CHAPTER 5

Synthesis of 16-dehydropregnenolone derivatives and their biological activity
5.1 Introduction

Malaria kills 1–2 million people each year and 300–500 million new clinical cases of malaria are reported annually.¹ Malaria is a particularly devastating disease in sub-Saharan Africa, where about 90% of cases and deaths occur. Malaria is also a serious public health problem in certain regions of South East Asia and South America. Human malaria transmitted by female Anopheles mosquitoes is caused by four species of *Plasmodium*, which are, *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. Most cases of malaria and deaths are caused by *P. falciparum*. The development of resistance to mainstay drugs like chloroquine, and controlled use of new artemisinin analogs have created an urgent need to discover new antimalarial agents. The life cycle, immunological defense mechanisms, and clinical development of malaria in humans is a complex process.² Clinical malaria is characterized by periodic fever, which follows the lysis of infected erythrocytes, and caused mainly by the induction of cytokines interleukin-1 and tumor necrosis factor. *P. falciparum* infection can have serious effects, for example, anemia, cerebral complications (from coma to convulsions), hypoglycemia and glomerulonephritis. The disease is most serious in the non-immune individuals, including children, pregnant women and tourists.

Pregnanes, the C-21 steroid derivatives, are an important class of bioactive compounds having diverse pharmacological activity and which has provided interesting ‘leads’ for the development of new drugs. These potent pregnane derivatives have been found to posses cytotoxic,³ antifeedant,⁴ anti-inflammatory,⁵,⁶ anti-asthamatic,⁷ lipid lowering⁸ and anti-viral⁹ activities. They also find use as neurosteroids¹⁰ and as inhibitors of testosterone ⁷ a reductase¹¹ which helps in the treatment of androgen sensitive prostate cancer in men.¹² Besides this, a number of pregnanes are not only similar to cardiac glycosides with respect to molecular and cellular site of action, but they have enhanced cardiac contractibility.¹³ Pregnane glycosides because of their remarkable pharmacological activities are one of the major components of traditional Chinese medicine.¹⁴ These biologically active compounds isolated chiefly from Asclepiadaceae¹⁵ family plants have been found to posses anti-cancer,¹⁶ anti-asthamatic,¹⁷ anti-tumor¹⁸ and anti-fungal activities.¹⁹ The synthetic derivatives of this class of compounds are larger, more hydrophilic, have increased efficacy and reduced toxicity relative to the parent compound ²⁰ and have primarily been used for the treatment of ulcerative colitis,²¹ Crohn’s disease²¹ and cardiac contractibility.²² Owing to the immense importance of these
medicinally important pregnane derivatives, considerable attention is being devoted to the synthesis and biological evaluation of this important class of compounds. In the search of newer derivatives, the synthesis of novel pregnane derivatives in excellent yields and anti-malarial activity is given below.

5.2 Chemical transformation of 16-dehydropregnenolone: The syntheses of amine analogues of pregnenolone were accomplished by subjecting the naturally isolated 16-dehydropregnenolone using various aromatic and aliphatic amine by employing Michael addition reaction at 45°C for 4 h to afford amine derivative of pregnenolone (1-9) in very good yield.
5.3 Anti-malarial Activity

Derivative of pregnenolone were screened for their *in-vitro* antimalarial activity against chloroquine (CQ) sensitive 3D7 strain of *P. falciparum*. Chloroquine was used as reference drug. Among the screen compounds (1-9), compound 4 showed activity. Activity was evaluated at 10, 2 and 1 μg/mL. Compounds with MIC value ≤ 10 μg/ml are given in Table 1.

Table 1. Anti-malarial activity of derivative of pregnenolone

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound No.</th>
<th>MIC μg/ml</th>
<th>IC&lt;sub&gt;50&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1A</td>
<td>10</td>
<td>&gt;500</td>
</tr>
<tr>
<td>2</td>
<td>1B</td>
<td>10</td>
<td>&gt;500</td>
</tr>
<tr>
<td>3</td>
<td>2A</td>
<td>2</td>
<td>415.2</td>
</tr>
<tr>
<td>4</td>
<td>2B</td>
<td>2</td>
<td>409.0</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>&gt;10</td>
<td>&gt;500</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>≤2</td>
<td>180.79</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>≤2</td>
<td>&gt;500</td>
</tr>
</tbody>
</table>

MIC= Minimum concentration inhibiting development of ring stage parasites into the schizonts

5.4 Experimental section:

5.4.1 Representative procedure for the preparation of N-propylamine derivative of 16-dehydropregnenolone (3β-Hydroxy-16α-(propylamino)pregn-5-en-20-one) (1)

Compound 1 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and N-propylamine. N-propylamine was also used as solvent. The reaction mixture was stirred for 4 h at 45°C. The reaction mixture was cooled, filtered and then extracted with EtOAc and H<sub>2</sub>O, the extract was evaporated under reduced pressure. Then the crude product was chromatographed on silica gel to afford the desired compound 1A and 1B.

