Chapter 2

Base induced synthesis of steroidal and nonsteroidal fused pyrimidines by three-component reaction

2.1 Introduction

Pyrimidines represent a class of nitrogen rich heterocyclic compounds, with two nitrogens at positions 1 and 3 in the diazine ring system. The pyrimidine ring system has wide occurrence in nature[1] as substituted and ring fused compounds and derivatives. In nucleic acids, the types of nucleobases with pyrimidine core are adenine, thymine, cytosine, uracil, and guanine. Pyrimidine ring is also found as main subunit in some vitamins, coenzymes, amino acids like thiamine, alloxan, folic acid, which are very essential for life processes.[2] Some other important pyrimidine derivatives isolated from nature[3] are orotic acid, 5-methylcytosine, lathyrine, bacimethrin and sparsomycin (Figure 2.1).

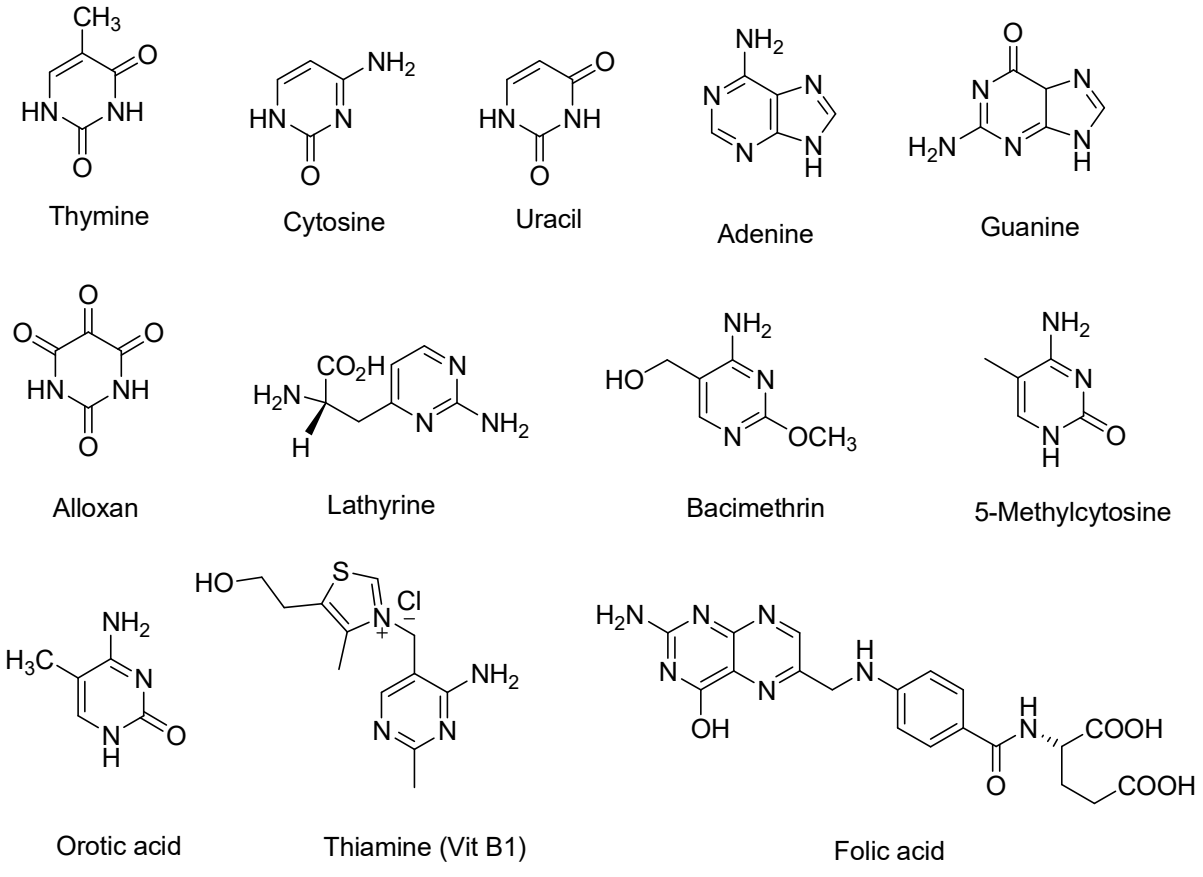


Figure 2.1 Examples of naturally occuring pyrimidine derivatives

Several therapeutically important synthetic molecules are found to have pyrimidine core besides naturally occurring derivatives. Pharmacophores based upon the pyrimidine structure finds immense importance in modern day medicinal chemistry as they possess numerous biological activities.[4-6]

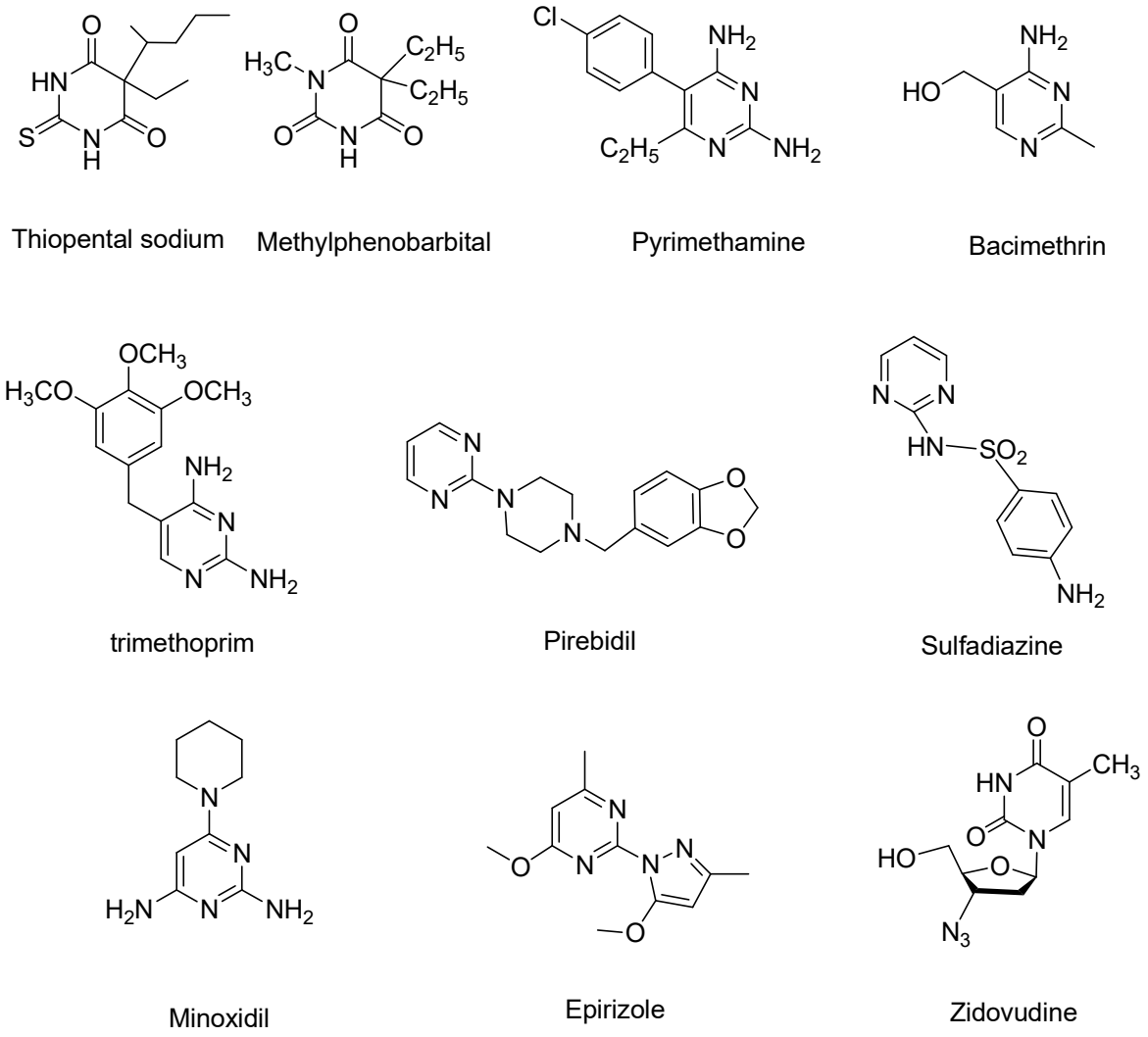
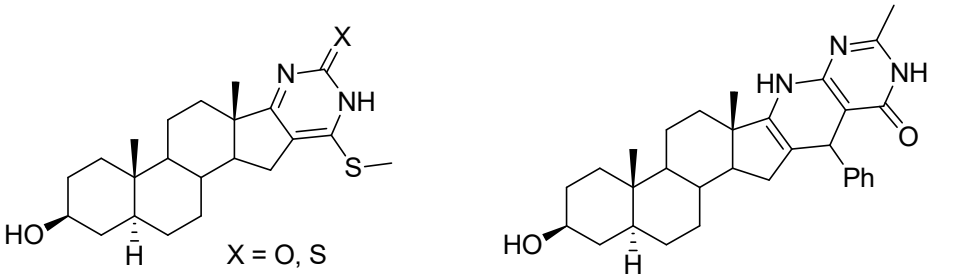


Figure 2.2 Some therapeutically important synthetic pyrimidine molecules

The above figure depicts some therapeutically important compounds bearing pyrimidine subunit such as the antibacterial bacimethrin, dopamine receptor stimulant pirebidil, the COX-2 inhibitor epirizole, general anesthetic thiopental sodium and antiepilepticum methylphenobarbital. Morever, some diaminopyrimidine, such as

pyrimethamine and trimethoprim are powerful antimalarial drugs. Zidovudine acts as anti HIV and minoxidil is used as antihypertensive whereas sulfadiazine is one of the chemotherapeutics containing pyrimidine moiety. Recently, Manohar *et al.* reported the 4-aminoquinoline-pyrimidine hybrids that have better antimalarial activity than standard drug chloroquine against plasmodium falciparum.[7] In an another recent report by Winter and co-workers trichloromethyl Pyrimidine is found to have good antitumoral activity against lymphoblastic leukemia.[8]

Apart from non steroidal pyrimidines, some steroidal pyrimidine derivatives have also come up recently as biologically significant molecules. For instance, the pyrimidino androstane derivatives **I** (Figure 2.3) have shown promising antibacterial activity[9] whereas compound **II** exibited potent antineuroinflammatory activity [10].



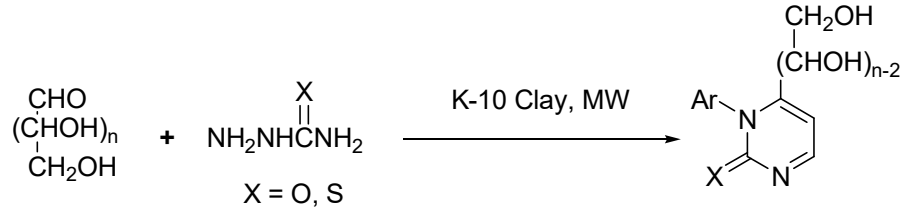
I (Antibacterial) **II** (Antineuroinflammatory agent)

Figure 2.3 Biologically significant steroidal pyrimidine molecules

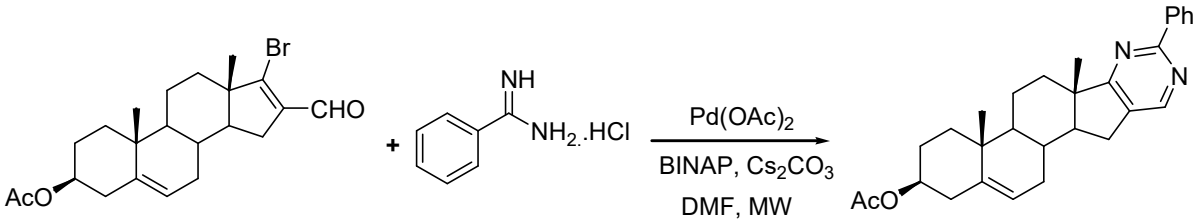
Because of the prevalence of this template in drug discovery, several comprehensive reports of pyrimidine study regarding library synthesis and pharmacological properties have appeared.[11,12] The classical Biginelli reaction[13] is found to be the predominant method for synthesis of pyrimidine core among all the methodology.

Functionalized pyrimidines were synthesized in excellent yields by aza-Michael addition of aromatic amines to aldose-derived 1,3-oxazin-2-ones followed by dehydrative

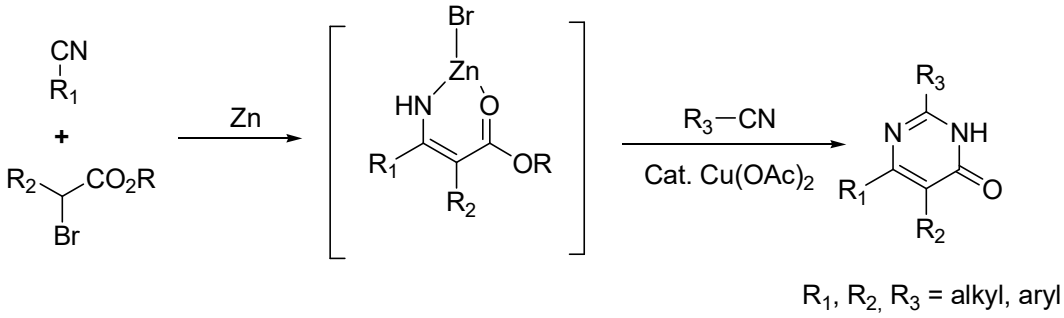
ring transformation. The reaction was proceeded under solvent-free microwave irradiation condition catalysed by Montmorillonite K-10 clay.[14]



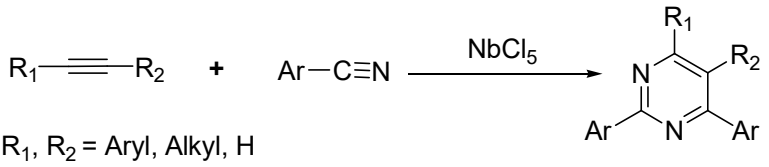
Boruah and co-workers[15] reported a Pd catalysed synthesis of steroidal pyrimidines from *β*-halo-*α,β*-unsaturated aldehydes under microwave irradiation.



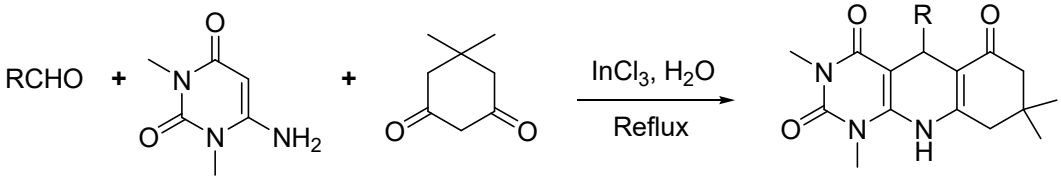
A tandem Blaise/Pinner-type reaction for the synthesis of pyrimidin-4-ones was described by Chun *et al.* The reaction was catalysed by $Cu(OAc)_2$ to afford pyrimidin-4-ones upto 80% yield.[16]



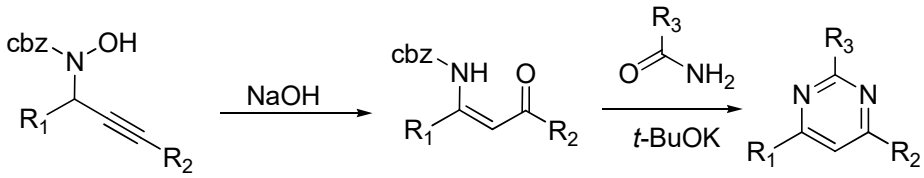
Intermolecular cycloaddition reaction of alkynes with aryl nitriles results substituted pyrimidine derivatives in high yields with excellent chemo- and regioselectivity. The reaction was catalysed by an $NbCl_5$ complex.[17]



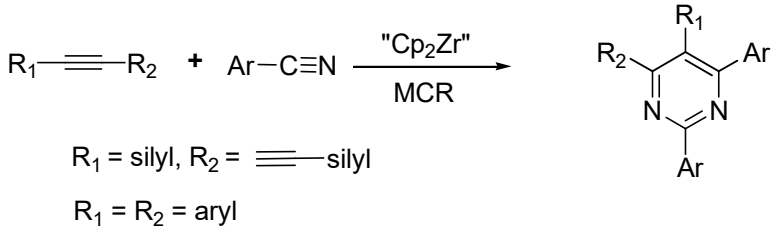
Khurana and co-workers[18] reported the synthesis of variety of pyrimidine derivatives from aldehydes, 1,3-dicarbonyl compounds and electron-rich amino heterocycles catalyzed by indium trichloride in water.



