_3). MS (LC–MS) *m/z*: 497 (M+H_2O), 478 (M^+), 461.99. Anal. Calcd for $C_{27}H_{42}O_3S_2$: C, 67.73; H, 8.84; S, 13.39. Found: C, 67.70; H, 8.46; S, 13.27.

4.1.4. 3β-Acetoxy-pregna-5-en-(20*R*)-20-dithiane (23). The solution of 3β-acetoxy-20(*R*)-hydroxy-pregna-5-en-20-dithiane **28** (0.239 g, 0.5 mmol) in dichloromethane (5 mL) was cooled to 0 °C. To it triethylsilane (0.48 mL, 3 mmol) was added, stirred for 10 min, and then borontrifluoride diethyl etherate (0.63 mL, 5 mmol) in dichloromethane (2 mL) was added dropwise. The mixture was stirred for 10 min and 10% sodium bicarbonate (10 mL) was added. The reaction mixture was extracted with dichloromethane (2×100 mL). The combined organic extracts were washed with brine (2×25 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford crude compound **23** (0.235 g). Flash chromatographic purification over silica gel using ethyl acetate–petroleum ether (1:99, R_f 0.5, 10% EA–PE) as an eluant gave pure compound **23** (0.204 g, 94%) as a colorless solid. From this 63 mg was crystallized in 3 mL of solvent (diethyl ether–hexane 2:8). Mp: 175–176 °C. $[\alpha]_D^{27.5}$ −32 (*c* 0.5, $CHCl_3$). IR (Nujol, cm^{-1}): 1730 (–$OCOCH_3$), 1236, 1045. ^1H NMR ($CDCl_3$, 200 MHz): δ 5.38 (d, 1H, *J*=6 Hz, 6-H), 4.62 (m, 1H, 3-H), 4.39 (d, 1H, *J*=4 Hz, 22-H), 2.85 (m, 4H, dithiane-CH_2), 2.04 (s, 3H, $OCOCH_3$), 1.05 (d, 1H, *J*=6 Hz, 21-H_3), 1.03 (s, 3H, 19-H_3), 0.71 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.3 (C), 139.6 (C), 122.5 (CH), 73.9 (CH), 56.2 (CH), 55.5 (CH), 52.0 (CH), 50.1 (CH), 42.5 (C), 40.4 (CH), 38.9 (CH_2), 38.1 (CH_2), 36.6 (C), 36.1 (CH_2), 31.9 (CH), 31.8 (CH_2), 31.7 (CH_2), 30.6 (CH_2), 27.7 (CH_2), 27.2 (CH_2), 26.4 (CH_2), 24.0 (CH_2), 21.3 (CH_3), 21.1 (CH_2), 19.3 (CH_3), 15.8 (CH_3), 12.1 (CH_3). MS (EI) *m/z*: 480.01 (M+H_2O), 464.02 (M+1). Anal. Calcd for $C_{27}H_{42}O_2S_2$: C, 70.69; H, 9.42; S, 14.54. Found: C, 70.27; H, 9.14; S, 14.15.

4.1.5. 3β-hydroxy-pregna-5-en-(20*R*)-20-dithiane (24). The procedure for the synthesis of **23** was followed. From **16** or **27** was obtained 90–92% of the title compound as a white solid. From this 38 mg was crystallized in 2 mL of solvent (ethyl acetate–hexane 4:6). Mp 184–185 °C. $[\alpha]_D^{25}$ −32 (*c* 0.75, $CHCl_3$). IR (Nujol, cm^{-1}): 3310 (–OH). ^1H NMR ($CDCl_3$, 200 MHz): δ 5.35 (d, 1H, *J*=6 Hz, 6-H), 4.39 (d, *J*=4 Hz, 1H, 22-H), 3.54 (m, 1H, 3-H), 2.84 (m, 4H, dithiane-CH_2), 2.30 (d, 2H, *J*=6 Hz, 4-H), 1.05 (d, 3H, *J*=6 Hz, 21-H_3), 1.02 (s, 3H, 19-H_3), 0.71 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.7 (C), 121.6 (CH), 71.8 (CH), 56.3 (CH), 55.6 (CH), 52.0 (CH), 50.2 (CH), 42.6 (C), 42.3 (CH_2), 40.5 (CH), 39.0 (CH_2), 37.3 (CH_2), 36.5 (C), 31.9 (CH), 31.8 (CH_2), 31.7 (CH_2), 31.7 (CH_2), 30.7 (CH_2), 27.3 (CH_2), 26.5 (CH_2), 20.5 (CH_2), 21.2 (CH_2), 19.4 (CH_3), 16.0 (CH_3), 12.1 (CH_3). MS (LC–MS) *m/z*: 438.02 (M+H_2O), 422.02 (M+2). Anal. Calcd for $C_{25}H_{40}OS_2$: C, 71.37; H, 9.58; S, 15.24. Found: C, 71.17; H, 9.62; S, 15.15.