Yield: 1A 45% and 1B 40%
3β-Acetoxy-16α-(propylamino)preg-5-en-20-one (1A)

IR (KBr): 2937, 1715, 1112 cm\(^{-1}\).

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta\) 5.29 (1H, m, H-6), 4.53 (1H, m, H-3), 4.12 (1H, m, H-16), 3.12 (br, NH) 2.71 (3H, m, H-17, 1'), 2.32 (2H, m, H-4), 2.23 (3H, s, H-21), 2.22 (3H, m, CH\(_3\)CO), 2.04 (1H, m, H-12), 1.97 (1H, m, H-7), 1.84 (4H, m, H-1, 2, 2'), 1.68 (1H, m, H-15), 1.62 (2H, m, H-11, 2), 1.57 (1H, m, H-7), 1.47 (1H, m, H-11), 1.46 (1H, m, H-8), 1.43 (1H, m, H-12), 1.23 (1H, m, H-15), 1.17 (1H, m, H-14), 1.10 (1H, m, H-9), 1.08 (1H, m, H-1), 0.96 (3H, s, H-18), 0.96 (3H, t, J = 7.0 Hz, H-3'), 0.57 (3H, s, H-19).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta\) 206.0 (C-20), 170.5 (O\(\text{COCH}_3\)), 139.6 (C-5), 121.9 (C-6), 73.7 (C-3), 67.5 (C-17), 57.1 (C-16), 53.9 (C-14), 49.2 (C-9), 49.0 (C-1'), 45.1 (C-13), 38.3 (C-4), 38.0 (C-12), 36.8 (C-1), 36.5 (C-10), 31.4 (C-8), 31.4 (C-7), 31.3 (C-2), 29.8 (C-21), 27.6 (C-15), 21.6 (O\(\text{COCH}_3\)), 20.7 (C-2'), 19.8 (C-11), 19.3 (C-18), 14.1 (C-19), 11.4 (C-3').

ESI-MS: (C\(_{26}\)H\(_{41}\)NO\(_3\)), \(m/z\) 416 [M+H]\(^+\).

3β-Hydroxy-16α-(propylamino)preg-5-en-20-one (2B)

IR (KBr): 3101, 1715, 1598, 1116 cm\(^{-1}\).

\(^1\)H NMR: (300 MHz, CD\(_3\)OD) \(\delta\) 5.35 (1H, m, H-6), 4.17 (1H, m, H-16), 3.37 (1H, m, H-3), 2.85 (3H, m, H-17, 1'), 2.27 (2H, m, H-4), 2.23 (3H, s, H-21), 2.04 (1H, m, H-12), 1.97 (1H, m, H-7), 1.84 (4H, m, C-1, 2, 2'), 1.68 (1H, m, H-15), 1.43 (1H, m, H-8), 1.43 (1H, m, H-12), 1.23 (1H, m, H-15), 1.17 (1H, m, H-14), 1.10 (1H, m, H-9), 1.08 (1H, m, H-1), 0.96 (3H, s, H-18), 0.96 (3H, t, J = 7.0 Hz, H-3'), 0.57 (3H, s, H-19).
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1.62 (1H, m, H-11), 1.57 (1H, m, H-7), 1.48 (1H, m, H-2), 1.46 (1H, m, H-8), 1.47 (1H, m, H-11), 1.43 (1H, m, H-12), 1.23 (1H, m, H-15), 1.17 (1H, m, H-14), 1.08 (1H, m, H-1), 1.03 (3H, s, H-18), 1.03 (3H, t, J = 6.9 Hz, H-3'), 0.98 (1H, s, H-9), 0.66 (3H, s, H-19).