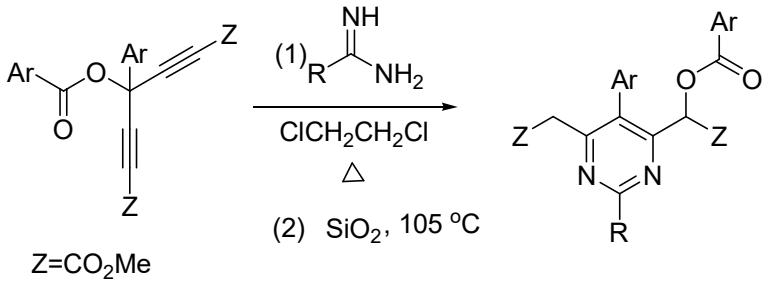
Gayon and co-workers[19] reported the synthesis of a series of pyrimidines from Cbz-protected β-enaminones based on NaOH catalyzed rearrangement of propargylic hydroxylamines.



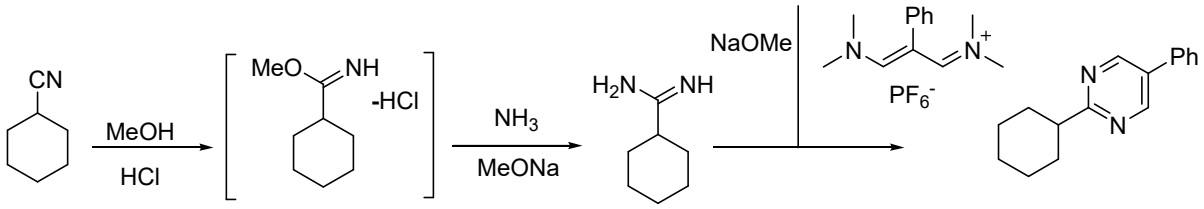
You and co-workers[20] synthesized functionalized pyrimidines by a multicomponent reaction of silylbutadiynes with aryl nitriles catalyzed by Zirconium catalyst.



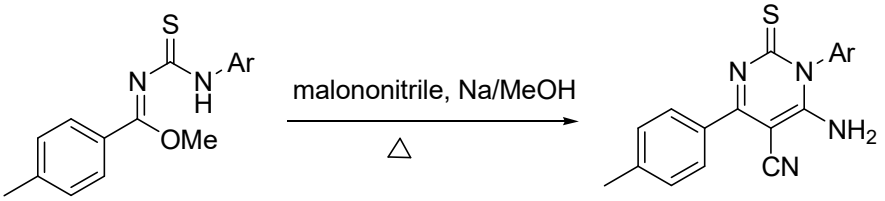
Tejedor *et al.* reported the synthesis of fully substituted pyrimidine derivatives using amidines as the nitrogen source and activated skipped diynes as the electrophilic reagent. The reaction pathway was a coupled domino strategy with aza-Michael addition followed by a [H]-shift and a [3,3]-sigmatropic rearrangement.[21]



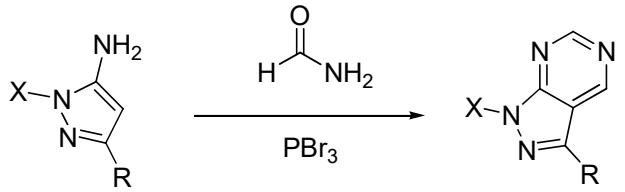
Frutos and his co-workers reported[22] one pot synthesis of 2,5-disubstituted Pyrimidines using nitriles as starting materials.



Najahi *et al.*[23] studied the atropisomerization of *N*-aryl-2(1*H*)-pyrimidin-(thi)ones synthesized by condensation of methyl *N*-(aminothiocarbonyl) imidates and malononitrile.



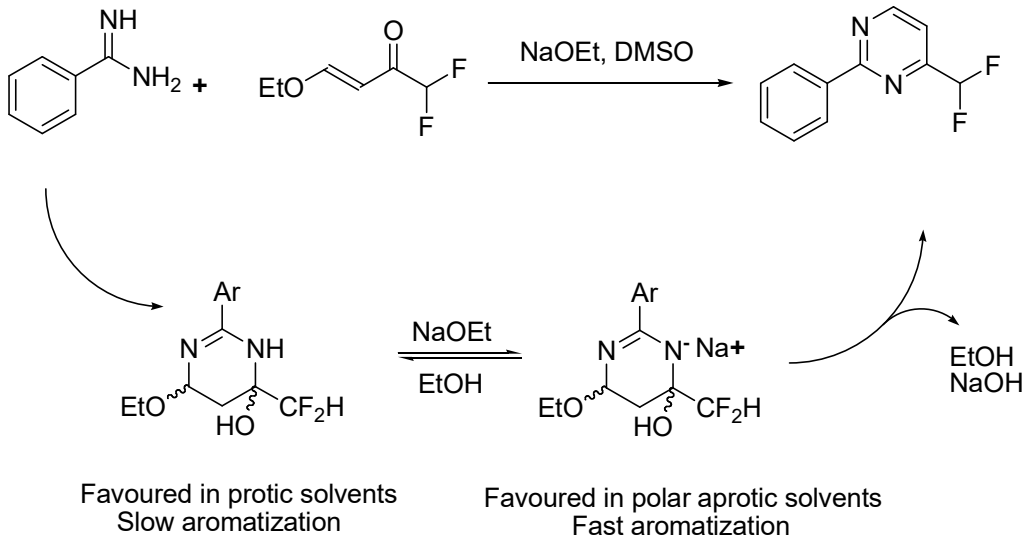
Wong and co-workers[24] synthesized heteroaromatic-fused pyrimidine derivatives by reacting heterocyclic substrates with formamide in the presence of PBr_3. The reaction was thought to be proceeded through three sequential steps *viz* amidination, electrophilic substitution imination and oxidative cyclization reaction.



X = aryl, 2-pyridinyl, 2-quinolinyl

R = Me, *t*-Bu, Ph, *p*-Me-Ph, *p*-Cl-Ph,

Recently, in a report by Fandrick and co-workers, the rate limiting aromatization step was addressed for pyrimidine synthesis (Scheme 2.12). Utilizing amidines and activated olefins as starting materials a strong solvent effect was elucidated for the reaction.[25]



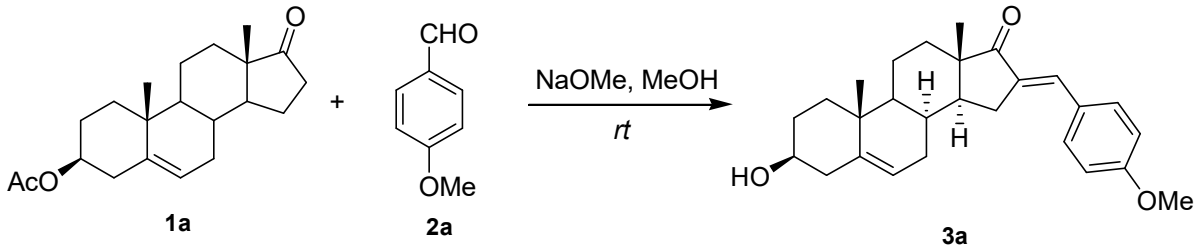
From the above discussion, it is noteworthy to mention that the pyrimidines constitute an interesting aza-heterocyclic class of compounds. New methodologies for pyrimidine ring construction are always important and their synthesis remains an active research area for organic chemist.

2.2 Results and Discussions

In this chapter a convenient preparation of A- and D-ring fused steroidal pyrimidines from the reaction of steroidal *α,β*-unsaturated ketone with different amidine is discussed. In this context, steroidal *α,β*-unsaturated ketones were prepared from corresponding steroidal ketones.

Preparation of steroidal *α,β*-unsaturated ketones:

The initial effort was directed towards developing a suitable method for the synthesis of steroidal *α,β*-unsaturated ketone. 3*β*-Acetoxy-5-en-androst-17-one (**1a**) and benzaldehyde (**2a**) were selected as model substrates for the Knoevenagel reaction to yield 16-benzylidine ketone (**3a**) (Scheme 2.1).



Scheme 2.1

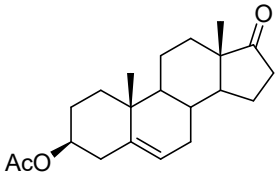
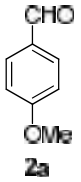
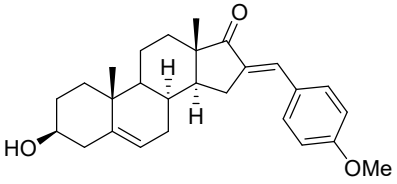
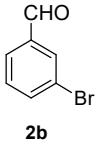
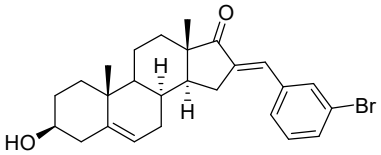
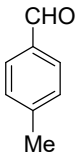
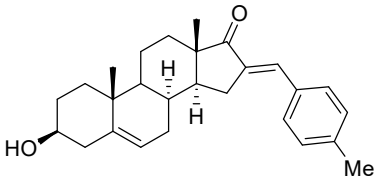
The structure of compound **3a** was confirmed by ^{1}H NMR, ^{13}C NMR and mass spectrometric analysis. The ^{1}H NMR of compound **3a** exhibited two characteristic aromatic doublet signals at δ 6.95 (d, J = 8.7 Hz, 2H) and 7.51 (d, J = 8.7 Hz, 2H) and a singlet at δ 7.40 (s, 1H). The ^{1}H NMR also showed a signal at δ 3.85 (s, 3H) for the methoxy protons.

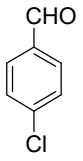
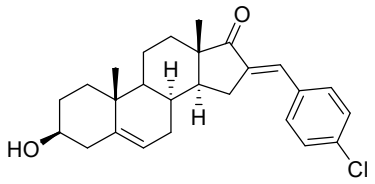
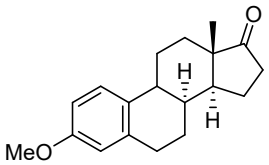
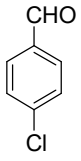
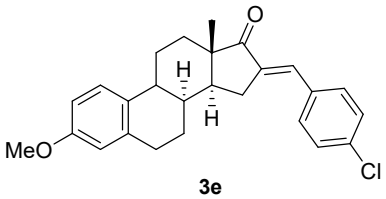
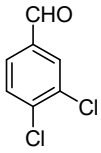
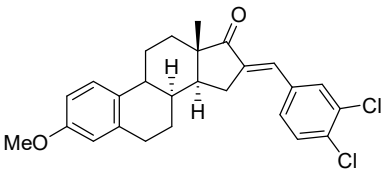
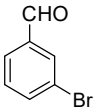
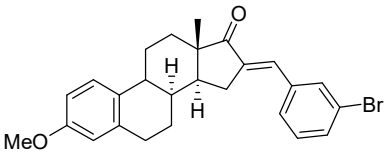
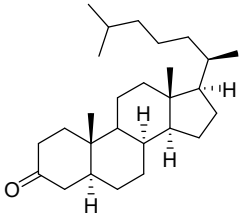
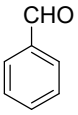
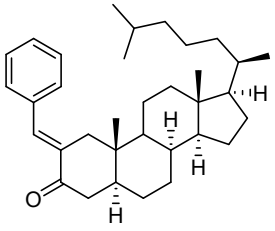
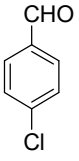
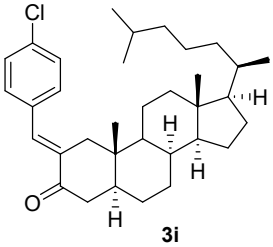
The ^{13}C NMR spectrum showed the presence of one carbonyl carbons at δ 209.8 and ten olefinic carbons at δ 114.2 (2C), 120.8, 128.3, 132.1 (2C), 132.9, 133.6, 141.2, 160.5. The mass spectra showed a strong molecular ion peak at m/z 406 $[M]^+$.

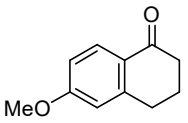
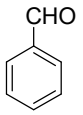
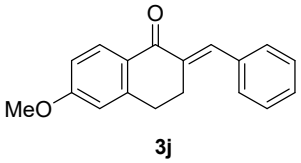
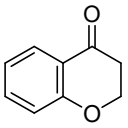
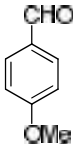
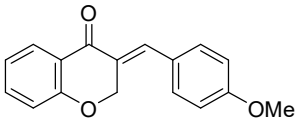
The scope of the reaction was then investigated by employing variety of aldehydes having both electron-deficient and electron-rich groups. Similarly *α,β*-unsaturated ketones in A-ring of the steroid were prepared, characterized and also extended to non-steroidal derivatives.

The results of this study are summarised in Table 2.1. In all cases, the products obtained were characterized by various spectroscopic means such as NMR, IR and mass spectrometric analysis.

Table 2.1 Steroidal and non steroidal benzylidine ketone **3a-k**

Entry	Ketone	Aldehyde	Product	Yield(%)[a]
1	 **1a**	 **2a**	 **3a**	80
2	**1a**	 **2b**	 **3b**	75
3	**1a**	 **2c**	 **3c**	85

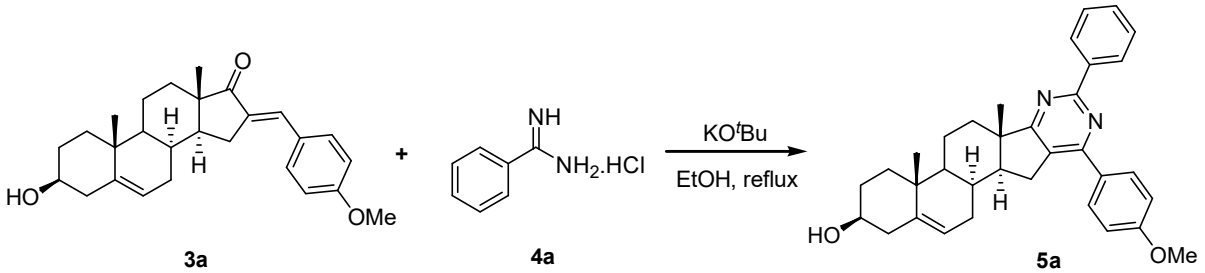
4	**1a**	 **2e**	 **3d**	82
5	 **1b**	 **2e**	 **3e**	75
6	**1b**	 **2f**	 **3f**	70
7	**1b**	 **2b**	 **3g**	75
8	 **1c**	 **2g**	 **3h**	70
9	**1c**	 **2e**	 **3i**	68

10	 **1d**	 **2g**	 **3j**	85
11	 **1e**	 **2a**	 **3k**	82

[a]Yield of the isolated product.