4.1.6. 3β-Acetoxy-pregna-5-en-(20*R*)-22-aldehyde (8). To a suspension of 3β-acetoxy-pregna-5-en-(20*R*)-20-dithiane **23** (0.231 g, 0.5 mmol) in CH_3CN (5 mL) and H_2O (0.5 mL), HgO (0.16 g, 0.75 mmol) and $HgCl_2$ (0.27 g, 1 mmol) were added. The reaction mixture was refluxed for 3 h with vigorous stirring. The solid mass was filtered through a pad of Celite and the residue was thoroughly washed with ethyl acetate. The filtrate was diluted with more ethyl acetate (100 mL). The total organic extracts were washed with brine (2×25 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give a solid (0.2 g), which was chromatographed over silica gel using ethyl acetate–petroleum ether (2:98, R_f 0.42, 10% EA–PE) as an eluant to afford pure compound **8** (0.18 g, 96%) as a colorless solid. From this 33 mg was crystallized in 2 mL of solvent (ethyl acetate–hexane 3:7). Mp: 118–120 °C (lit.[15] 120–121 °C). $[\alpha]_D^{24.6}$ −57.14 (*c* 0.385, $CHCl_3$). IR (Nujol, cm^{-1}): 2960, 1730 (–$OCOCH_3$), 1710 (CHO), 1247. ^1H NMR ($CDCl_3$, 500 MHz): δ 9.55 (d, 1H, *J*=5 Hz, CHO), 5.38 (d, 1H, *J*=6 Hz, 6-H), 4.60 (m, 1H, 3-H), 2.03 (s, 3H, $OCOCH_3$), 1.03 (d, 1H, *J*=6 Hz, 21-H_3), 1.01 (s, 3H, 19-H_3), 0.69 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 205.6 (CH), 170.4 (C), 139.8 (C), 122.3 (CH), 73.9 (CH), 56.2 (CH), 52.0 (CH), 50.1 (CH), 48.8 (CH), 42.2 (CH), 38.5 (C), 38.1 (C), 37.0 (CH_2), 31.9 (CH_2), 31.8 (CH), 29.7 (CH_2), 27.8 (CH_2), 26.5 (CH_2), 23.9 (CH_2), 21.4 (CH_3), 20.8 (CH_2), 19.3 (CH_3), 13.5 (CH_3), 12.8 (CH_3). MS (LC–MS) *m/z*: 391.02 (M+H_2O), 373.03 (M+1), 313.03. Anal. Calcd for $C_{24}H_{36}O_3$: C, 77.37; H, 9.74. Found: C, 77.13; H, 9.83.

4.1.7. 3α,5-*cyclo*-6β-Methoxy-pregna-(20*R*)-22-aldehyde (9). To a solution of 3α,5-*cyclo*-6β-methoxy-pregna-(20*R*)-20-dithiane **26** (0.043 g, 0.1 mmol) in 1 mL of 8:1:1 MeCN–CH_2Cl_2–H_2O was added Dess–Martin periodinane reagent (0.085 g, 0.2 mmol) in one portion. The reaction mixture was stirred at room temperature, exposed to air, for 5 h. The reaction was quenched with 5 mL of 50% $NaHCO_3$ and extracted with dichloromethane (2×50 mL). The combined organic extracts were washed with brine (2×25 mL), dried over Na_2SO_4, and concentrated under reduced pressure followed by purification of the product by preparative thin-layer chromatography affords (0.02 g, 55%) the desired C-22 aldehyde **9** as a gum. $[\alpha]_D^{27}$ +42.97 (*c* 0.605, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ 9.55 (d, 1H, *J*=6 Hz, CHO), 3.33 (s, 1H, OCH_3), 1.03 (d, 3H, *J*=5 Hz, 21-H_3), 1.01 (s, 3H, 19-H_3), 0.73 (s, 3H, 18-H_3). The ^1H NMR data of **9** is similar to the reported[39] one.

4.1.8. 16-Dehydropregnenolone (29). To a stirred solution of 16-dehydropregnenolone acetate **12** (5.340 g, 15 mmol) in *tert*-butanol (125 mL) was added solution of KOH (4.2 g, 75 mmol) in H_2O (5 ml). The reaction mixture was stirred for 10 h at 30 °C and *tert*-butanol was removed under reduced pressure, crushed ice was added to it. The solid was

filtered and washed with cold water (5×25 mL). It was then dried to yield 16-dehydropregnenolone **29** (4.52 g, 96%) as a colorless solid. From this 100 mg was crystallized in 5 mL of solvent (methanol–dichloromethane 9:1). Mp: 214–215 °C (lit.[40] 216 °C). $[\alpha]_D^{22.5}$ −27.27 (*c* 0.66, CH_3OH). IR (Nujol, cm^{-1}): 1654 (C═O), 3390 (–OH). ^1H NMR (300 MHz, $CDCl_3$): δ 6.72 (t, 1H, *J*=3 Hz, 16-H), 5.37 (d, 1H, *J*=5 Hz, 6-H), 3.53 (m, 1H, 3-H), 2.26 (s, 3H, $COCH_3$), 1.05 (s, 3H, 19-H_3), 0.92 (s, 3H, 18-H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.7 (C), 155.4 (C), 144.2 (CH), 141.4 (C), 120.9 (CH), 71.6 (CH), 56.4 (CH), 50.5 (CH), 46.1 (C), 42.2 (CH_2), 37.1 (CH_2), 36.7 (CH), 34.7 (CH_2), 32.2 (CH_2), 31.6 (CH_2), 31.5 (CH_2), 30.2 (CH), 27.0 (CH_3), 20.6 (CH_2), 19.2 (CH_3), 15.7 (CH_3). MS (LC–MS) *m/z*: 315 (M+1), 337 (M+Na), 353 (M+K). Anal. Calcd for $C_{21}H_{30}O_2 \cdot 0.5CH_4O$: C, 78.13; H, 9.76. Found: C, 78.12; H, 9.78.