$^{13}$C NMR: (75 MHz, CD$_3$OD) δ 207.4 (C-20), 142.6 (C-5), 121.86 (C-6), 72.4 (C-3), 68.9 (C-17), 58.4 (C-16), 55.6 (C-14), 51.6 (C-9), 49.9 (C-1'), 46.3 (C-13), 43.0 (C-4), 39.5 (C-12), 38.5 (C-1), 37.8 (C-10), 32.8 (C-8), 32.6 (C-7), 32.3 (C-2), 31.5 (C-21), 30.6 (C-15), 22.0 (C-2'), 21.0 (C-11), 19.9 (C-18), 14.4 (C-19), 11.4 (C-3').

ESI-MS:  (C$_{24}$H$_{39}$N$_O_2$), m/z 374 [M+H]$^+$. 

5.4.2 Phenyl-1-propylamine derivative of 16-dehydropregnenolone (2A & 2B): using similar procedure as described for 1A, compound 2A and 2B were obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and 3-phenylpropan-1-amine.

Yield: 2A 30% and 2B 40%.

3β-Acetoxy-16α-(3-phenylpropylamino)pregn-5-en-20-one (2A)

1H NMR:  (300 MHz, CDCl$_3$) δH 7.24 (2H, m, H-6', 8'), 7.14 (3H, m, H-5', 7', 9'), 5.30 (1H, m, H-6), 4.55 (1H, m, H-3), 4.01 (1H, m, H-16), 2.92 (1H, d= 6.1Hz, H-17), 2.79 (1H, m, H-1'), 2.68 (1H, m, H-1'), 2.58 (2H, t, J = 7.8 Hz, H-3'), 2.29 (2H, m, H-4), 2.16 (2H, m, H-7, 12) 2.08 (3H, s, H-21), 2.00 (3H, m, CH$_3$CO ), 1.84 (4H, H-1, 2, 2'), 1.67 (1H, m, H-15), 1.63 (2H, m, H-11, 2), 1.57 (1H, m, H-7), 1.46 (1H, m, H-8), 1.46 (1H, m, H-11), 1.36 (1H, m, H-12), 1.23 (1H, m, H-15), 1.08 (2H, m, H-1, 14), 0.95 (3H, s, H-18), 0.90 (1H, m, H-9), 0.53 (3H, s, H-19).

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$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$ 205.9 (C-20), 170.5 (OCOCH$_3$), 139.9 (C-5), 139.6 (C-4'), 128.7 (C-6', 8'), 128.5 (C-5', 9'), 126.5 (C-7'), 122.1 (C-6), 73.9 (C-3), 67.9 (C-17), 57.3 (C-16), 54.0 (C-14), 49.2 (C-9), 47.2 (C-1'), 44.9 (C-13), 38.2 (C-4), 38.0 (C-12), 36.8 (C-1), 36.5 (C-10, 3'), 31.3 (C-8), 31.3 (C-7), 31.3 (C-2), 29.7 (C-21), 28.0 (C-2'), 27.7 (C-15), 21.5 (OCOCH$_3$), 20.8 (C-11), 19.3 (C-18), 14.1 (C-19).

ESI-MS: (C$_{32}$H$_{45}$N$_3$O$_3$), $m/z$ 492 [M+H]$^+$.  

3β-Hydroxy-16α-(3-phenylpropylamino) pregn-5-en-20-one (2B)  

![Chemical structure of 3β-Hydroxy-16α-(3-phenylpropylamino) pregn-5-en-20-one (2B)](image)

$^1$H NMR: (300 MHz, CD$_3$OD) $\delta$H 7.29 (2H, m, H-6', 8'), 7.20 (3H, m, H-5', 7', 9'), 5.32 (1H, m, H-6), 4.05 (1H, m, H-16), 3.47 (1H, m, H-3), 3.06 (1H, d, J = 8.2 Hz, H-17), 2.80 (1H, m, H-1'), 2.74 (1H, m, H-1'), 2.69 (2H, t, J = 7.8 Hz, H-3'), 2.28 (2H, m, H-4), 2.20 (3H, s, H-21), 2.16 (2H, m, H-7, 12), 2.05 (3H, m, H-1, 2'), 1.88 (1H, m, H-2) 1.81 (1H, m, H-15), 1.70 (2H, m, H-11, 2), 1.67 (1H, m, H-7), 1.46 (1H, m, H-8), 1.44 (1H, m, H-11), 1.36 (1H, m, H-12), 1.26 (1H, m, H-15), 1.13 (2H, m, H-1, 14), 0.99 (3H, s, H-18), 0.88 (1H, m, H-9), 0.60 (3H, s, H-19).