Preparation of steroidal pyrimidines from *α,β*-unsaturated ketones:

The steroidal pyrimidine derivatives have been prepared by exploring the reaction of steroidal *α,β*-unsaturated ketone **3a** with benzimidine (**4a**) (Scheme 2.2). Accordingly, the reaction was performed by refluxing a mixture of ketone **3a** and benzimidine (**4a**) in ethanol in presence of base potassium tertiary butoxide for five hours.



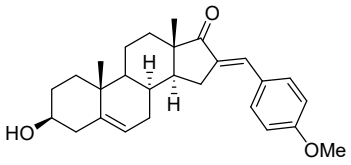
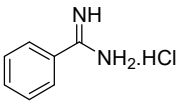
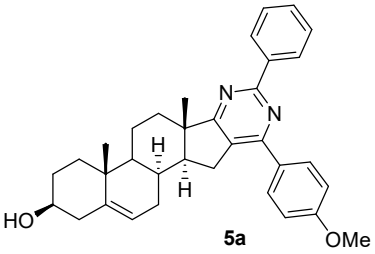
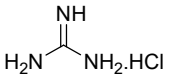
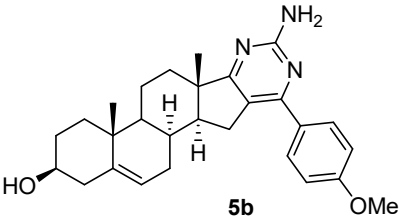
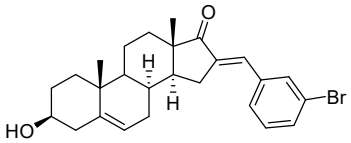
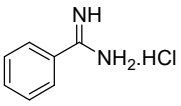
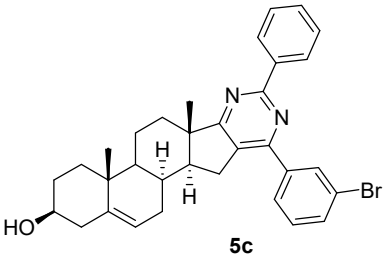
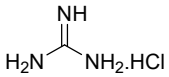
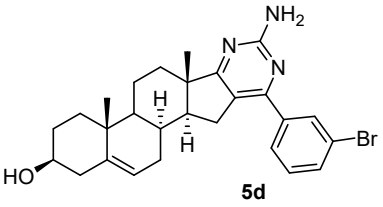
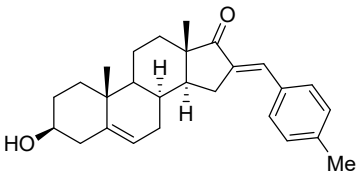
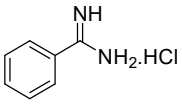
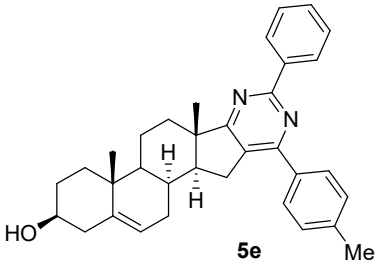
Scheme 2.2

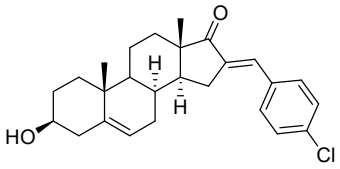
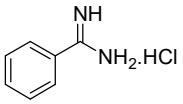
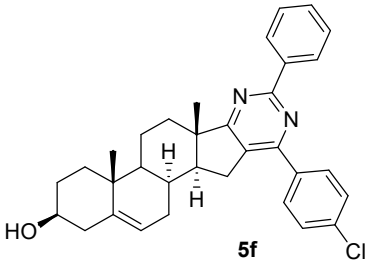
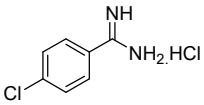
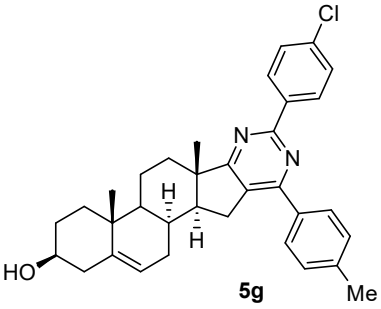
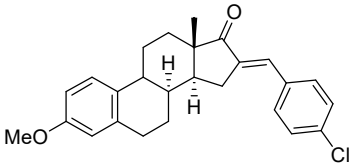
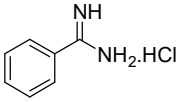
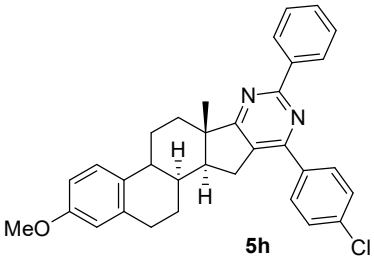
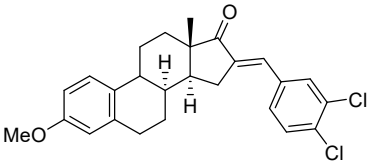
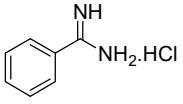
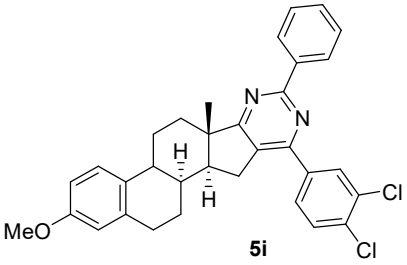
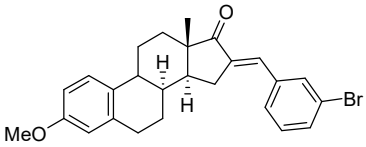
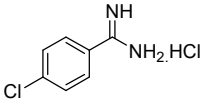
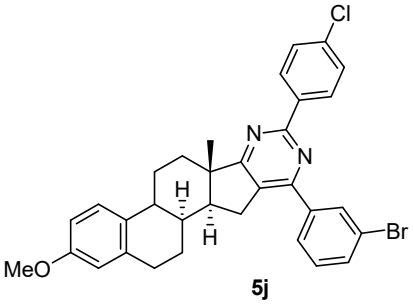
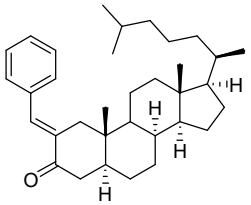
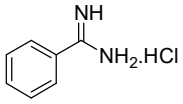
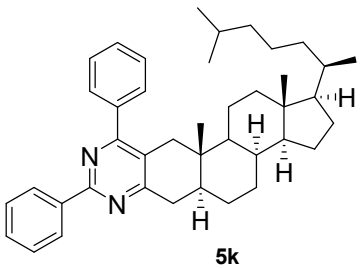
The product **5a** was obtained in 75% yield as white solid and characterized by ^{1}H NMR, ^{13}C NMR and mass spectral data. The ^{1}H NMR of compound **5a** exhibited three characteristic aromatic doublet signals at δ 7.05 (*J* = 8.7 Hz, 2H), 8.05 (*J* = 8.7 Hz, 2H), 8.57 (*J* = 7.9 Hz, 2H) and a multiplet at δ 7.46-7.50 (3H). The ^{1}H NMR also showed a singlet signal at δ 3.90 (s, 3H) for the methoxy protons. The ^{13}C NMR spectrum of **5a** showed eleven signals in the aromatic region at δ 113.9, 120.9, 127.3, 128.3, 128.7, 130.1, 130.3, 130.5,

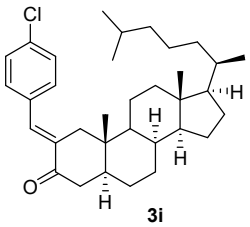
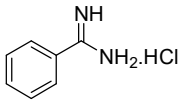
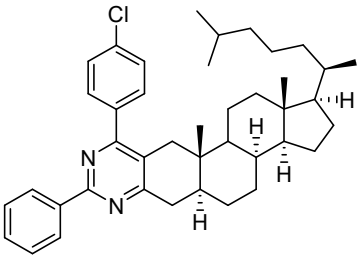
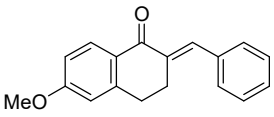
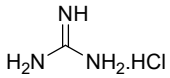
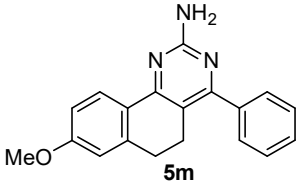
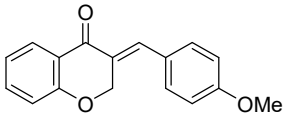
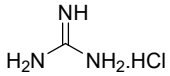
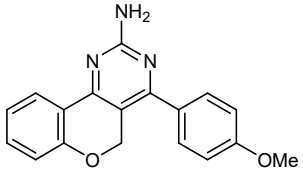
138.4, 141.3 and 161.1. The ESI mass spectra showed a sharp $[M+1]^+$ molecular ion peak at m/z = 507, which finally confirmed the formation of compound **5a**.

Comparative study on different bases such as KO^{t}Bu, NaOMe, NaH and KOH showed that KO^{t}Bu was the best base to perform this multi-component reaction to afford the pyrimidine derivative **5a**. When NaOMe, NaH and KOH were used in place of KO^{t}Bu, yield of **5a** was obtained 35%, 41% and 27%, respectively. The reaction was also performed with other amidine derivative and amidine analogues. For example, the reaction of α,β-unsaturated ketone (**3a**) and guanidine hydrochloride (**4b**) provided 74% yield of steroidal pyrimidine derivative **5b** (Entry 2, Table 2.2), whereas ketone **3d** and 4-chlorobenzamidine hydrochloride (**4c**) provided 70% yield of pyrimidine derivative **5g** (Entry 7, Table 2.2). Furthermore, the reaction was performed with 3-methyl ether derivative of estrone (**3e-g**) with amidine derivatives **4a** and **4c** under the above reaction conditions to obtain steroidal pyrimidines **5h-j** in 70-75% yields (Entries 8-10, Table 2.2). Similarly, reaction of steroidal A-ring ketone cholestanone (**3h and 3i**), with benzamidine hydrochloride (**4a**) afforded pyrimidines fused in A-ring of steroid (**5k-l**, 68-70%, Entries 11-12, Table 2.2). Reaction of nonsteroidal ketone **3j** with guanidine hydrochloride (**4b**) provided nonsteroidal pyrimidine **5m** in 80% yield (Entry 13, Table 2.2). Similar reaction of nonsteroidal ketone **3k** with guanidine hydrochloride (**4b**) provided nonsteroidal pyrimidine **5n** in 82% yield (Entry 14, Table 2.2).

Table 2.2 Steroidal and non steroidal pyrimidines **5a-n**

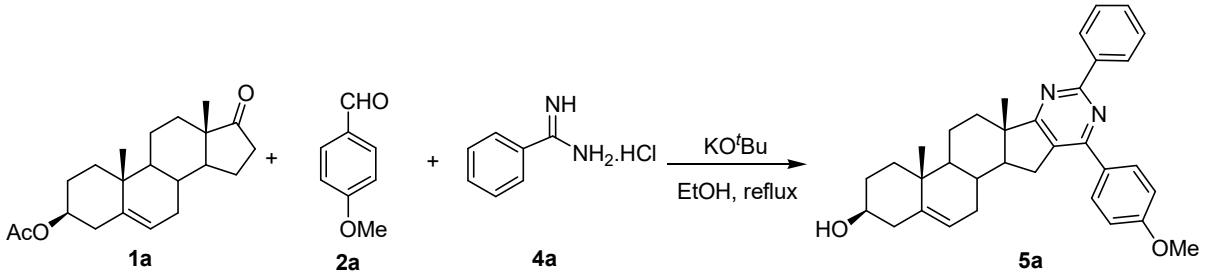
Entry	Ketone	Amidine	Product	Yield (%)[a]
1	 **3a**	 **4a**	 **5a**	75
2	**3a**	 **4b**	 **5b**	74
3	 **3b**	 **4a**	 **5c**	72
4	**3b**	 **4b**	 **5d**	72
5	 **3c**	 **4a**	 **5e**	70

6	 **3d**	 **4a**	 **5f**	73
7	**3d**	 **4c**	 **5g**	70
8	 **3e**	 **4a**	 **5h**	70
9	 **3f**	 **4a**	 **5i**	75
10	 **3g**	 **4c**	 **5j**	71
11	 **3h**	 **4a**	 **5k**	70

12	 **3i**	 **4a**	 **5l**	68
13	 **3j**	 **4b**	 **5m**	80
14	 **3k**	 **4b**	 **5n**	82

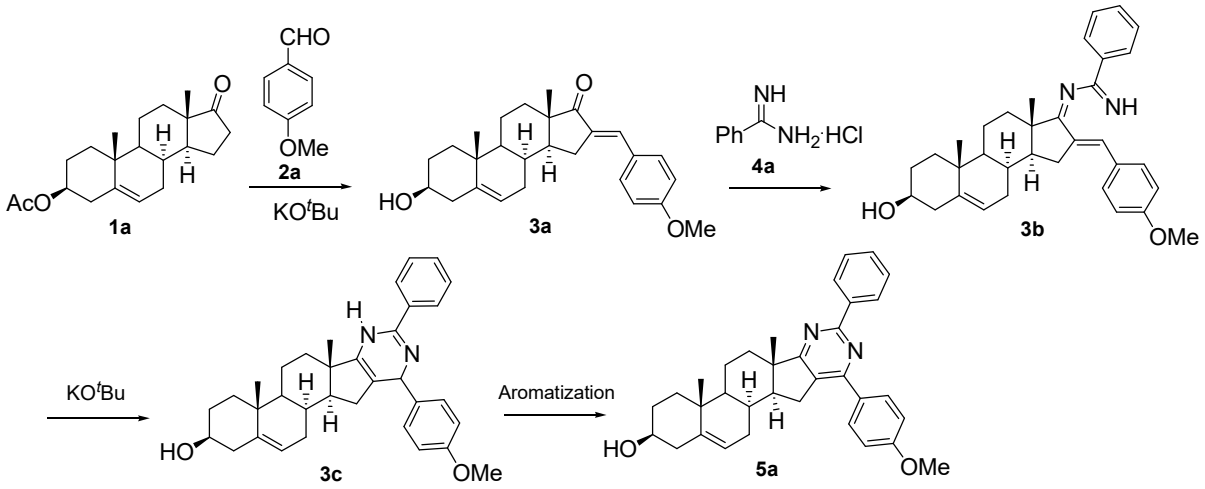
[a]Yield of the isolated product.

After having the product **5a**, the reaction was tried in multi-componenet fashion, without isolating the *α*,*β*-unsaturated ketone intermediate **3a** (Scheme 2.3). First, ketone **1a** and aldehyde **2a** in ethanol were refluxed for half an hour in presence of base potassium tertiary butoxide. After that, amidine **4a** was added to the reaction mixture and refluxed for another five hours. Formation of desired pyrimidine derivative was observed by comparing TLC with authentic compound **5a** and confirmed by ^{1}H NMR, ^{13}C NMR and mass spectral data which was same as **5a**.