4.1.9. 3β-Hydroxy-5α,17α-pregna-20-one (30). To a solution of 16-dehydropregnenolone **29** (1.572 g, 5 mmol) in ethanol (100 mL) was added Pd–C catalyst (0.157 g, 10%) and hydrogenation was carried out using Parr apparatus at 55 psi pressure at 30 °C for 12 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure to obtain 3β-hydroxy-5α,17α-pregna-20-one **30** (1.576 g, 99%) as a colorless solid. From this 150 mg was crystallized in 10 mL of solvent (methanol–dichloromethane 9:1). Mp: 193–195 °C (lit.[41a] 193–195 °C, lit.[41b] 192–195 °C, and lit.[42] 194 °C). $[\alpha]_D^{23}$ +90.78 (*c* 0.70, CH_3OH) (lit.[42] +93 and +91). IR (Nujol, cm^{-1}): 1691 (C═O), 3388 (–OH). ^1H NMR (200 MHz, $CDCl_3$): δ 3.60 (m, 1H, 3-H), 2.11 (s, 3H, $COCH_3$), 0.81 (s, 3H, 19-H_3), 0.60 (s, 3H, 18-H_3). ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.7 (C), 70.9 (CH), 63.7 (CH), 56.5 (CH), 54.1 (CH), 44.7 (CH), 44.1 (C), 38.9 (CH_2), 37.9 (CH_2), 36.9 (CH_2), 35.3 (C), 35.3 (CH), 31.9 (CH_2), 31.4 (CH_3), 31.2 (CH_2), 28.5 (CH_2), 24.3 (CH_2), 22.6 (CH_2), 21.1 (CH_2), 13.3 (CH_3), 12.2 (CH_3). MS (LC–MS) *m/z*: 319 (M+1), 341 (M+Na), 357 (M+K). Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.75. Found: C, 78.89; H, 11.03.

4.1.10. 3β-*tert*-Butyldimethylsilyloxy-5α,17α-pregna-20-one (31). To a solution of 3β-hydroxy-5α,17α-pregna-20-one **30** (3.185 g, 10 mmol) in dry DMF (90 mL) under nitrogen atmosphere were added imidazole (1.020 g, 15 mmol) and *tert*-butyldimethylsilyl chloride (1.875 g, 12.5 mmol). The mixture was stirred at 30 °C for 10 h. The resulting suspension was quenched with cold water and extracted with diethyl ether (2×200 mL) and washed with saturated sodium bicarbonate (2×75 mL), 1 M HCl (2×25 mL), and water (2×50 mL). The organic extracts were washed with brine (2×50 mL) and dried over Na_2SO_4. Removal of solvent under reduced pressure afforded crude compound (4.340 g). Column chromatographic purification over silica gel using ethyl acetate–petroleum ether (3:97; R_f 0.4, 10% EA–PE) as an eluant afforded 3β-*tert*-butyldimethylsilyloxy-5α,17α-pregna-20-one **31** (4.197 g, 97%) as a colorless solid. From this 200 mg was crystallized in 10 mL of solvent (methanol–dichloromethane 9:1). Mp: 140–141 °C (lit.[37] 139–140 °C). $[\alpha]_D^{23.4}$ +70.17 (*c* 0.57, $CHCl_3$). IR (Nujol, cm^{-1}): 1708 (C═O). ^1H NMR (200 MHz, $CDCl_3$): δ 3.55 (m, 1H, 3-H), 2.11 (s, 3H, $COCH_3$), 0.89 (s, 9H, $SiCMe_3$), 0.80 (s, 3H, 19-H_3), 0.60 (s, 3H, 18-H_3), 0.05 (s, 6H, $SiMe_2$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.6 (C), 72.0 (CH), 63.8 (CH), 56.7 (CH), 54.3 (CH), 45.0 (CH), 44.2 (C), 39.1 (CH_2), 38.6 (CH_2), 37.1 (CH_2), 35.5 (C), 35.4 (CH), 32.0 (CH_2), 31.9 (CH_2), 31.5 (CH_3), 28.6 (CH_2), 25.9 (3×CH_3), 24.4 (CH_2), 22.7 (CH_2), 21.2 (CH_2), 18.2 (C), 13.4 (CH_3), 12.3 (CH_3), −4.6 (2×CH_3). Anal. Calcd for $C_{27}H_{48}O_2Si$: C, 74.93; H, 11.17. Found: C, 75.00; H, 11.37.