ESI-MS: (C$_{30}$H$_{43}$NO$_2$), $m/z$ 450 [M+H]$^+$.  

5.4.3 Morpholine derivative of 16-dehydropregnenolone (3): By similar procedure as described for 1, compound 3 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and morpholine.
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3β-Acetoxy-16α-(morpholino)pregn-5-en-20-one (3)

\[
\text{\textbf{1H NMR:} (300 MHz, CDCl}_3\text{)} \delta \text{H} 5.35 (1H, m, H-6), 4.58 (1H, m, H-3), 3.71 (4H, t, J = 4.4 Hz, H-3', 5'), 3.61 (1H, m, H-16), 2.74 (1H, d, J = 8.6 Hz, H-17), 2.53 (2H, m, H-2', 6'), 2.32 (4H, m, H-4, 2', 6'), 2.18 (3H, s, H-21), 2.02 (3H, m, CH}_3\text{CO\text{), 2.02 (1H, m, H-12), 1.97 (1H, m, H-7), 1.84 (4H, H-1, 2), 1.68 (1H, m, H-15), 1.62 (2H, m, H-11, 2), 1.57 (1H, m, H-8), 1.50 (1H, m, H-11), 1.50 (1H, m, H-12), 1.18 (1H, m, H-15), 1.13 (1H, m, H-14), 1.04 (1H, m, H-1), 1.00 (3H, s, H-18), 0.86 (1H, m, H-9), 0.64 (3H, s, H-19).}
\]

**ESI-MS: (C\text{27}H\text{41}N\text{O4}, m/z 444 [M+H]^+.**

**Yield: 50%**

Dodecan-1-amine derivative of 16-dehydropregnenolone (4): By similar procedure as described for 1, compound 4 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and dodecan-1-amine.

3β-Hydroxy-16α-(dodecylamino) pregn-5-en-20-one (4)

\[
\text{\textbf{1H NMR:} (300 MHz, CD}_3\text{OD) } \delta \text{H} 5.27 (1H, m, H-6), 4.02 (1H, m, H-16), 3.44 (1H, m, H-3), 2.90 (1H, d, J = 7.1 Hz, H-17), 2.68 (2H, m, H-1'), 2.22 (2H, m, H-4), 2.22 (3H, s, H-21), 2.04 (1H, m, H-12), 1.96 (1H, m, H-7), 1.83 (4H, m, H-1, 2, 2'), 1.69 (1H, m, H-15), 1.64 (1H, m, H-11), 1.55 (1H, m, H-7), 1.47 (1H,}
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\[ m, H-2), 1.47 (1H, m, H-11), 1.46 (1H, m, H-8), 1.44 (1H, m, H-12), 1.25-1.18 (20H, H-14, 15, 3'-11') 1.08 (1H, m, H-1), 0.95 (3H, s, H-18), 0.84 (3H, t, J = 6.9 Hz, H-12'), 0.98 (1H, s, H-9), 0.58 (3H, s, H-19).

\[ ^{13}C \text{NMR:} \ (75 \text{ MHz, } \text{CD}_3\text{OD}) \delta 206.4 \text{ (C-20), 140.8 (C-5), 121.1 (C-6), 71.5 (C-3), 68.2 (C-17), 57.1 (C-16), 54.1 (C-14), 49.5 (C-9), 47.6 (C-1'), 45.1 (C-13), 42.1 (C-4), 38.5 (C-12), 37.2 (C-1), 36.7 (C-10), 32.0 (C-8), 32.0 (C-7), 31.6 (C-2), 31.5 (C-21), 30.0 (C-15), 29.8-29.3 (C-3'-10') 26.5 (C-2'), 22.8 (C-11'), 21.0 (C-11), 19.5 (C-18), 14.2 (C-19), 14.2 (C-12').

Yield: 50%.

ESI-MS: \((C_{33}H_{57}NO_{2}) \ m/z \ 500 \ [M+1]^+\)

5.4.5 Di-Methylamino ethylamine derivative of 16-dehydropregnenolone (5): By similar procedure as described for 1, compound 5 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and N,N-dimethylethane-1,2-diamine.