Scheme 2.3

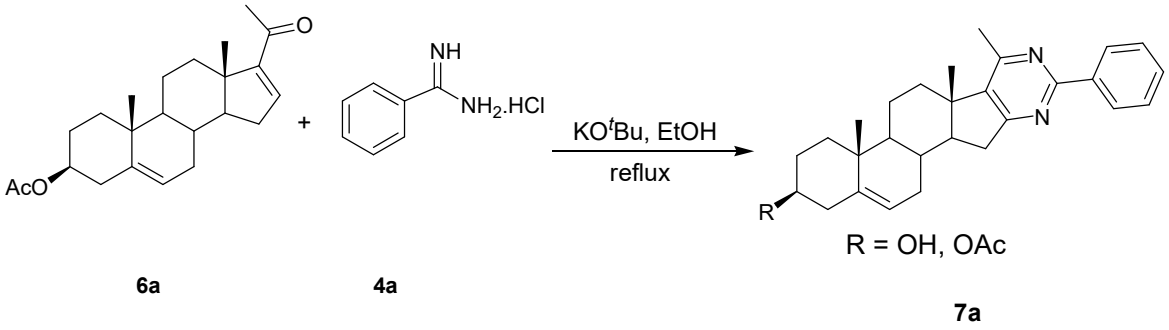
A probable mechanism for the formation of aryl substituted pyrimidine derivative **5a** is shown (Scheme 2.4). Initially, ketone **1a** undergoes base catalyzed condensation with aldehyde **2a** to give intermediate 16-benzylidene ketone **3a**. The intermediate **3a** then reacts with benzamidine **4a** to produce the imine intermediate **3b**. Deprotonation of the imine under basic reaction conditions followed by intramolecular aza-Michael addition and aromatisation of the Michael adduct afforded the desired product **5a**.



Scheme 2.4

Apart from preparing benzylidine ketone, 16-dehydropregnanolone acetate (16-DPA) and 1-acetylcyclohexene were also employed directly as *α,β*-unsaturated ketone source for the preparation of steroidal and non-steroidal aryl substituted pyrimidines. Focusing on minimum synthetic steps a library of pyrimidine compounds were synthesised in good yield under same reaction condition.

The reaction of 16-DPA (**6a**) and benzamidine hydrochloride (**4a**) afforded pyrimidine derivative **7a** as shown in Scheme 2.5.

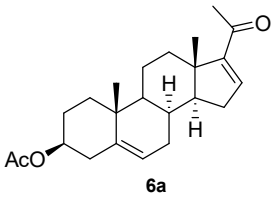
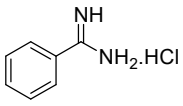
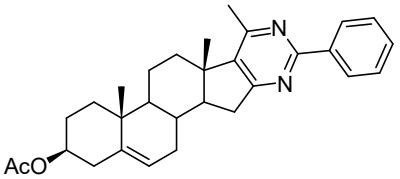
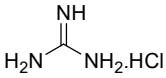
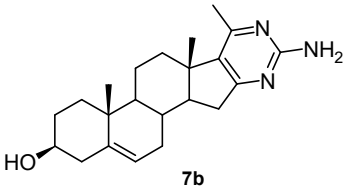
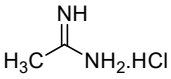
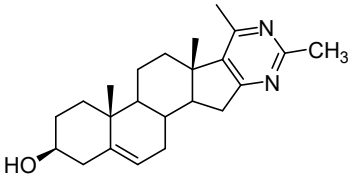
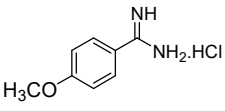
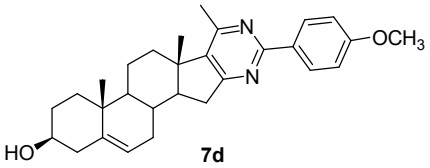
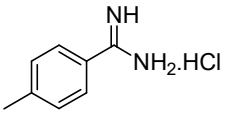
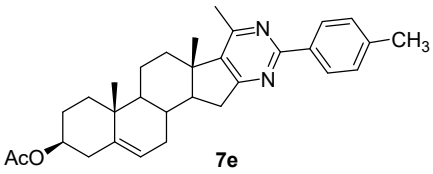
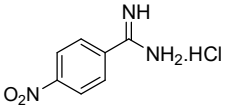
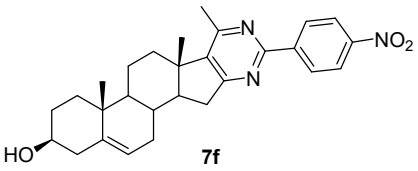
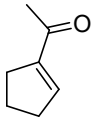
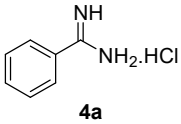
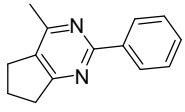


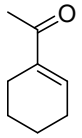
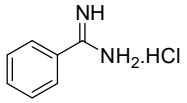
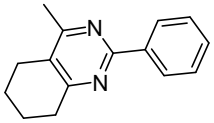
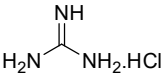
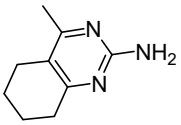
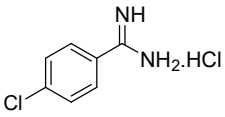
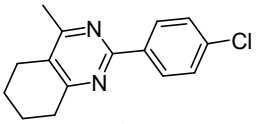
6a **4a** **7a**

Scheme 2.5

The product **7a** was identified and characterized by ^{1}H NMR, ^{13}C NMR and mass spectral data. The ^{1}H NMR of compound **7a** exhibited a characteristic aromatic doublet signals at δ 7.46 (d, *J* = 5.46 Hz, 2H), and a multiplet at δ 8.39-8.42 (m, 2H). The ^{1}H NMR also showed a singlet signal at δ 2.18 (s, 3H) for the methyl protons. The ^{13}C NMR spectrum of **5a** showed nine signals for twelve olefinic carbon at δ 115.4, 121.9, 128.2 (2C), 128.5 (2C), 129.6, 130.3, 139.9, 160.3 (2C), 170.6. The ESI mass spectra showed a sharp $[M+1]^{+}$ molecular ion peak at m/z = 457 which finally confirmed the formation of compound **7a**. The other generalized products are summarised in Table 2.3. In all cases, the product obtained was characterized by various spectroscopic means such as NMR, IR and mass spectrometric analysis.

Table 2.3 Synthesis of Steroidal and non steroidal pyrimidines derivatives **7a–j**

Entry	Ketone	Amidine	Product	Yield (%)[a]
1	 **6a**	 **4a**	 **7a**	78
2	**6a**	 **4b**	 **7b**	80
3	**6a**	 **4d**	 **7c**	75
4	**6a**	 **4e**	 **7d**	78
5	**6a**	 **4f**	 **7e**	80
6	**6a**	 **4g**	 **7f**	75
7	 **6b**	 **4a**	 **7g**	78

8	 **6c**	 **4a**	 **7h**	80
9	**6c**	 **4b**	 **7i**	78
10	**6c**	 **4h**	 **7j**	80

[a]Yield of the isolated product.

2.3 Conclusion

In conclusion, an efficient methodology is developed for the facile synthesis of fused steroidal/nonsteroidal pyrimidines by reacting *α,β*-unsaturated ketone with amidine derivatives. The methodology is simple, efficient and high yielding and represents a new preparation of steroidal as well as non-steroidal aryl substituted pyrimidines using easily available *α,β*-unsaturated ketone as starting material. This protocol can be utilized as an effective alternative method for the synthesis of aryl substituted pyrimidine derivatives.

2.4 Experimental

General experimental Procedure

Melting points were measured with a Buchi B-540 melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer FT-IR-2000 spectrometer. NMR spectra were recorded on Bruker Avance DPX 300 MHz FT-NMR spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on Trace DSQ GC-MS instrument or Bruker ESQUIRE 3000 LCMS instrument. All the commercially available reagents were used as received. All experiments were monitored by thin layer

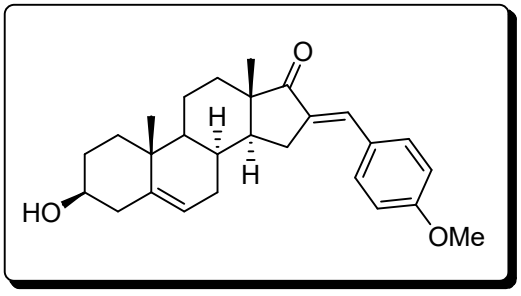
chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck). Column chromatography was performed on silica gel (100-200 mesh, Merck) using ethyl acetate: hexane as eluent.

(a) Preparation and characterization of α,β-unsaturated ketone

To a stirred solution of ketone (**1**, 1.0 mmol) in ethanol 2.0 mmol of sodium methoxide was added at room temperature. After formation of a turbid solution, aldehyde (**2**, 1.0 mmol) was added slowly to the reaction mixture and then the reaction mixture was stirred for another 8 hours. On completion of the reaction (*vide* TLC), the solvent was removed from the reaction mixture, treated with water (50 mL) and extracted with dichloromethane (30 mL × 3). The organic portion was washed with water, dried over anhydrous sodium sulfate and the solvent was removed in vacuo to obtain the product **3** as white solid in 80% yield with R_f value of 0.6-0.8(10 % EtOAc in hexane).

Characterization of 16-benzylidine ketone (3)

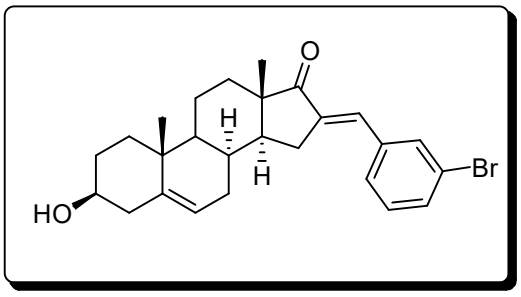
3β-Hydroxy-16-(*p*-OMe-benzylidene)androst-17-one (3a)



White solid, Yield 80%; m.p. 213-216 °C; IR ($CHCl_3$, cm^{-1}): 3415, 2934, 2858, 1709, 1624, 1601, 1511, 1440, 1255, 1175, 1095, 831, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.97 (s, 3H), 1.07(s, 3H), 1.09-2.85 (m, 18H), 3.53 (s, 1H), 3.85 (s, 3H), 5.40 (s, 1H), 6.95 (d, J = 8.7 Hz, 2H), 7.40 (s, 1H), 7.51 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.3, 19.5, 20.4,

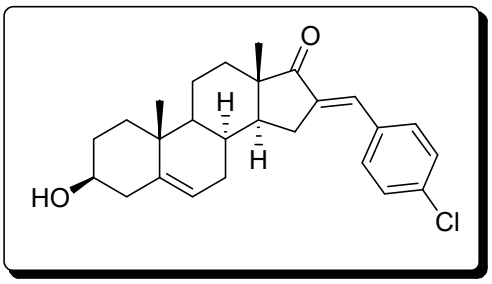
29.3, 30.9, 31.2, 31.6, 36.7, 37.1, 42.2, 47.3, 49.9, 50.4, 55.4, 71.6, 114.2, 120.8, 128.3, 132.1, 132.9, 133.6, 141.2, 160.5, 209.8; MS (GCMS, *m/z*) = 406 $[M]^+$.

3*β*-Hydroxy-16-(*m*-bromo-benzylidene)androst-17-one (3b)



White solid, Yield 75%; m.p. 175-179 °C; IR ($CHCl_3$, cm^{-1}): 3414, 2932, 2856, 1718, 1628, 1559, 1471, 1374, 1277, 1086, 1010, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.98 (s, 3H), 1.07 (s, 3H), 1.08-2.87 (m, 17H), 3.55 (s, 1H), 5.40 (s, 1H), 7.27-7.74 (m, 5H), 7.66 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.2, 19.5, 20.4, 29.2, 30.9, 31.2, 31.6, 36.7, 37.1, 42.2, 47.4, 49.8, 50.3, 71.6, 120.7, 122.8, 128.8, 130.2, 131.4, 132.0, 132.8, 137.3, 137.7, 141.2, 209.3; MS (GCMS, *m/z*) = 450 $[M]^+$.

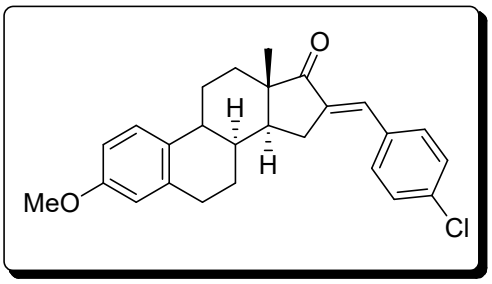
3*β*-Hydroxy-16-(*p*-chloro-benzylidene)androst-17-one (3d)



White solid, Yield 82%; m.p. 209-214 °C; IR ($CHCl_3$, cm^{-1}): 3231, 2930, 2856, 1712, 1630, 1590, 1491, 1376, 1090, 1064, 1010, 826, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.98 (s, 3H), 1.07(s, 3H), 0.88-2.88 (m, 18H), 3.54 (s, 1H), 5.40 (s, 1H), 7.26-7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.2, 19.5, 20.4, 29.3, 30.9, 31.2, 31.5, 31.6, 36.7, 37.1, 42.2, 47.4, 49.8,

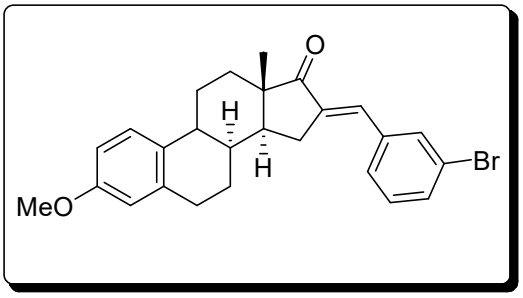
50.3, 71.6, 120.7, 128.9, 131.4, 131.7, 134.1, 135.1, 136.5, 141.2, 209.4; MS (GCMS, *m/z*) = 410 $[M]^+$.

3-Methoxy-16-(*p*-chloro-benzylidene)-estra-1,3,5-triene-17-one (3e)



Yellow solid, Yield 75%; m.p. 165-168 °C; IR ($CHCl_3$, cm^{-1}): 2932, 2858, 1717, 1631, 1611, 1492, 1372, 1256, 1092, 1039, 1012, 993, 825, 756; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.99 (s, 3H), 1.47-2.96 (m, 13H), 3.76 (s, 3H), 6.66 (s, 1H), 6.72 (d, *J* = 2.6 Hz, 1H), 6.75 (d, *J* = 2.6 Hz, 1H), 7.21-7.50 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.5, 25.9, 26.8, 29.1, 29.6, 31.7, 37.9, 44.1, 47.9, 48.5, 55.2, 111.6, 113.9, 126.3, 128.9, 131.4, 131.8,131.9, 134.1, 135.2, 136.5, 137.6, 157.6, 209.3; MS (GCMS, *m/z*) = 406 $[M]^+$.