4.1.11. 3β-*tert*-Butyldimethylsilyloxy-(20*R*)-20-hydroxy-5α-pregna-20-dithiane (32) and 3β-*tert*-butyl-dimethylsilyloxy-(20*S*)-20-hydroxy-20-butyl-5α-pregnane (33). Compounds **32** (2.2673 g, 82%) and **33** (0.123 g, 5%) were obtained from compound **31** (2.163 g, 5 mmol) following identical experimental procedure adopted for the preparation of compounds **16** and **17** from compound **15**.

4.1.11.1. Compound 32. Mp: 217–219 °C (acetone). $[\alpha]_D^{23.7}$ −17.39 (*c* 0.57, $CHCl_3$). IR (Nujol, cm^{-1}): 3388 (–OH). ^1H NMR (200 MHz, $CDCl_3$): δ 4.14 (s, 1H, 22-H), 3.52 (m, 1H, 3-H), 2.90 (m, 4H, dithiane-CH_2), 1.42 (s, 3H, 21-H_3), 0.88 (s, 9H, $SiCMe_3$), 0.85 (s, 3H, 19-H_3), 0.79 (s, 3H, 18-H_3), 0.05 (s, 6H, $SiMe_2$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 78.0 (C), 72.4 (CH), 61.5 (CH), 56.8 (CH), 55.5 (CH), 54.6 (CH), 45.2 (CH), 43.5 (C), 40.7 (CH_2), 38.9 (CH_2), 37.4 (CH_2), 35.7 (C), 35.1 (CH), 32.2 (2×CH_2), 31.8 (CH_2), 31.1 (CH_2), 29.0 (CH_2), 26.3 (CH_2), 26.2 (3×CH_3), 24.4 (CH_3), 23.9 (CH_2), 21.9 (CH_2), 21.4 (CH_2), 18.5 (C), 13.9 (CH_3), 12.6 (CH_3), −4.3 (2×CH_3). Anal. Calcd for $C_{31}H_{56}O_2SiS_2$: C, 67.33; H, 10.20; S, 11.59. Found: C, 67.22; H, 9.96; S, 11.33.

4.1.11.2. Compound 33. Mp: 124–126 °C (ethyl acetate–hexane). $[\alpha]_D^{31}$ +3.36 (*c* 0.59, $CHCl_3$). IR (Nujol, cm^{-1}): 3392 (–OH). ^1H NMR ($CDCl_3$, 200 MHz): δ 3.52 (m, 1H, 3-H), 1.24 (s, 3H, 21-H_3), 0.86 (s, 9H, $SiCMe_3$), 0.81 (s, 3H, 19-H_3), 0.78 (s, 3H, 18-H_3), 0.03 (s, 6H, $SiMe_2$). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 75.2 (C), 72.1 (CH), 57.7 (CH), 56.7 (CH), 54.4 (CH), 45.0 (CH), 43.7 (CH_2), 42.9 (C), 40.4 (CH), 48.6 (CH_2), 37.2 (CH_2), 35.5 (C), 34.8 (CH), 32.0 (CH_2), 31.9 (CH_2), 28.8 (CH_2), 26.5 (CH_2), 26.4 (CH_3), 25.9 (3×CH_3), 23.7 (CH_2), 23.3 (CH_2), 22.3 (CH_2), 21.1 (CH_2), 18.2 (C), 14.1 (CH_3), 13.8 (CH_3), 12.4 (CH_3), −4.6 (2×CH_3). Anal. Calcd for $C_{31}H_{58}O_2Si$: C, 75.85; H, 11.91. Found: C, 75.70; H, 11.56.

4.1.12. 3β,20(*R*)-Dihydroxy-5α-pregna-20-dithiane (34). The procedure for the synthesis of **27** was followed. From **32** was obtained 93% of the title compound as a white solid. From this 50 mg was crystallized in 4 mL of solvent (methanol–dichloromethane 9:1). Mp: 198–200 °C. $[\alpha]_D^{24}$ −13.63 (*c* 0.44, $CHCl_3$). IR (Nujol, cm^{-1}): 3328 (–OH). ^1H NMR (200 MHz, $CDCl_3$): δ 4.14 (s, 1H, 22-H), 3.59 (m, 1H, 3-H), 2.88 (m, 4H, dithiane-CH_2), 1.42 (s, 3H, 21-H_3), 0.85 (s, 3H, 19-H_3), 0.80 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 76.7 (C), 71.1 (CH), 61.1 (CH), 56.4 (CH), 55.1 (CH), 54.1 (CH), 44.7 (CH), 43.1 (C), 40.2 (CH_2), 38.0 (CH_2), 36.9 (CH_2), 35.3 (C), 34.7 (CH), 31.8 (CH_2), 31.4 (CH_2), 31.3 (CH_2), 30.7 (CH_2), 28.6 (CH_2), 25.9 (CH_2), 24.0 (CH_3), 23.5 (CH_2), 21.5 (CH_2), 21.0 (CH_2), 13.5 (CH_3), 12.2 (CH_3).