3β-Acetoxy-16α-(2-(dimethylamino)ethylamino) pregn-5-en-20-one(5)

\[ ^1H \text{NMR:} \ (300 \text{ MHz, } \text{CDCl}_3) \delta_H 5.30 (1H, m, H-6), 3.92 (1H, m, H-16), 3.46 (1H, m, H-3), 2.90 (2H, t, J = 6.0 Hz, H-1'), 2.75 (1H, m, H-17), 2.50 (2H, t, J = 6.0 Hz, H-2') 2.42 (6H, s, H-3'), 2.17 (2H, m, H-4), 2.16 (3H, s, H-21), 2.03 (3H, m, CH_3CO), 1.94 (1H, m, H-7), 1.90 (1H, m, H-12), 1.85 (1H, m, H-2), 1.82 (1H, m, H-1), 1.68 (1H, m, H-15), 1.62 (2H, m, H-11, 2), 1.60 (2H, m, H-15), 1.57 (1H, m, H-7), 1.57 (1H, m, H-12), 1.47 (1H, m, H-11), 1.46 (1H, m, H-8), 1.14 (1H, m, H-14), 1.02 (1H, m, H-1), 1.00 (1H, m, H-9), 0.96 (3H, s, H-18), 0.58 (3H, s, H-19).
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$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$ 209.5 (C-20), 179.9 (OCOCH$_3$), 142.4 (C-5), 122.1 (C-6), 72.4 (C-3), 72.0 (C-17), 58.3 (C-16), 57.0 (C-2'), 55.9 (C-14), 51.0 (C-9), 38.0 (C-1'), 45.9 (C-13), 45.4 (C-4'), 43.0 (C-4), 39.4 (C-12), 37.7 (C-1), 37.6 (C-10), 31.4 (C-8), 32.3 (C-7), 31.3 (C-2), 31.5 (C-21), 24.5 (C-15), 21.6 (OCOCH$_3$), 19.8 (C-11), 19.3 (C-18), 14.4 (C-19).

ESI-MS: (C$_{27}$H$_{44}$N$_2$O$_3$), $m/z$ 445 [M+H$^+$].

Yield: 50%.

5.4.6 Benzylamine derivative of 16-dehydropregnenolone (6): By similar procedure as described for 1, compound 6 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and phenylmethanamine.

$\beta$-Hydroxy-16$\alpha$-(benzylamino) pregn-5-en-20-one (6)

![Chemical Structure]

$^1$H NMR: (300 MHz, CD$_3$OD) $\delta_H$ 7.34-7.21 (5H, $m$), 5.35 (1H, $m$, H-6), 3.85 (1H, $m$, H-16), 3.71 (1H, $d$, $J = 12.2$ Hz, H-1'), 3.59 (1H, $d$, $J = 12.2$ Hz, H-1'), 3.51 (1H, $m$, H-3), 2.5 (1H, $d$= 6.5 Hz, H-17), 2.27 (2H, $m$, H-4), 2.16 (3H, $s$, H-21), 2.16 (1H, $m$, H-12), 1.97 (1H, $m$, H-7), 1.84 (2H, $m$, H-1, 2), 1.68 (1H, $m$, H-15), 1.62 (1H, $m$, H-11), 1.57 (1H, $m$, H-7), 1.48 (1H, $m$, H-2), 1.46 (1H, $m$, H-8), 1.46 (1H, $m$, H-11), 1.43 (1H, $m$, H-12), 1.24 (1H, $m$, H-15), 1.16 (1H, $m$, H-14), 1.08 (1H, $m$, H-1), 1.01 (3H, $s$, H-18), 0.98 (1H, $s$, H-9), 0.66 (3H, $s$, H-19).

$^{13}$C NMR: (75 MHz, CD$_3$OD) $\delta$ 208.8 (C-20), 141.0 (C-5), 139.5 (C-2'), 128.7 (C-3', 7'), 128.5 (C-4', 6'), 127.4 (C-5'), 121.4 (C-6), 72.2 (C-3), 71.7 (C-17), 57.7 (C-16), 54.8 (C-14), 53.0 (C-1'), 50.1 (C-9), 45.1 (C-13), 42.4 (C-4), 39.0 (C-12), 37.4 (C-1), 36.1 (C-10), 32.8 (C-8), 32.0 (C-7), 31.7 (C-2), 31.7 (C-21), 31.7 (C-15), 21.0 (C-11), 19.6 (C-18), 14.6 (C-19).
MS (EISMS): (C_{28}H_{39}NO_2) m/z 422 [M+1]^+.  
Yield: 60%.