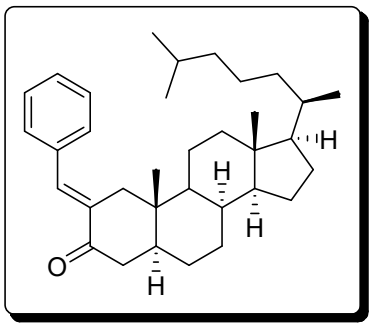
3-Methoxy-16-(*m*-bromo-benzylidene)-estra-1,3,5-triene-17-one (3g)



Yellow solid, Yield 75%; m.p. 154-157 °C; IR ($CHCl_3$, cm^{-1}): 2932, 2858, 1718, 1629, 1610, 1558, 1499, 1256, 1082, 1052, 995, 785, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.99 (s, 3H), 1.21-2.97 (m, 1H), 3.78 (s, 3H), 6.66 (s, 1H), 6.72 (d, *J* = 2.6 Hz, 1H), 6.75 (d, *J* = 2.6 Hz, 1H), 7.22-7.54 (m, 4H), 7.68 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.5, 25.9, 26.8, 28.9,

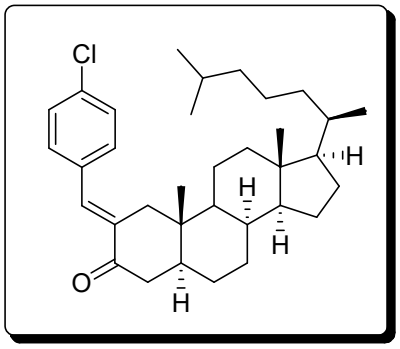
29.6, 31.7, 37.9, 44.1, 47.9, 48.5, 55.2, 111.6, 113.9, 122.3, 126.3, 128.9, 130.2, 131.5, 131.9, 132.0, 132.7, 137.4, 137.6, 137.8, 157.7, 209.2; MS (GCMS, *m/z*) = 450$[M]^+$.

2-Benzylidenecholestan-3-one (3h)



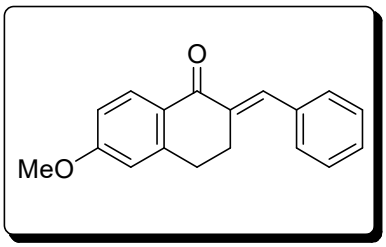
Light yellow solid, Yield 70%; m.p. 109-110 ^{0}C; IR ($CHCl_3$, cm^{-1}) 2929, 1678, 1445, 1192, 696; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.64-2.49 (m, 42H), 3.08-3.13 (d, 2H), 7.26 (s, 1H), 7.28-7.60 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.8, 12.0, 18.7, 21.4, 22.8, 23.8, 24.3, 28.3, 28.7, 31.5, 35.4, 35.8, 35.9, 36.2, 39.5, 39.9, 42.4, 42.8, 53.6, 56.4, 66.4, 66.7, 128.4, 128.6, 128.9, 129.6, 129.7, 135.4, 135.7, 137.1, 201.5; MS (GCMS, *m/z*) 474 $[M]^+$.

2-(*p*-Chloro-Benzylidene)-cholestan-3-one (3i)



Yellow solid, Yield 68%; m.p. 113-114 °C, IR ($CHCl_3$, cm^{-1}): 2929, 1676, 1442, 1190, 695; ^{1}H NMR ($CDCl_3$, 300 MHz): 0.65-2.41 (m, 42H), 3.00-3.05 (d, 2H), 7.26 (s, 1H), 7.28-7.54 (m, 4H);^{13}C NMR ($CDCl_3$, 75 MHz): 11.8, 11.9, 18.7, 22.6, 22.8, 23.8, 24.2, 28.0, 28.2, 28.7, 35.4, 35.8, 35.9, 36.2, 39.5, 39.9, 42.4, 42.5, 42.8, 53.6, 56.3, 128.6, 131.5, 134.2, 135.7, 136.1, 201.1; MS (GCMS, *m/z*) = 508 $[M]^+$.

2-Benzylidene-3,4-dihydro-6-methoxynaphthalen-1(2*H*)-one (3j)



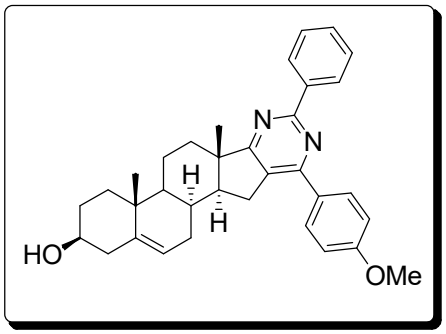
White solid, Yield 85%; m.p. 95-99 °C; IR ($CHCl_3$, cm^{-1}): 2942, 1667, 1493, 1186, 952, 770; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.88-2.93 (m, 2H), 3.08-3.12 (m, 2H), 3.86 (s, 3H), 6.70 (s, 1H), 6.87(d, *J* = 7.9 Hz, 1H), 7.25-7.42 (m, 5H), 7.68 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 23.4, 27.2, 29.3, 30.2, 38.9, 55.5, 112.3, 113.4, 127.0, 128.4, 129.8, 130.8, 135.6, 135.9, 145.8, 163.6, 186.8, 197.2; MS (GCMS, *m/z*) = 264 $[M]^+$.

(b) Preparation and characterization of pyrimidines from α,β-unsaturated ketone:

To a solution of benzylidine ketone (**3**, 1.0 mmol) in ethanol, 1.0 mmol of amidine hydrochloride (**4**) and 2.0 mmol of potassium tertiary butoxide was added and the reaction mixture was allowed to reflux slowly. On completion of the reaction (*vide* TLC), the solvent was removed from the reaction mixture, treated with water (50 mL) and extracted with dichloromethane (30 mL × 3). The organic portion was washed with water, dried over anhydrous sodium sulphate. The solvent was removed in vacuo to obtain the crude mixture which was further purified by silica gel column chromatography using EtOAc/hexane (2:3) as the eluant. The purified product **5** was obtained in good yield with R_f value of 0.3-0.4.

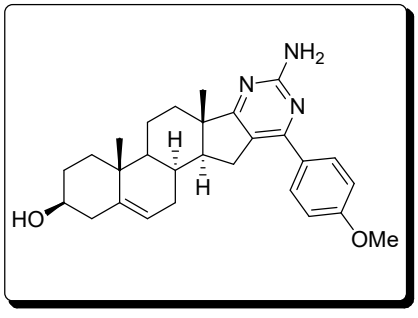
Characterization of pyrimidines (5)

3*β*-Hydroxy-2'-(phenyl)-4'-(*p*-methoxyphenyl)-androst-[16,17-*e*]pyrimidine (5a)



Yellow solid, Yield 75%; m.p. 151-153 °C; IR ($CHCl_3$, cm^{-1}): 3383, 2924, 1585, 1509, 1376, 1251, 1038, 770; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.13 (s, 3H), 1.15 (s, 3H), 0.80-2.95 (m, 17H), 3.45-3.60 (m, 1H), 3.90 (s, 3H), 5.35-5.42 (m, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 7.46-7.50 (m, 3H), 8.05 (d, *J* = 8.7 Hz, 2H), 8.57 (d, *J* = 7.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 17.0, 19.5, 20.6, 22.7, 29.0, 29.2, 29.4, 30.8, 31.0, 31.4, 31.6, 31.9, 33.2, 36.8, 37.2, 42.3, 45.9, 50.7, 55.4, 55.8, 71.6, 113.9, 120.9, 127.3, 128.3, 128.7, 130.1, 130.3, 130.5, 138.4, 141.3, 161.1; MS (ESI, m/z) = 507 $[M+1]^+$. Anal. calcd. for $C_{34}H_{38}N_2O_2$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.60; H, 7.48; N, 5.29.

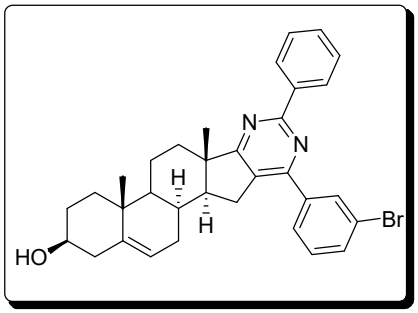
3*β*-Hydroxy-2'-amino-4'-(*p*-methoxyphenyl)-androst-[16,17-*e*]pyrimidine (5b)



Yellow solid, Yield 74%; m.p. 155-158 °C; IR ($CHCl_3$, cm^{-1}): 3384, 2933, 1602, 1512, 1377, 1254, 1033, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.98 (s, 3H), 1.08 (s, 3H), 0.85-2.95 (m, 17H), 3.45-3.58 (m, 1H), 3.85 (s, 3H), 5.35-5.45 (m, 1H), 6.94 (d, *J* = 8.7 Hz, 2H), 7.41 (s,

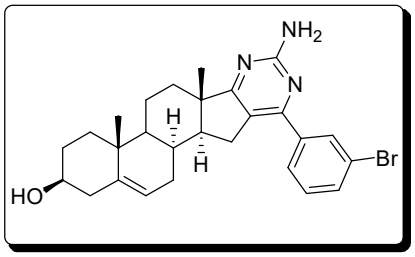
2H), 7.51 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.3, 16.8, 19.4, 20.5, 30.1, 30.7, 30.9, 31.1, 31.2, 31.6, 32.8, 36.7, 37.1, 42.2, 46.0, 47.3, 50.5, 55.4, 55.5, 71.5, 114.1,114.2, 120.8, 128.2, 130.2, 132.9, 141.3, 161.4; MS (ESI, m/z) = 446 $[M+1]^+$. Anal. calcd. for $C_{28}H_{35}N_3O_2$: C, 75.47; H, 7.92; N, 9.43. Found: C, 75.28; H, 7.65; N, 9.43.

3*β*-Hydroxy-2'-(phenyl)-4'-(*m*-bromophenyl)-androst-[16,17-*e*]pyrimidine (5c)



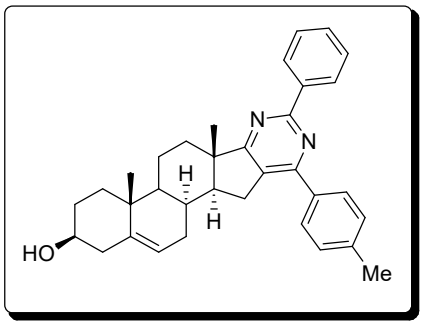
Yellow solid, Yield 72%; m.p. 127-129 °C; IR ($CHCl_3$, cm^{-1}): 3392, 2927, 1547, 1376, 1053, 771; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.13 (s, 3H), 1.15 (s, 3H), 0.85-2.90 (m, 17H), 3.45-3.58 (m, 1H), 5.32-5.42 (m, 1H), 7.48 (m, 3H), 7.92 (d, *J* = 7.7 Hz, 2H), 8.04 (d, *J* = 6.5 Hz, 2H), 8.20 (s, 1H), 8.56 (d, *J* = 9.01 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 17.0, 19.5, 20.5, 29.7, 30.6, 30.9, 31.4, 31.6, 33.2, 36.8, 37.2, 42.3, 45.9, 50.7, 55.8, 71.6, 120.9, 122.8, 128.3, 128.4, 128.5, 128.8, 129.9, 130.3, 131.7, 138.2, 140.1, 141.3, 163.0; MS (ESI, m/z) = 555 $[M+1]^+$. Anal. calcd. for $C_{28}H_{35}N_3O_2$: C, 75.47; H, 7.92; N, 9.43. Found: C, 75.28; H, 7.65; N, 9.43.

3*β*-Hydroxy-2'-amino-4'-(*m*-bromophenyl)-androst-[16,17-*e*]pyrimidine (5d)



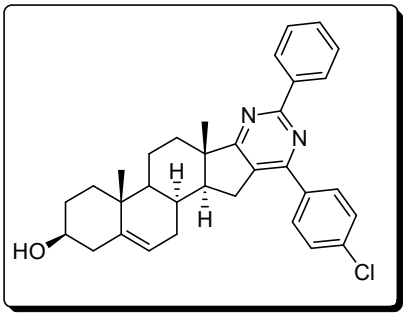
Yellow solid, Yield 72%; m.p. 127-130 °C; IR ($CHCl_3$, cm^{-1}): 3333, 2932, 1561, 1453, 1376, 1041, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.10 (s, 3H), 1.12 (s, 3H), 0.85-2.80 (m, 17H), 3.50-3.60 (m, 1H), 5.35-5.45 (m, 1H), 7.36 (s, 2H), 7.40 (m, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.9 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 16.8, 19.4, 20.4, 29.6, 30.7, 30.9, 32.8, 36.7, 37.1, 39.8, 40.0, 40.3, 40.6, 42.2, 45.9, 50.4, 55.5, 71.2, 120.5, 122.7, 127.1, 130.1, 131.4, 133.1, 141.5, 161.0; MS (ESI, m/z) = 495 $[M+1]^+$. Anal. calcd. for $C_{33}H_{35}BrN_2O$: C, 71.34; H, 6.35; N, 5.04. Found: C, 71.65; H, 6.18; N, 5.28.

3*β*-Hydroxy-2'-phenyl-4'-tolyl-androst-[16,17-*e*]pyrimidine (5e)



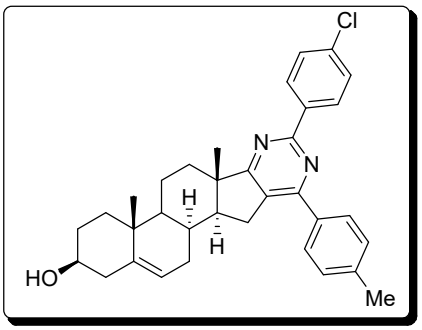
Yellow solid, Yield 70%; m.p. 127-130 °C; IR ($CHCl_3$, cm^{-1}): 3397, 2926, 1547, 1375, 755; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.13 (s, 3H), 1.15 (s, 3H), 0.80-2.95 (m, 20H), 3.48-3.60 (m, 1H), 5.35-5.45 (m, 1H), 7.07-7.49 (m, 5H), 7.94 (d, *J* = 7.9 Hz, 2H), 8.57 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 14.3, 17.0, 19.5, 20.6, 21.5, 29.4, 29.7, 30.9, 31.2, 31.9, 36.7, 42.2, 45.9, 47.3, 49.9, 50.7, 55.9, 71.6, 121.0, 128.3, 128.7, 129.5, 130.4, 132.8, 133.2, 134.9, 139.6, 141.1, 161.3; MS (ESI, m/z) = 491 $[M+1]^+$. Anal. calcd. for $C_{34}H_{38}N_2O$: C, 83.22; H, 7.81; N, 5.71. Found: C, 83.01; H, 7.66; N, 5.28.

3*β*-Hydroxy-2'-phenyl-4'-(*p*-chlorophenyl)-androst-[16,17-*e*]pyrimidine (5f)



White solid, Yield 73%; m.p. 126-129 °C; IR ($CHCl_3$, cm^{-1}): 3387, 2929, 1548, 1491, 1376, 1043, 771; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.85-2.87 (m, 25H), 3.50-3.54 (m, 1H), 5.35-5.45 (m, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.46-7.53 (m, 2H), 7.99 (d, *J* = 8.7 Hz, 2H), 8.54-8.57 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 17.0, 19.4, 20.6, 22.7, 29.3, 29.7, 30.9, 31.5, 31.9, 32.5, 36.8, 37.1, 42.2, 45.9, 49.8, 50.3, 55.5, 71.7, 120.8, 121.3, 128.3, 128.5, 128.7, 129.7, 130.1, 130.2, 130.4, 131.3, 140.6, 140.8, 140.3, 146.7, 161.0; MS (ESI, m/z) = 511 $[M+1]^+$. Anal. calcd. for $C_{33}H_{35}ClN_2O$: C, 77.55; H, 6.90; C N, 5.48. Found: C, 77.42; H, 6.67; N, 5.18.