4.1.13. 3β-Acetoxy-20(*R*)-hydroxy-5α-pregna-20-dithiane (35). The procedure for the synthesis of **28** was

followed. From **34** was obtained 97% of the title compound as a white solid. From this 60 mg was crystallized in 6 mL of solvent (methanol–dichloromethane 4:1). Mp: 243–244 °C. $[\alpha]_D^{24}$ −17.02 (*c* 0.7, $CHCl_3$). IR (Nujol, cm^{-1}): 3436 (–OH), 1730 (–$OCOCH_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 4.68 (m, 1H, 3-H), 4.13 (s, 1H, 22-H), 2.90 (m, 4H, dithiane-CH_2), 2.02 (s, 3H, $OCOCH_3$), 1.42 (s, 3H, 21-H_3), 0.85 (s, 3H, 19-H_3), 0.82 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.6 (C), 76.7 (C), 73.6 (CH), 61.1 (CH), 56.4 (CH), 55.1 (CH), 54.0 (CH), 44.5 (CH), 43.1 (C), 40.2 (CH_2), 36.6 (CH_2), 35.3 (C), 34.8 (CH), 33.9 (CH_2), 31.7 (CH_2), 31.5 (CH_2), 30.8 (CH_2), 28.5 (CH_2), 27.4 (CH_2), 26.0 (CH_2), 24.0 (CH_3), 23.6 (CH_2), 21.5 (CH_2), 21.4 (CH_3), 21.0 (CH_2), 13.5 (CH_3), 12.1 (CH_3). MS (LC–MS) *m/z*: 503 (M+Na). Anal. Calcd for $C_{27}H_{44}O_3S_2$: C, 67.45; H, 9.22; S, 13.33. Found: C, 67.08; H, 9.13; S, 13.56.

4.1.14. 3β-Acetoxy-5α-pregna-(20*R*)-20-dithiane (36). Deoxygenation of C-20 *tert*-alcohol of **35** to compound **36** (0.874 g, 94%) was carried out following the procedure (Et_3SiH, $BF_3\cdot OEt_2$, DCM, 0 °C, 10 min.) used for deoxygenation of compound **28** to compound **23**. From this 40 mg was crystallized in 4 mL of solvent (methanol–dichloromethane 9:1). Mp: 176–178 °C. $[\alpha]_D^{24.5}$ +11.82 (*c* 1.01, $CHCl_3$). IR (Nujol, cm^{-1}): 1730 (–$OCOCH_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 4.68 (m, 1H, 3-H), 4.37 (d, 1H, *J*=2 Hz, 22-H), 2.84 (m, 4H, dithiane-CH_2), 2.02 (s, 3H, $OCOCH_3$), 1.06 (d, 3H, *J*=6 Hz, 21-H_3), 0.82 (s, 3H, 19-H_3), 0.67 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.5 (C), 73.6 (CH), 55.9 (CH), 55.4 (CH), 54.1 (CH), 51.9 (CH), 44.5 (CH), 42.7 (C), 40.4 (CH), 39.0 (CH_2), 36.6 (CH_2), 35.4 (C), 35.4 (CH), 33.9 (CH_2), 31.8 (CH_2), 31.6 (CH_2), 30.5 (CH_2), 28.5 (CH_2), 27.4 (CH_2), 27.2 (CH_2), 26.3 (CH_2), 23.9 (CH_2), 21.3 (CH_3), 21.2 (CH_2), 15.9 (CH_3), 12.2 (CH_3), 12.1 (CH_3). MS (LC–MS) *m/z*: 464 (M^+). Anal. Calcd for $C_{27}H_{44}O_2S_2$: C, 69.77; H, 9.54; S, 13.79. Found: C, 69.87; H, 9.52; S, 13.74.

4.1.15. 3β-Acetoxy-pregna-(20*R*)-22-aldehyde (10). Oxidative hydrolysis of C-20 dithiane **36** (0.464 g, 1 mmol) to the C-22 aldehyde **10** (0.360 g, 96%) was carried out by following identical procedure adopted for compound **8** from **23**.

Mp: 142–145 °C (ethyl acetate–hexane). IR (Nujol, cm^{-1}): 1731 (–$OCOCH_3$), 1716 (CHO). ^1H NMR ($CDCl_3$, 200 MHz): δ 9.52 (d, 1H, *J*=6 Hz, CHO), 4.68 (m, 1H, 3-H), 2.02 (s, 3H, $OCOCH_3$), 1.03 (d, 1H, *J*=8 Hz, 21-H_3), 0.81 (s, 3H, 19-H_3), 0.66 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 205.8 (CH), 170.7 (C), 73.6 (CH), 55.9 (CH), 54.2 (CH), 52.0 (CH), 48.5 (CH), 44.6 (CH), 42.3 (C), 38.6 (CH_2), 36.7 (CH_2), 35.4 (C), 35.5 (CH), 33.9 (CH_2), 31.9 (CH_2), 28.5 (CH_2), 27.4 (CH_2), 26.4 (CH_2), 23.8 (CH_2), 21.4 (CH_3), 20.8 (CH_2), 13.5 (CH_3), 13.0 (CH_3), 12.1 (CH_3). MS (LC–MS) *m/z*: 398 (M+Na), 414 (M+K). Anal. Calcd for $C_{24}H_{36}O_3$: C, 76.96; H, 10.22. Found: C, 76.90; H, 10.18.