5.4.7 **Propane-1,3-diamine derivative of 16-dehydropregnenolone (7):** By similar procedure as described for 1, compound 7 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and propane-1,3-diamine.

**3β-Hydroxy-16α-(3-aminopropylamino) pregn-5-en-20-one (7)**

![Chemical Structure](image)

$^1$H NMR: (300 MHz, CD$_3$OD) $\delta$H 5.33 (1H, m, H-6), 4.00 (1H, m, H-16), 3.57 (1H, m, H-1'), 3.37 (1H, m, H-3), 2.85 (2H, t, $J = 5.9$ Hz, H-3'), 2.55 (1H, d, $J = 8.8$ Hz, H-17), 2.27 (2H, m, H-4), 2.23 (3H, s, H-21), 2.05 (1H, m, H-12), 1.96 (1H, m, H-7), 1.85 (4H, m, C-1, 2, 2'), 1.67 (1H, m, H-15), 1.62 (1H, m, H-11), 1.57 (1H, m, H-7), 1.48 (1H, m, C-2), 1.47 (1H, m, H-11), 1.45 (1H, m, C-8), 1.43 (1H, m, H-12), 1.22 (1H, m, H-15), 1.17 (1H, m, H-14), 1.08 (1H, m, C-1), 1.03 (3H, s, H-18), 1.03 (3H, t, $J = 6.9$ Hz, H-3'), 0.98 (1H, s, H-9), 0.66 (3H, s, H-19).

ESI-MS: (C_{24}H_{40}N_2O_2), m/z 389 [M+]^+.
Yield: 40%.

5.4.8 **Heptan-2-amine derivative of 16-dehydropregnenolone (8):** By similar procedure as described for 1, compound 8 was obtained from 16-dehydropregnenolone acetate (100 mg, 0.28 mmol) and heptan-2-amine.
3β-Hydroxy-16α-(heptan-2-ylamino) pregn-5-en-20-one (8)

\[
\begin{align*}
\text{H NMR: } & (300 \text{ MHz, CD}_3\text{OD}) \delta_H 5.37 (1H, m, H-6), 4.17 (1H, m, H-16), 3.37 (1H, m, H-3), 2.85 (2H, m, H-17, 2'), 2.27 (2H, m, H-4), 2.24 (3H, s, H-21), 2.04 (1H, m, H-12), 1.96 (1H, m, H-7), 1.84 (4H, m, H-1, 2, 3'), 1.68 (1H, m, H-15), 1.62 (1H, m, H-11), 1.57 (1H, m, H-7), 1.48 (1H, m, H-2), 1.47 (1H, m, H-11), 1.46 (1H, m, H-8), 1.43 (1H, m, H-12), 1.31 (2H, m, H-6'), 1.23 (1H, m, H-15), 1.22 (4H, m, H-4', 5') 1.17 (1H, m, H-14), 1.08 (1H, m, H-1), 1.02 (3H, s, H-18), 1.00 (3H, t, J = 6.8, H-7'), 0.99 (1H, s, H-9), 0.67 (3H, s, H-19).
\end{align*}
\]

MS (ESIMS): (C\textsubscript{28}H\textsubscript{47}NO\textsubscript{2}), \textit{m/z} 430 [M+H]\textsuperscript{+}.

Yield: 40\%.

5.4.9 Di-ethylamino propylamine derivative of 16-dehydroprogrenolone (9): By similar procedure as described for 1, compound 9 was obtained from 16-dehydroprogrenolone acetate (100 mg, 0.28 mmol) and N,N-diethylpropene-1,3-diamine.