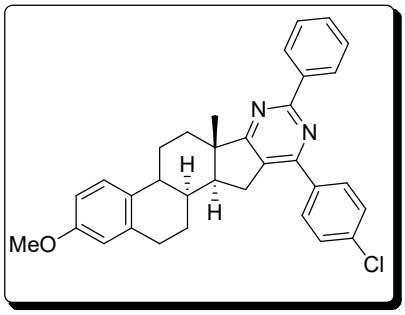
3*β*-Hydroxy-2'-(*p*-chlorophenyl)-4'-(tolyl)-androst-[16,17-*e*]pyrimidine (5g)



Yellow solid, Yield 70%; m.p. 74-76 °C; IR ($CHCl_3$, cm^{-1}): 3397, 2926, 1621, 1375, 1019, 772; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.07 (s, 3H), 1.15 (s, 3H), 0.85-2.95 (m, 20H), 3.45-3.55 (m, 1H), 5.35-5.45 (m, 1H), 7.2 (d, *J* = 7.9 Hz, 1H) 7.34 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 8.53 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz):

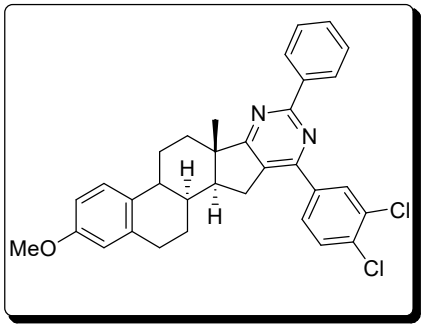
14.3, 19.5, 20.4, 21.5, 29.4, 29.7, 30.8, 30.9, 31.2, 31.6, 36.7, 37.1, 42.2, 47.3, 49.9, 50.4, 71.6, 120.8, 128.6, 128.8, 129.4, 129.5, 129.9, 130.4, 139.6, 140.6, 141.2, 141.3, 157.7, 161.9; MS (ESI, m/z) = 525 $[M+1]^+$. Anal. calcd. for $C_{34}H_{37}ClN_2O$: C, 77.77; H, 7.10; N, 5.33. Found: C, 77.92; H, 7.28; N, 5.49.

3-Methoxy-2'-phenyl-4'-(*p*-chlorophenyl)-estra-1,3,5-triene(10)-[16,17-*e*]pyrimidine (5h)



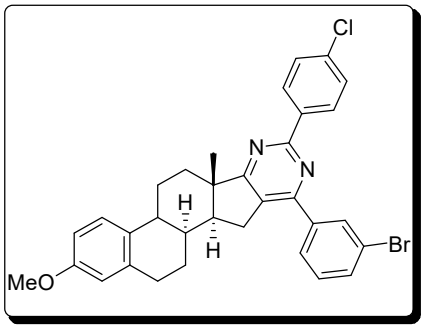
Yellow solid, Yield 80%; m.p. 79-82 °C; IR ($CHCl_3$, cm^{-1}): 2929, 1549, 1498, 1377, 1255, 1047, 733; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.17 (s, 3H), 0.85-3.00 (m, 13H), 3.80 (s, 3H), 6.67 (s, 1H), 6.74 (d, J = 8.7 Hz, 2H), 7.48-7.52 (m, J = 7.2 Hz, 5H), 8.05 (d, J = 6.4 Hz, 2H), 8.60 (d, J = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 17.4, 26.2, 27.5, 29.7, 30.5, 33.3, 37.7, 44.4, 46.4, 54.9, 55.2, 111.6, 113.9, 126.2, 128.3, 128.5, 128.8, 130.1, 132.4, 137.4, 137.7, 137.9, 138.1, 138.5, 157.6, 159.2, 162.9; MS (ESI, m/z) = 507 $[M+1]^+$. Anal. calcd. for $C_{33}H_{31}ClN_2O$: C, 78.17; H, 6.16; N, 5.52. Found: C, 78.46; H, 6.31; N, 5.72.

3-Methoxy-2'-phenyl-4'-(3″,4″-dichlorophenyl)-estra-1,3,5-triene(10)-[16,17-*e*] pyrimidine (5i)



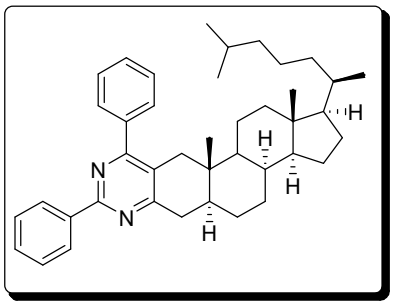
Yellow solid, Yield 75%; m.p. 86-89 °C; IR ($CHCl_3$, cm^{-1}): 2928, 1549, 1453, 1377, 1055, 758; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.14 (s, 3H), 0.85-2.95 (m, 11H), 3.80 (s, 3H), 6.67 (d, *J* = 2.2 Hz, 2H), 6.75 (d, *J* = 6.1 Hz, 2H), 7.20-7.30 (m, 1H), 7.50 (d, *J* = 6.8 Hz, 1H), 7.60 (d, *J* = 5.94 Hz, 1H), 7.88 (d, *J* = 6.6 Hz, 2H), 8.17 (s, 2H), 8.56 (d, *J* = 2.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.1, 19.2, 23.4, 24.2, 24.6, 24.7, 28.4, 29.7, 33.4, 36.6, 36.8, 37.3, 44.4, 54.8, 55.2, 61.4, 61.6, 90.2, 92.1, 100.8, 111.6, 113.9, 126.2, 128.1, 128.3, 128.4, 132.2, 132.9, 137.6, 138.0, 157.6; MS (ESI, m/z) = 541 $[M+1]^+$. Anal. calcd. for $C_{33}H_{30}Cl_2N_2O$: C, 73.19; H, 5.58; N, 5.17. Found: C, 73.34; H, 5.78; N, 5.42.

3-Methoxy-2'-(*p*-chlorophenyl)-4'-(*m*-bromophenyl)-estra-1,3,5-triene(10)-[16,17-*e*]pyrimidine (5j)



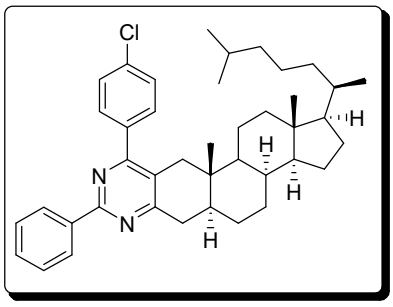
Yellow solid, Yield 71%; m.p. 78-81 °C; IR ($CHCl_3$, cm^{-1}): 2928, 1546, 1499, 1376, 1219, 1014, 772; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.14 (s, 3H), 0.85-2.95 (m, 13H), 3.77 (s, 3H), 6.66 (s, 1H), 6.74 (d, *J* = 8.7 Hz, 1H), 7.24 (d, *J* = 4.6 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.91 (d, *J* = 7.7 Hz, 1H), 8.18 (s, 1H), 8.54 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 17.4, 26.2, 27.5, 29.6, 30.4, 33.2, 37.6, 44.4, 46.4, 54.8, 55.2, 111.6, 113.9, 122.9, 126.2, 127.3, 128.6, 129.7, 130.1, 131.7, 132.2, 132.8, 136.4, 136.7, 137.7, 139.9, 157.6, 162.1; MS (ESI, m/z) = 585 $[M+1]^+$. Anal. calcd. for $C_{33}H_{30}BrClN_2O$: C, 67.64; H, 5.16; N, 4.78;. Found: C, 67.27; H, 5.43; N, 4.67.

2′,4′-Diphenyl-5α-cholest[2,3-*e*]pyrimidine (5k)



Yellow solid, Yield 70%; m.p. 187-189 °C; IR ($CHCl_3$, cm^{-1}): 2929, 1740, 1544, 1445, 1397, 1242, 1027, 909; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.64 (s, 3H), 0.72 (s, 3H), 0.60-2.80 (m, 38H), 7.10-7.49 (m, 6H), 7.66 (d, *J* = 5.1 Hz, 2H), 8.46 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 11.4, 11.8, 18.5, 21.2, 22.6, 22.7, 23.7, 24.1, 27.9, 28.1, 28.2, 29.6, 31.4, 35.1, 35.2, 35.3, 35.6, 35.9, 39.2, 39.4, 42.2, 42.3, 42.5, 53.5, 56.2, 124.2, 125.5, 127.7, 128.0, 128.2, 128.8, 128.9, 129.0, 129.2, 129.8, 138.0, 138.6, 161.1, 165.4, 165.9; MS (ESI, m/z) = 575 $[M + 1]^+$. Anal. calcd. for $C_{41}H_{54}N_2$: C, 85.66; H, 9.47; N, 4.87. Found: C, 85.46; H, 9.21; N, 4.65.

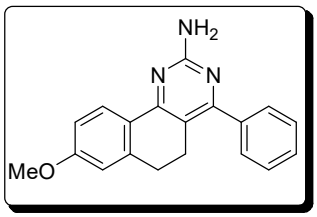
2′-Phenyl-4′-(*p*-chlorophenyl)-5α-cholest[2,3-*e*]pyrimidine (5l)



Yellow solid, Yield 68%; 205-209 °C; IR ($CHCl_3$, cm^{-1}): 2928, 1538, 1445, 1395, 1090, 910; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.64 (s, 3H), 0.72 (s, 3H), 0.60-2.80 (m, 38H), 7.40-7.51 (m, 5H), 7.64 (d, *J* = 4.5 Hz, 2H), 8.43 (d, *J* = 4.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 11.4, 11.8, 18.6, 21.2, 22.5, 22.6, 22.7, 23.7, 24.1, 27.9, 28.1, 28.4, 29.6, 31.4, 35.2, 35.4, 35.7, 36.0, 36.6, 39.4, 39.8, 40.6, 41.1, 42.3, 53.5, 56.2, 124.7, 128.1, 128.3, 128.5, 128.6, 129.0,

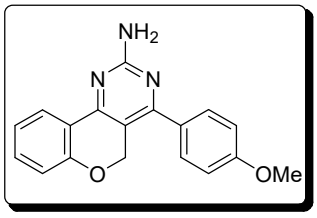
129.1, 129.4, 136.2, 138.3, 160.0, 165.9; MS (ESI, m/z) = 609 $[M + 1]^+$. Anal. calcd. for $C_{41}H_{53}ClN_2$: C, 80.82; H, 8.77; N, 4.60. Found: C, 80.68; H, 8.54; N, 4.38.

8-Methoxy-4-phenyl-5,6-dihydro-benzo[h]quinazolin-2-amine (5m)



Brown solid, Yield 80%; m.p. 73-75 °C; IR ($CHCl_3$, cm^{-1}): 3312, 3189, 2936, 1606, 1546, 1250, 773; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.80-2.88 (m, 4H), 3.87 (s, 3H), 5.35-5.45 (m, 2H), 6.75 (s, 1H), 6.90 (d, *J* = 6.2 Hz, 1H), 7.40-7.60 (m, 2H), 7.56 (d, *J* = 4.8 Hz, 2H), 8.24 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 24.1, 28.7, 55.4, 112.7, 112.9, 115.2, 125.9, 127.6, 128.3, 128.6, 129.0, 138.1, 141.7, 161.2, 161.8, 164.7; MS (EI, m/z) = 304 $[M+1]^+$. Anal. calcd. for $C_{19}H_{17}N_3O$: C, 75.23; H, 5.65; N, 13.85. Found: C, 75.55; H, 5.73; N, 13.99.

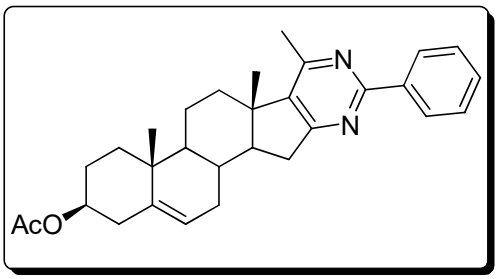
4-(*p*-Methoxyphenyl)-5H-chromeno[3,4-*e*]pyrimidin-2-amine (5n)



Yellow solid, Yield 82%; m.p. 76-79 °C; IR ($CHCl_3$, cm^{-1}): 3395, 2945, 1665, 1602, 1567, 1509, 1453, 1369, 1247, 771; ^1H NMR ($CDCl_3$, 300 MHz): δ 3.80 (s, 3H), 3.99 (s, 2H), 5.60 (s, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 7.02 (d, *J* = 8.9 Hz, 2H), 7.22-7.35 (m, 2H), 8.18 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 35.1, 55.3, 114.3, 118.1, 119.0, 120.8, 129.5, 129.9, 131.5, 132.2, 158.3, 159.1, 162.7, 164.2; MS (EI, m/z) = 306 $[M+1]^+$; Anal. calcd. for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76; Found: C, 70.66; H, 4.64; N, 13.48.

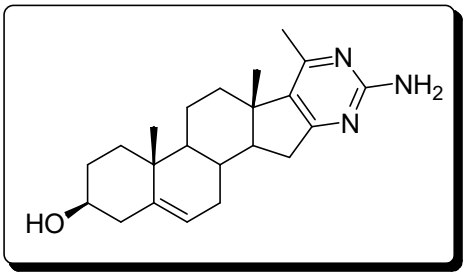
Characterization of pyrimidines (7)

3*β*-Acetoxy-2'-(phenyl)-6'-(methyl)-androst-[16,17-*d*]pyrimidine (7a)



Brown solid, Yield 78%; m.p. 160-165 °C; IR ($CHCl_3$, cm^{-1}): 2944, 2854, 1732, 1555, 1436, 1384, 1245, 1032, 758; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.08 (s, 3H), 1.12 (s, 3H), 2.18 (s, 3H), 2.57 (s, 3H), 1.05-2.92 (m, 17H), 4.61 (m, 1H), 5.43 (s, 1H), 6.84 (m, 1H), 7.46 (d, *J* = 5.46 Hz, 2H), 8.39-8.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 16.7, 19.3, 20.6, 21.4, 21.7, 27.7, 30.4, 30.9, 31.5, 34.3, 35.6, 36.8, 38.1, 44.3, 50.1, 55.2, 73.8, 115.4, 121.9, 128.2, 128.5, 129.6, 130.3, 139.9, 160.3, 170.6, 173.5; MS (ESI, m/z) = 457 $[M + 1]^+$. Anal. calcd. for $C_{30}H_{36}N_2O_2$: C, 78.91; H, 7.95; N, 6.13. Found: C, 78.77; H, 7.69; N, 6.01.

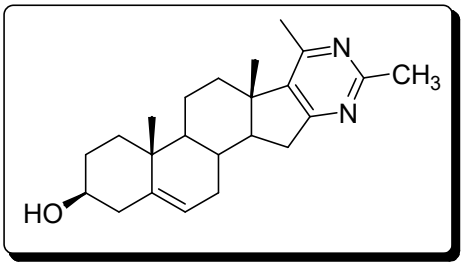
3*β*-Hydroxy-2'-(amino)-6'-(methyl)-androst-[16,17-*d*]pyrimidine (7b)



White solid, Yield 80%; m.p. 312-315 °C; IR ($CHCl_3$, cm^{-1}): 2929, 2855, 1650, 1560, 1478, 1384, 1245, 1045, 798; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.02 (s, 3H), 1.08 (s, 3H), 2.38 (s, 3H), 1.10-2.65 (m, 20H), 3.50 (m, 1H), 5.77 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.8, 24.1, 25.3, 35.0, 36.2, 38.9, 40.7, 41.4, 41.8, 47.0, 48.2, 54.9, 59.8, 75.5, 125.0, 135.7, 146.4,

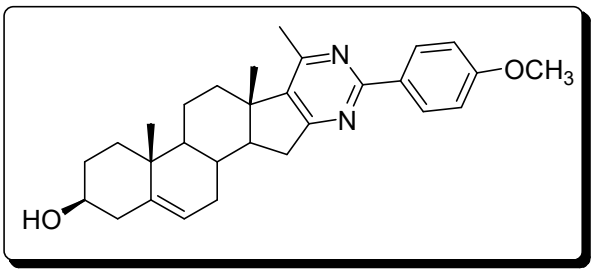
165.6; MS (ESI, m/z) = 354 $[M+1]^+$. Anal. calcd. for $C_{22}H_{31}N_3O$: C, 74.75; H, 8.84; N, 11.89. Found: C, 74.98; H, 8.96; N, 11.91.