4.1.16. 3β-Acetoxy-5α,17α-pregna-20-one (37). The procedure for the synthesis of **30** was followed. From **12** was obtained 98% of the title compound as a colorless solid. Mp: 144–146 °C (methanol). $[\alpha]_D^{31}$ +67 (*c* 0.92, $CHCl_3$). IR (Nujol, cm^{-1}): 1731 (–$OCOCH_3$), 1704 (C=O). ^1H NMR (200 MHz, $CDCl_3$): δ 4.68 (m, 1H, 3-H), 2.11 (s, 3H, $COCH_3$), 2.02 (s, 3H, $OCOCH_3$), 0.82 (s, 3H, 19-H_3), 0.60 (s, 3H, 18-H_3). ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.3 (C), 170.5 (C), 73.4 (CH), 63.6 (CH), 56.5 (CH), 53.9 (CH), 44.5 (CH), 44.0 (C), 38.9 (CH_2), 36.6 (CH_2), 35.3 (CH_2), 35.3 (C), 33.8 (CH_2), 31.8 (CH_2), 31.4 (CH_3), 28.3 (CH_2), 27.3 (CH_2), 24.2 (CH_2), 22.6 (CH_2), 21.3 (CH_3), 21.0 (CH_2), 13.3 (CH_3), 12.1 (CH_3). MS (LC–MS) *m/z*: 360 (M^+). Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.06. Found: C, 76.62; H, 10.36.

4.1.17. Methyl (20*S*,22*E*)-3β-acetoxychola-5,22-dienoate (4). To a solution of 3β-acetoxy-pregna-5-en-(20*R*)-22-aldehyde **8** (0.370 g, 1 mmol) in dry tetrahydrofuran (10 mL) was added carbomethoxymethylenetriphenylphosphorane ($Ph_3P{=}CHCO_2Me$) (1.336 g, 4 mmol) and it was refluxed for 48 h. The reaction mixture was concentrated in vacuo and the residue was extracted with ethyl acetate (2× 100 mL). The organic extracts were washed with brine (2× 25 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give a solid (1.7 g), which was chromatographed over silica gel using ethyl acetate–petroleum ether (4:96, R_f 0.42, 10% EA–PE) as eluant to afford compound **4** (0.407 g, 95%) as a colorless long needles. From this 125 mg was crystallized in 5 mL of solvent (methanol–dichloromethane 4:1). Mp: 151–152 °C. $[\alpha]_D^{25.7}$ −84.4 (*c* 0.91, $CHCl_3$). IR (Nujol, cm^{-1}): 1733 (–$OCOCH_3$) 1718 (–$COOCH_3$). ^1H NMR ($CDCl_3$, 200 MHz): δ 6.90 (dd, 1H, *J*=16 and 10 Hz, 22-H), 5.81 (d, 1H, *J*=16 Hz, 23-H), 5.38 (d, 1H, *J*=4 Hz, 6-H), 4.61 (m, 1H, 3-H), 3.73 (s, 3H, $COOCH_3$), 2.03 (s, 3H, $OCOCH_3$), 0.99 (d, 3H, *J*=4 Hz, 21-H_3), 0.97 (s, 3H, 19-H_3), 0.64 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.5 (C), 167.2 (C), 155.7 (CH), 139.7 (C), 122.4 (CH), 118.4 (CH), 73.9 (CH), 56.3 (CH), 55.9 (CH), 51.3 (CH), 49.9 (CH), 42.2 (C), 39.9 (CH_3), 38.6 (CH_2), 38.0 (CH_2), 36.9 (CH_2), 36.5 (C), 31.8 (CH_2), 31.8 (CH), 27.7 (CH_2), 27.6 (CH_2), 24.0 (CH_2), 21.4 (CH_3), 20.7 (CH_2), 20.1 (CH_3), 19.2 (CH_3), 12.1 (CH_3). Anal. Calcd for $C_{27}H_{40}O_4$: C, 75.66; H, 9.40. Found: C, 75.38; H, 9.68.