3β-Hydroxy-16α-(3-(diethylamino)propylamino) pregn-5-en-20-one (9)
Chapter-5  Synthesis of 16-dehydropregnenolone derivatives and their biological activity

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 5.30 (1H, m, H-6), 4.08 (1H, m, H-16), 3.36 (1H, m, H-3), 3.20 (2H, m, H-1'), 3.13 (2H, t, $J = 6.9$ Hz, H-3'), 3.14 (4H, m, H-5') 2.92 (1H, d, $J = 7.0$ Hz, H-17), 2.20 (2H, m, H-4), 2.23 (3H, s, H-21), 2.02 (1H, m, H-12), 1.97 (1H, m, H-7), 1.89 (2H, m, H-2'), 1.85 (2H, m, H-1, 2), 1.70 (1H, m, H-15), 1.64 (1H, m, H-11), 1.62 (1H, m, H-7), 1.48 (1H, m, H-2), 1.46 (1H, m, H-8), 1.45 (1H, m, H-11), 1.43 (1H, m, H-12), 1.23 (6H, t, $J = 6.9$ Hz, H-6'), 1.12 (1H, m, H-15), 1.05 (1H, m, H-14), 1.00 (1H, m, H-1), 0.93 (3H, s, H-18), 0.82 (1H, s, H-9), 0.55 (3H, s, H-19).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 209.3 (C-20), 142.8 (C-5), 122.4 (C-6), 72.5 (C-3), 69.3 (C-17), 58.5 (C-16), 55.5 (C-14), 51.1 (C-9), 52.1 (C-3'), 48.6 (2 X C-5'), 46.3 (C-13), 43.0 (C-4), 39.5 (C-12), 37.8 (C-1), 37.6 (C-1'), 37.7 (C-10), 33.4 (C-7), 32.8 (C-8), 32.8 (C-21), 32.3 (C-2), 25.3 (C-2'), 22.9 (C-15), 21.9 (C-11), 19.9 (C-18), 14.5 (C-19), 9.6 (2 X C-6').

ESI-MS: (C$_{28}$H$_{46}$N$_2$O$_2$), $m/z$ 445 [M+H]$^+$. Yield: 40%.
Chapter 5 Synthesis of 16-dehydropregnenolone derivatives and their biological activity

ESI-MS of compound 1A

\[ \text{1H NMR spectrum (300 MHz, CDCl}_3\) of compound 1A} \]
Chapter 5 Synthesis of 16-dehydropregnenolone derivatives and their biological activity

ESI-MS spectrum of compound 1B

$^1$H NMR spectrum (300 MHz, CD$_3$OD) of compound 1B in CD$_3$OD
Chapter 5  Synthesis of 16-dehydropregnenolone derivatives and their biological activity

C13CPD C13OH+D2O (Driedr1) user S1

13C NMR spectrum (75 MHz, CD3OD) of compound 1B

ESI-MS of compound 2A
Chapter 5  Synthesis of 16-dehydropregnenolone derivatives and their biological activity

PROTON CDCl₃ (D:edri) user 51

[Image of proton NMR spectrum]

1H NMR spectrum (300 MHz, CDCl₃) of compound 2A

13C NMR (75 MHz, CDCl₃) spectrum of compound 2A
Chapter 5  Synthesis of 16-dehydropregnenolone derivatives and their biological activity

ESI-MS of compound 2B

1H NMR spectrum (300 MHz, CD3OD) of compound 2B
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Original Data Path: 912/MAY36905120316.120439.RAW
Sample ID: 36905120316
Sample Name: 1144A
Analysis Date: 9/12/2009 2:26:23 PM

T: = c ESI Full ms [50.00-500.00]

ESI-MS of compound 3

PROTON CDC13 (D:\cdci) user 44

H NMR spectrum (300 MHz, CDCl3) of compound 3
Chapter 5 Synthesis of 16-dehydropregnenolone derivatives and their biological activity

PROTON CDCl₃ [D/dedr] user 18

1H NMR (300 MHz, CDCl₃) spectrum of compound 4

13C NMR spectrum (75 MHz, CDCl₃) of compound 4
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ESI-MS of compound 4

ESI-MS of compound 5
Chapter-5  Synthesis of 16-dehydroprogesterone derivatives and their biological activity

![Graph of Relative Abundance vs m/z]

ESI-MS of compound 6

![Graph of 1H NMR spectrum (300 MHz, CDCl₃)]

$^{1}$H NMR (300 MHz, CDCl$_3$) spectrum of compound 6
Chapter 5  Synthesis of 16-dehydropregnenolone derivatives and their biological activity

$^{13}$C NMR spectrum (75 MHz, CDCl$_3$) of compound 6

ESI-MS of compound 7
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**ESI-MS of compound 8**

**ESI-MS of compound 9**
5.5 References:


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