3*β*-Hydroxy-2',6'-dimethyl-androst-[16,17-*d*]pyrimidine (7c)



Yiellow solid, Yield 75%; m.p. 166-170 °C; IR ($CHCl_3$, cm^{-1}): 2929, 2899, 1732, 1693, 1638, 1568, 1384, 1059, 836; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.06 (s, 3H), 1.09 (s, 3H), 1.92 (s, 3H), 2.16 (s, 3H), 1.50-2.31 (m, 18H), 3.52 (m, 1H), 5.34 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 16.7, 19.4, 20.6, 21.2, 25.3, 29.7, 30.4, 31.5, 34.1, 35.6, 36.7, 37.0, 42.2, 44.2, 50.2, 55.3, 71.4, 121.0, 138.9, 141.2, 164.9, 169.9, 173.6; MS (ESI, m/z) = 353 $[M+1]^+$. Anal. calcd. for $C_{23}H_{32}N_2O$: C, 78.36; H, 9.15; N, 7.95. Found: C, 78.65; H, 9.34; N, 7.78.

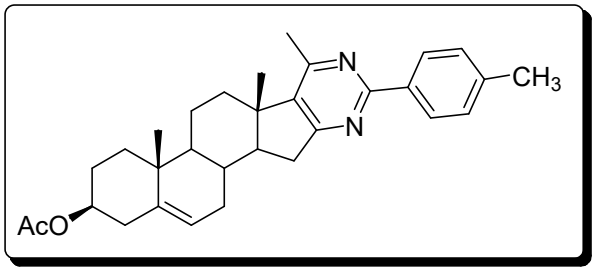
3*β*-Hydroxy-2'-(*p*-methoxyphenyl)-6'-(methyl)-androst-[16,17-*d*]pyrimidine (7d)



White gum, Yield 78%; IR ($CHCl_3$, cm^{-1}): 2955, 2849, 1728, 1540, 1429, 1388, 1241, 1039, 745; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.05 (s, 3H), 1.08 (s, 3H), 0.62-2.80 (m, 18H), 2.52 (s, 3H), 3.50 (m, 1H), 3.86 (s, 3H), 5.33 (s, 1H), 6.96 (d, J = 8.79 Hz, 2H), 8.34 (d, J = 8.76 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 16.7, 19.4, 20.6, 21.7, 30.4, 31.5, 34.3, 35.7, 36.7, 37.0, 42.2, 44.1, 50.2, 55.3, 71.5, 113.7, 120.9, 129.5, 130.9, 139.0, 141.1, 159.9, 161.2, 162.2,

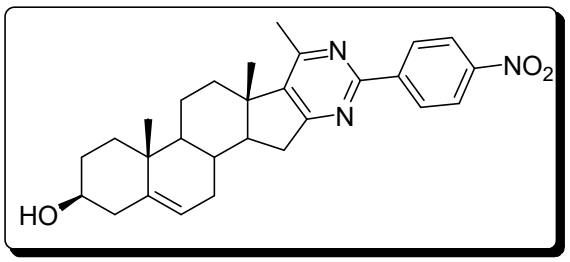
173.3; MS (ESI, m/z) = 445[M + 1]$^+$. Anal. calcd. for $C_{29}H_{36}N_2O_2$: C, 78.34; H, 8.16; N, 6.30. Found: C, 78.18; H, 8.26; N, 6.45.

3*β*-Acetoxy-2'-(*p*-methylphenyl)-6'-(methyl)-androst-[16,17-*d*]pyrimidine (7e)



White gum, Yield 80%; IR ($CHCl_3$, cm^{-1}): 2948, 2855, 1730, 1550, 1431, 1379, 1241, 1030, 757; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.09 (s, 3H), 1.10 (s, 3H), 1.11-2.90 (m, 13H), 2.21 (s, 3H), 2.61 (s, 3H), 2.90 (s, 3H), 4.59 (s, 3H), 5.40 (s, 1H), 7.45 (s, *J* = 4.20 Hz, 2H), 8.39 (d, *J* = 5.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 16.7, 19.3, 20.9, 21.5, 21.7, 24.9, 27.7, 30.4, 30.9, 31.6, 34.3, 35.6, 36.8, 38.1, 44.3, 50.1, 55.3, 73.3, 113.4, 121.9, 126.3, 126.6, 129.6, 130.2, 136.9, 169.9; MS (ESI, m/z) = 471 [M + 1]$^+$. Anal. calcd. for $C_{31}H_{38}N_2O_2$: C, 79.11; H, 8.14; N, 5.95. Found: C, 79.32; H, 8.43; N, 5.77.

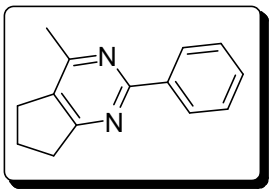
3*β*-Hydroxy-2'-(*p*-nitrophenyl)-6'-(methyl)-androst-[16,17-*d*]pyrimidine (7f)



Yellow gum, Yield 75%; IR ($CHCl_3$, cm^{-1}): 2929, 2846, 1728, 1685, 1628, 1560, 1377, 1044, 741; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.91 (s, 3H), 1.09 (s, 3H), 0.67-2.85 (m, 18H), 2.52 (s, 3H), 3.37 (s, 1H), 5.32 (s, 1H), 7.76 (d, *J* = 8.65 Hz, 2H), 8.23 (d, *J* = 8.55 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 20.1, 22.6, 24.2, 25.4, 30.4, 32.5, 32.8, 33.3, 36.2, 36.7, 41.7, 50.2, 52.2, 55.2, 71.5, 121.1, 128.9, 131.2, 138.9, 140.7, 148.5, 169.1, 172.2, 175.2; MS (ESI, m/z)

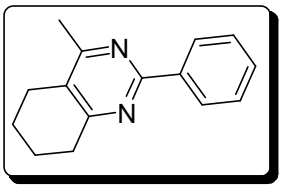
= 460 $[M+1]^+$. Anal. calcd. for $C_{28}H_{33}N_3O_3$: C, 73.18; H, 7.24; N, 9.14. Found: C, 73.42; H, 7.56; N, 9.44.

6,7-Dihydro-4-methyl-2-phenyl-5H-cyclopenta[d]pyrimidine (7g)



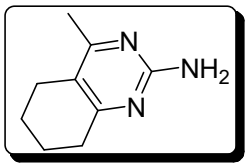
White solid, Yield 78%; m.p. 83-86 °C; IR ($CHCl_3$, cm^{-1}): 2958, 2920, 1563, 1390, 1058, 743; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.15 (m, 2H), 2.49 (s, 3H), 2.92 (m, 2H), 3.05 (m, 2H), 7.45 (m, 3H), 8.40 (d, J = 7.65 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.8, 28.3, 34.2, 128.0, 128.4, 129.9, 130.7, 138.4, 161.8, 163.2, 174.3; MS (ESI, m/z) = 211 $[M+1]^+$. Anal. calcd. for $C_{14}H_{14}N_2$: C, 79.97; H, 6.71; N, 13.32. Found: C, 79.82; H, 6.66; N, 13.12.

5,6,7,8-Tetrahydro-4-methyl-2-phenylquinazoline (7h)



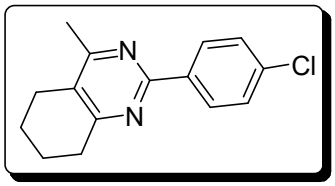
White solid, Yield 80%; m.p. 92-96 °C; IR ($CHCl_3$, cm^{-1}): 2946, 2865, 1552, 1400, 1017, 744; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.75 (m, 2H), 1.89 (m, 2H), 2.48 (s, 3H), 2.67 (m, 2H), 2.92 (m, 2H), 7.45 (m, 3H), 8.37 (d, J = 7.95 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.8, 22.3, 22.6, 24.9, 32.6, 125.9, 127.9, 128.4, 129.8, 138.4, 161.2, 164.9, 165.3; MS (ESI, m/z) = 225 $[M + 1]^+$. Anal. calcd. for $C_{15}H_{16}N_2$: C, 80.32; H, 7.19; N, 12.49. Found: C, 80.18; H, 7.32; N, 12.24.

5,6,7,8-Tetrahydro-4-methylquinazolin-2-amine (7i)



White solid, Yield 78%; m.p. 105-110 °C; IR ($CHCl_3$, cm^{-1}): 2925, 1662, 1447, 1017, 772; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.26 (m, 2H), 1.62 (m, 2H), 2.23 (s, 3H), 2.28 (m, 4H), 6.91 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.5, 21.9, 22.9, 25.2, 26.1, 139.7, 141.0, 170.5, 174.9; MS (ESI, m/z) = 164 $[M+1]^+$. Anal. calcd. for $C_9H_{13}N_3$: C, 66.23; H, 8.03; N, 25.74. Found: C, 66.54; H, 8.28; N, 25.65.

2-(4-Chlorophenyl)-5,6,7,8-tetrahydro-4-methylquinazoline (7j)



White solid, Yield 80%; m.p. 104-108 °C; IR ($CHCl_3$, cm^{-1}): 2936, 1579, 1395, 1087, 776; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.70 (m, 2H), 1.88 (m, 2H), 2.46 (s, 3H), 2.67 (m, 2H), 2.89 (m, 2H), 7.40 (d, J = 8.34 Hz, 2H), 8.33 (d, J = 8.35 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.8, 22.3, 22.6, 24.9, 32.5, 126.2, 128.5, 129.3, 135.9, 136.9, 160.1, 164.9, 165.4; MS (ESI, m/z) = 259 $[M+1]^+$. Anal. calcd. for $C_{15}H_{15}ClN_2$: C, 69.63; H, 5.84; N, 10.83. Found: C, 69.36; H, 5.54; N, 10.65.

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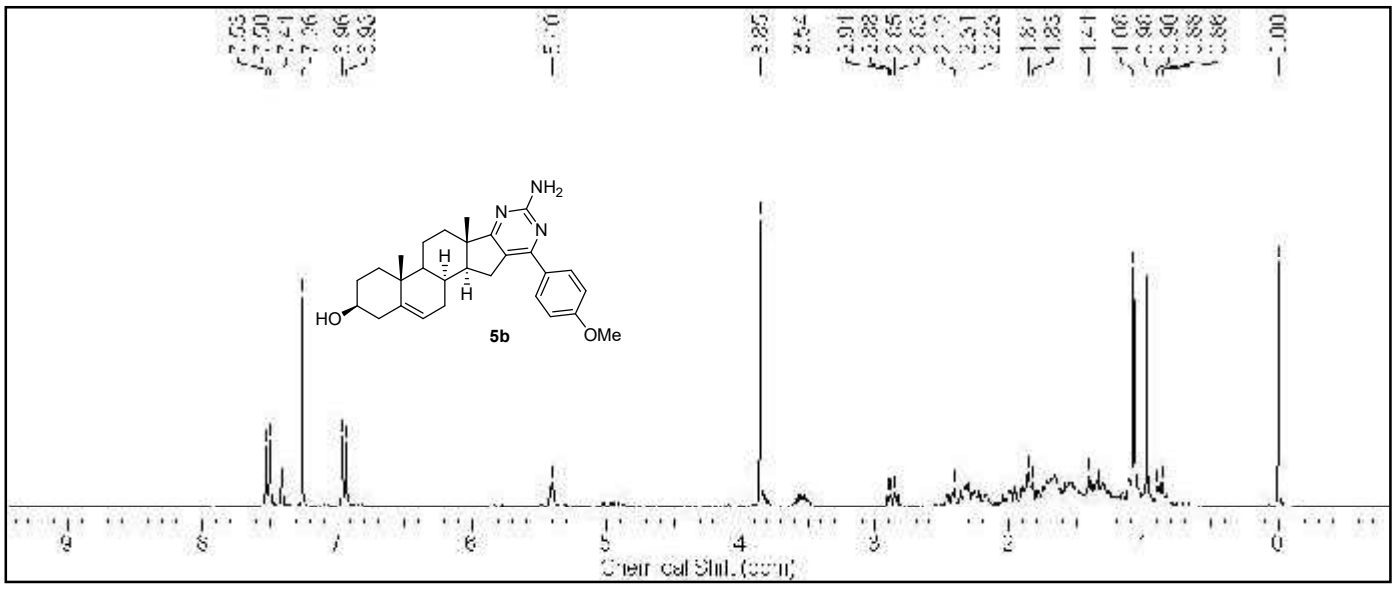
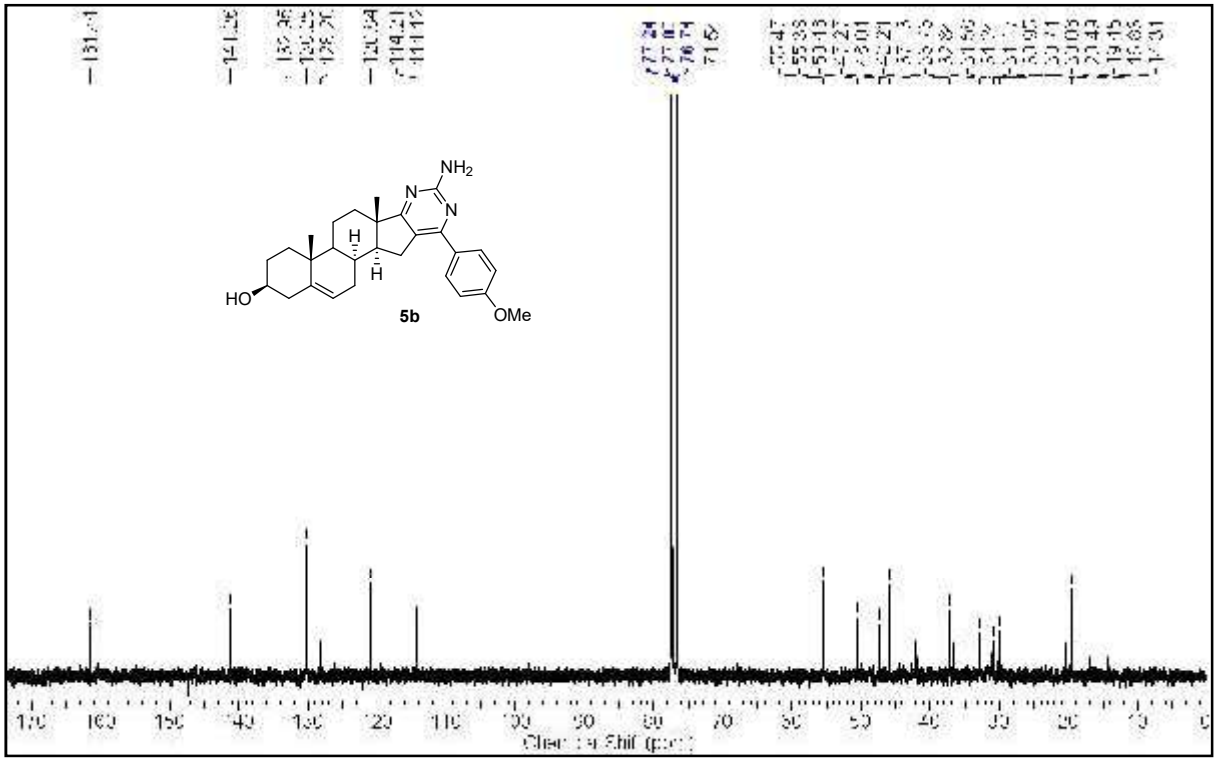
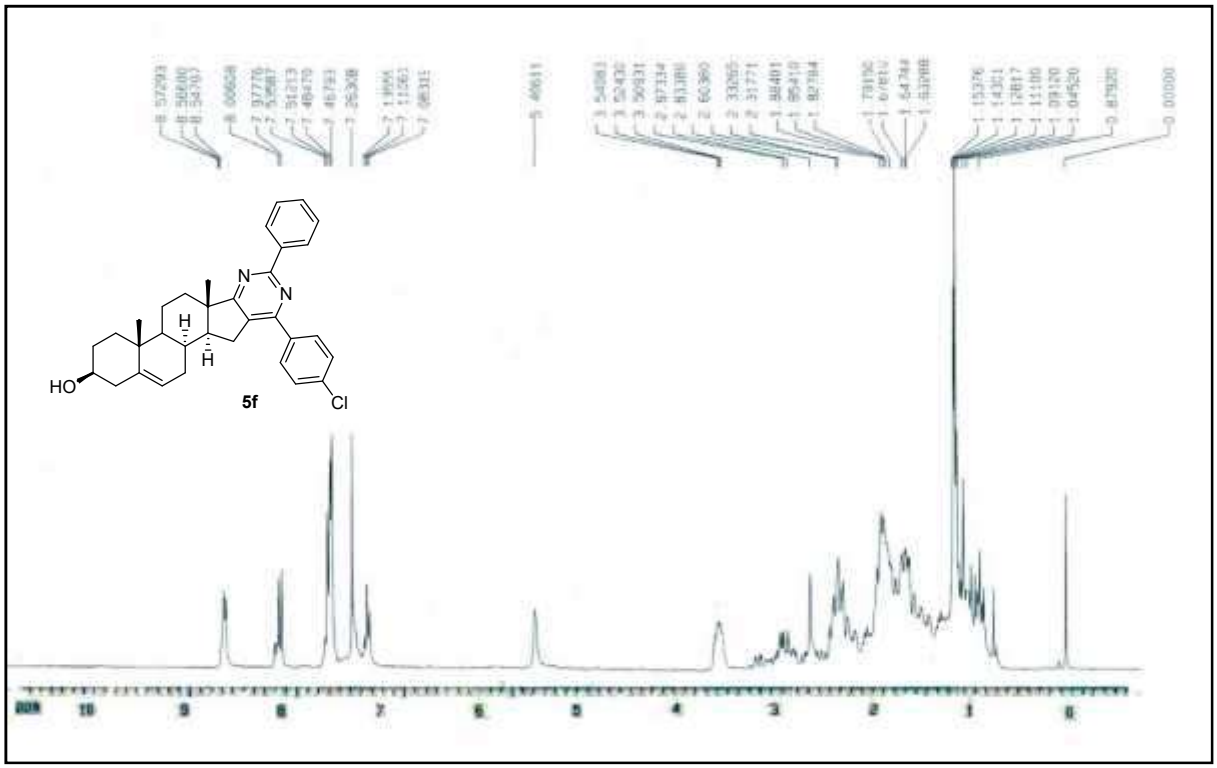
^{1}H NMR and ^{13}C NMR of some selected pyrimidine compounds