4.1.18. Methyl (20*S*)-3β-acetoxychol-5-enoate (5). To a solution of methyl (20*S*,22*E*)-3β-acetoxychola-5,22-dienoate **4** (0.086 g, 0.2 mmol) in ethyl acetate (7 mL) was added 0.09 g of 10% Pd–C catalyst and hydrogenation was carried out using Parr apparatus at 45 psi pressure, at 30 °C for 10 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure to obtain methyl (20*S*)-3β-acetoxychol-5-enoate **5** (0.087 g, 98%) as a colorless solid. From this 25 mg was crystallized in 2 mL of solvent (methanol–dichloromethane 9:1). Mp: 120–121 °C. $[\alpha]_D^{25.7}$ −52.28 (*c* 0.76, $CHCl_3$). IR (Nujol, cm^{-1}): 1733 (–$OCOCH_3$), 1725 (–$COOCH_3$). ^1H NMR ($CDCl_3$, 200 MHz): δ 5.38 (d, 1H, *J*=4 Hz, 6-H), 4.63 (m, 1H, 3-H), 3.67 (s, 3H, $COOCH_3$), 2.03 (s, 3H, $OCOCH_3$), 1.02 (s, 3H, 19-H_3), 0.85 (d, 3H, *J*=4 Hz, 21-H_3), 0.69 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 174.7 (C), 170.5 (C), 139.6 (C), 122.5 (CH), 73.9 (CH), 56.6 (CH), 55.4 (CH), 51.4 (CH), 49.9 (CH), 42.3 (C), 39.5 (CH_2), 38.1 (CH_2), 36.9 (CH_2), 36.5 (C), 34.6 (CH_3), 31.8 (CH_2), 31.8 (CH), 31.0 (CH_2), 30.3 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 24.1 (CH_2), 21.4 (CH_3), 21.0 (CH_3), 19.3 (CH_3), 18.3 (CH_3), 11.9 (CH_3). Anal. Calcd for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.21; H, 9.81.

4.1.19. Methyl (20*S*,22*E*)-3β-acetoxy-5α-chol-22-enoate (6). Wittig olefination of the aldehyde **10** was carried out for compound **6** following the procedure for the preparation of compound **4** from the aldehyde **8**.

Yield: 93%. Mp: 121–122 °C (MeOH). $[\alpha]_D^{24}$ +18.18 (*c* 0.55, $CHCl_3$). IR (Nujol, cm^{-1}): 1731(–$OCOCH_3$), 1718 (–$COOCH_3$). ^1H NMR ($CDCl_3$, 200 MHz): δ 6.89 (dd, 1H, *J*=16 and 10 Hz, 22-H), 5.76 (d, 1H, *J*=16 Hz, 23-H), 4.67 (m, 1H, 3-H), 3.73 (s, 3H, $COOCH_3$), 2.02 (s, 3H, $OCOCH_3$), 0.97 (d, 3H, *J*=6 Hz, 21-H_3), 0.80 (s, 3H, 19-H_3), 0.61 (s, 3H, 18-H_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.7 (C), 167.3 (C), 155.8 (CH), 118.4 (CH), 73.7 (CH), 56.1 (CH), 54.2 (CH), 51.4 (CH), 44.6 (CH), 42.6 (C), 40.0 (CH), 38.9 (CH_2), 36.9 (CH_2), 36.7 (CH_2), 35.4 (C), 35.4 (CH_3), 34.0 (CH_2), 31.9 (CH_2), 28.5 (CH_2), 27.6 (CH_2), 27.4 (CH_2), 24.0 (CH_2), 21.4 (CH_3), 20.9 (CH_2), 20.1 (CH_3), 12.3 (CH_3), 12.2 (CH_3). Anal. Calcd for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found: C, 75.23; H, 9.86.

4.1.20. Methyl (20*S*)-3β-acetoxy-5α-cholanate (7). Catalytic hydrogenation of compound **6** to compound **7** was carried out following the procedure adopted for the hydrogenation of compound **4** to compound **5**.

Yield: 97%. Mp: 132–134 °C (CH_3OH). $[\alpha]_D^{31}$ +5.71 (*c* 0.35, $CHCl_3$). IR (Nujol, cm^{-1}): 1731. ^1H NMR ($CDCl_3$, 200 MHz): δ 4.69 (m, 1H, 3-H), 3.67 (s, 3H, $COOCH_3$), 2.31 (m, 2H, 23-H_2), 2.02 (s, 3H, $OCOCH_3$), 0.83 (d, 3H, *J*=4 Hz, 21-H_3), 0.82 (s, 3H, 19-H_3), 0.66 (s, 3H, 18-H_3). Anal. Calcd for $C_{27}H_{44}O_4$: C, 74.96; H, 10.25. Found: C, 75.16; H, 10.18.

4.2. Crystal structure analysis

Crystals of all the compounds were obtained from methanol by slow evaporation. Crystals of all the compounds were thin plates and best amongst them were selected using Leica polarizing microscope. X-ray intensity data of all the compounds were collected on a Bruker SMART APEX CCD diffractometer with omega and phi scan mode, $\lambda_{Mo\ K\alpha}$= 0.71073 Å at *T*=133(2) K. All the data were corrected for Lorentzian, polarization, and absorption effects using Bruker's SAINT and SADABS programs. The crystal structures were solved by direct method using SHELXS-97 and the refinement was performed by full matrix least squares of F^2 using SHELXL-97.[43] Hydrogen atoms were included in the refinement as per the riding model.

Crystal data for **4** ($C_{27}H_{40}O_4$): *M*=428.59, crystal dimensions 0.23×0.08×0.01 mm^3, monoclinic, space group $P2_1$, *a*=12.017(13), *b*=6.259(7), *c*=16.890(18) Å, β= 104.61(2)°, *V*=1229(2) $Å^3$, *Z*=2, ρ_{calcd}=1.158 g cm^{-3}, μ(Mo Kα)=0.076 mm^{-1}, *F*(000)=468, $2\theta_{max}$=50.00°, 8729 reflections collected, 4146 unique, 2750 observed ($I>2\sigma(I)$) reflections, 285 refined parameters, *R* value 0.1146, *wR*2=0.2481 (all data *R*=0.1590, *wR*2=0.2707), *S*= 1.215, minimum and maximum transmission 0.9826 and 0.9989, respectively, maximum and minimum residual electron densities +0.347 and −0.220 e$Å^{-3}$, CCDC no. 606455.

Crystal data for **6** ($C_{27}H_{42}O_4$): *M*=430.61, crystal dimensions 0.43×0.27×0.05 mm^3, orthorhombic, space group $P2_12_12_1$, *a*=6.590(3), *b*=12.750(6), *c*=30.150(12) Å, *V*=2533.5(19) $Å^3$, *Z*=4, ρ_{calcd}=1.129 g cm^{-3}, μ(Mo Kα)= 0.074 mm^{-1}, *F*(000)=944, $2\theta_{max}$=50.00°, 18,276 reflections collected, 4436 unique, 2775 observed ($I>2\sigma(I)$) reflections, 286 refined parameters, *R* value 0.0812, *wR*2=0.1477 (all data *R*=0.1334, *wR*2=0.1681), *S*=1.075, minimum and maximum transmission 0.9691 and 0.9967, respectively, maximum and minimum residual electron densities +0.132 and −0.150 e$Å^{-3}$, CCDC no. 606456.

Crystal data for compound **16** ($C_{27}H_{44}O_3$): *M*=416.62, crystal dimensions 0.49×0.15×0.11 mm^3, orthorhombic, space group $P2_12_12_1$, *a*=9.202(4), *b*=12.334(6), *c*= 21.928(10) Å, *V*=2489(2) $Å^3$, *Z*=4, ρ_{calcd}=1.112 g cm^{-3}, μ(Mo Kα)=0.070 mm^{-1}, $2\theta_{max}$=50.0°, *F*(000)=920, 12,394 reflections collected, 4370 unique, 2597 observed ($I>2\sigma(I)$) reflections, 277 refined parameters, *R* value 0.0431, *wR*2=0.0841 (all data *R*=0.0874, *wR*2=0.0934), *S*=0.889, minimum and maximum transmission 0.9665 and 0.9927, maximum and minimum residual electron densities +0.109 and −0.093 e$Å^{-3}$, CCDC no. 606460.

Crystal data for **31** ($C_{27}H_{48}O_2Si$): *M*=432.74, crystal dimensions 0.42×0.16×0.09 mm^3, orthorhombic, space group $P2_12_12_1$, *a*=7.289(3), *b*=21.177(9), *c*=35.260(15) Å, *V*= 5443(4) $Å^3$, *Z*=8, ρ_{calcd}=1.056 gcm^{-3}, μ(Mo Kα)=0.105 mm^{-1}, *F*(000)=1920, $2\theta_{max}$=50.00°, 44,081 reflections collected, 9588 unique, 4245 observed ($I>2\sigma(I)$) reflections, 557 refined parameters, *R* value 0.0727, *wR*2=0.1515 (all data *R*=0.1900, *wR*2=0.1911), *S*=0.988, minimum and maximum transmissions 0.9569 and 0.9905, respectively, maximum and minimum residual electron densities +0.411 and −0.274 e$Å^{-3}$, CCDC no. 606457.

Crystal data for **34** ($C_{25}H_{42}O_2S_2\cdot 2(CH_3OH)$): *M*=502.79, crystal dimensions 0.80×0.54×0.02 mm^3, orthorhombic, space group $P2_12_12_1$, *a*=7.5351(17), *b*=10.129(2), *c*= 37.329(8) Å, *V*=2849.2(11) $Å^3$, *Z*=4, ρ_{calcd}=1.172 g cm^{-3}, μ(Mo Kα)=0.216 mm^{-1}, *F*(000)=1104, $2\theta_{max}$=50.00°, 19,132 reflections collected, 4990 unique, 3908 observed ($I>2\sigma(I)$) reflections, 307 refined parameters, *R* value 0.1002, *wR*2=0.1629 (all data *R*=0.1309, *wR*2=0.1715), *S*=1.274, minimum and maximum transmission 0.8469 and 0.9968, respectively, maximum and minimum residual electron densities +0.324 and −0.202 e$Å^{-3}$, CCDC no. 606458.

Acknowledgements

B.B.S. thanks the University Grants Commission, New Delhi for Research Fellowship. The Emeritus Scientist Scheme awarded to B.G.H. by the Council of Scientific and Industrial Research, New Delhi is gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.04.014.

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