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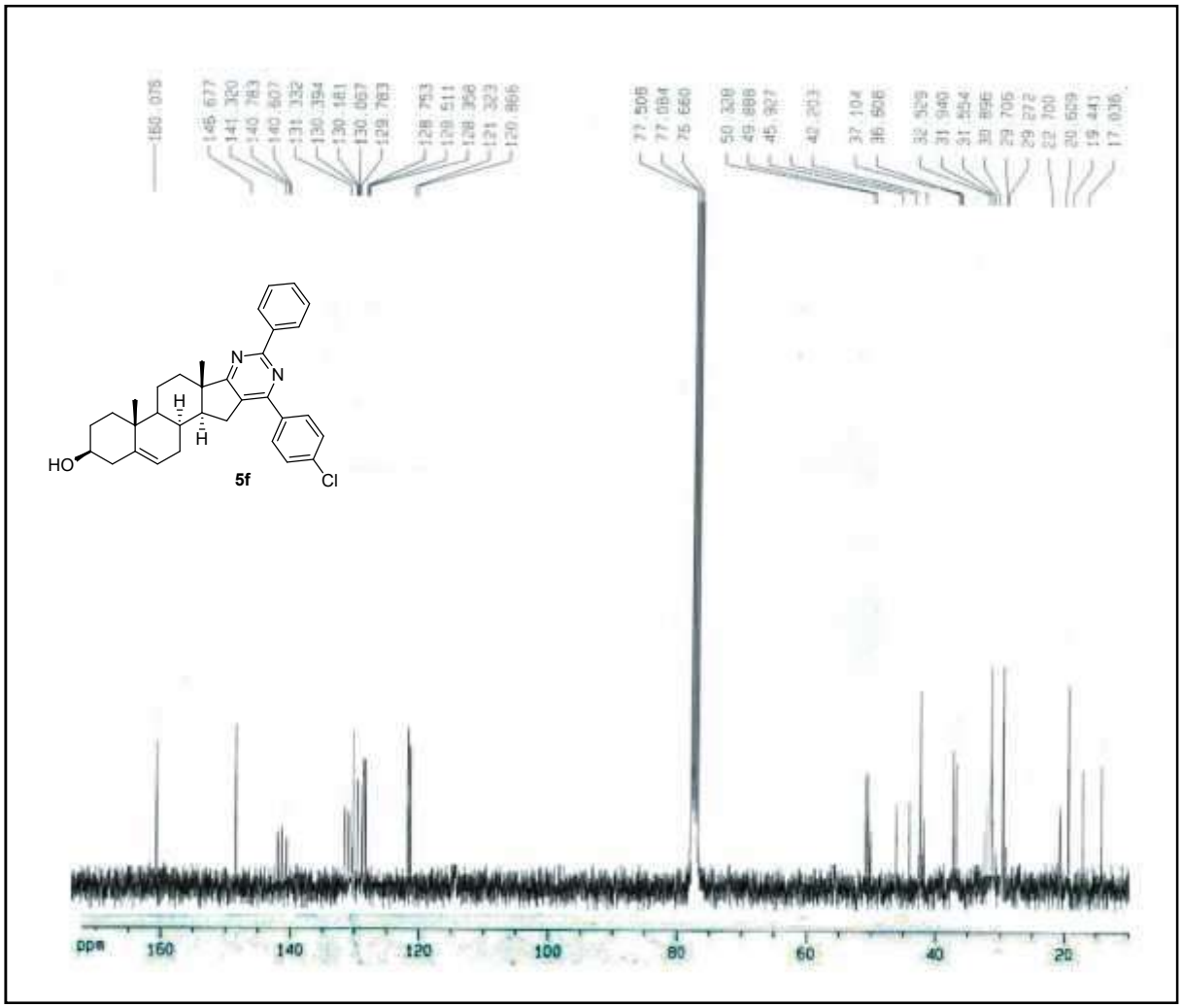
Cl
5f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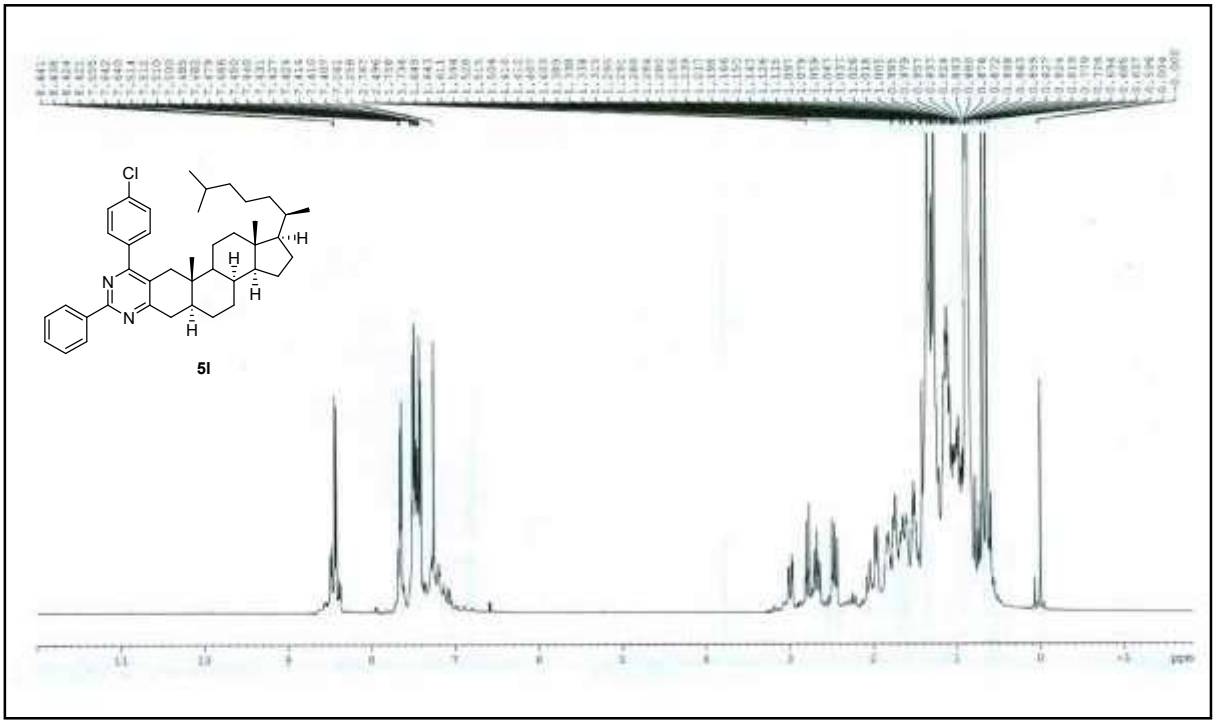
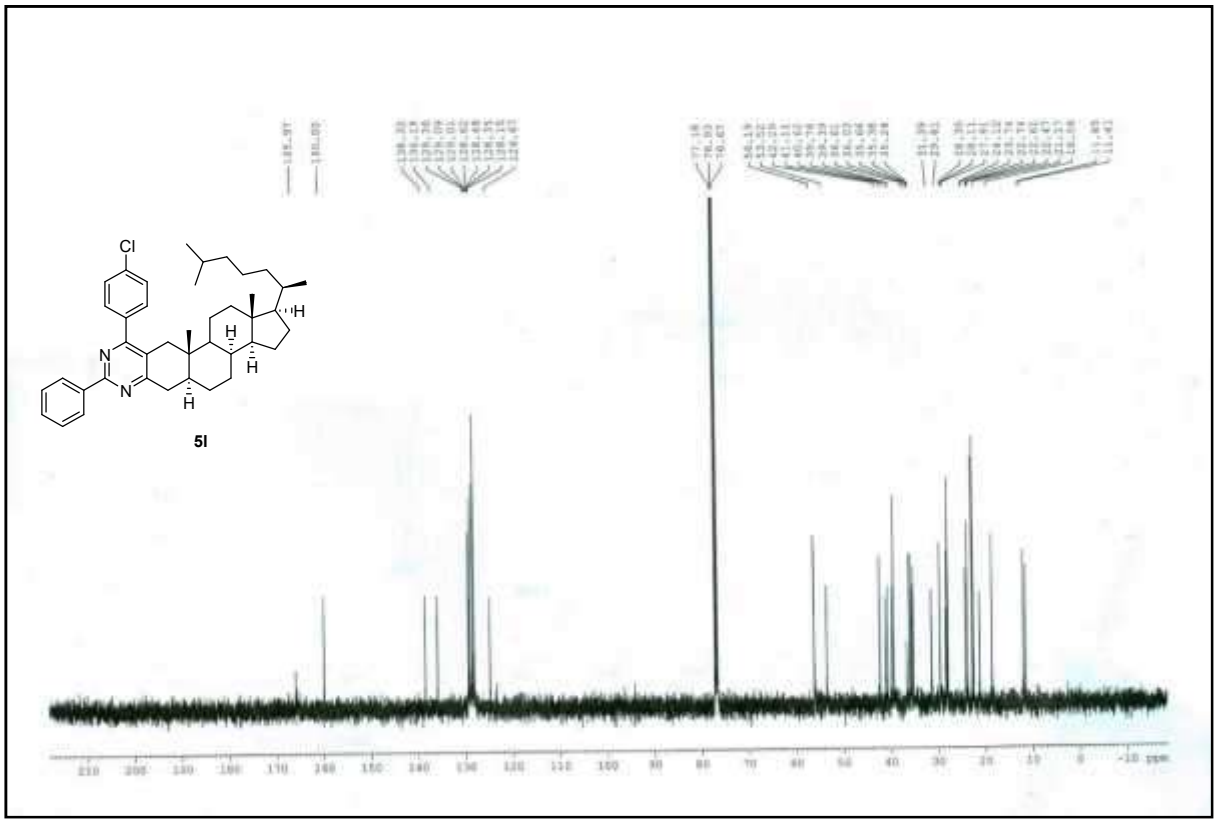


5l



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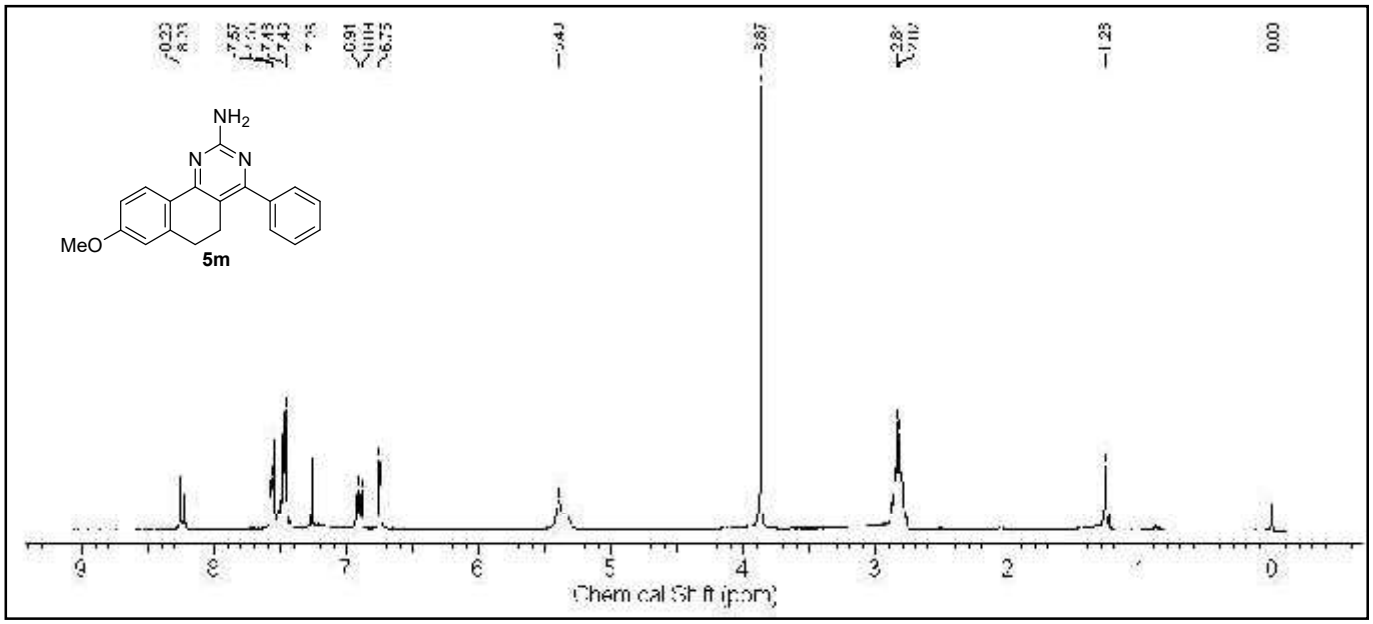
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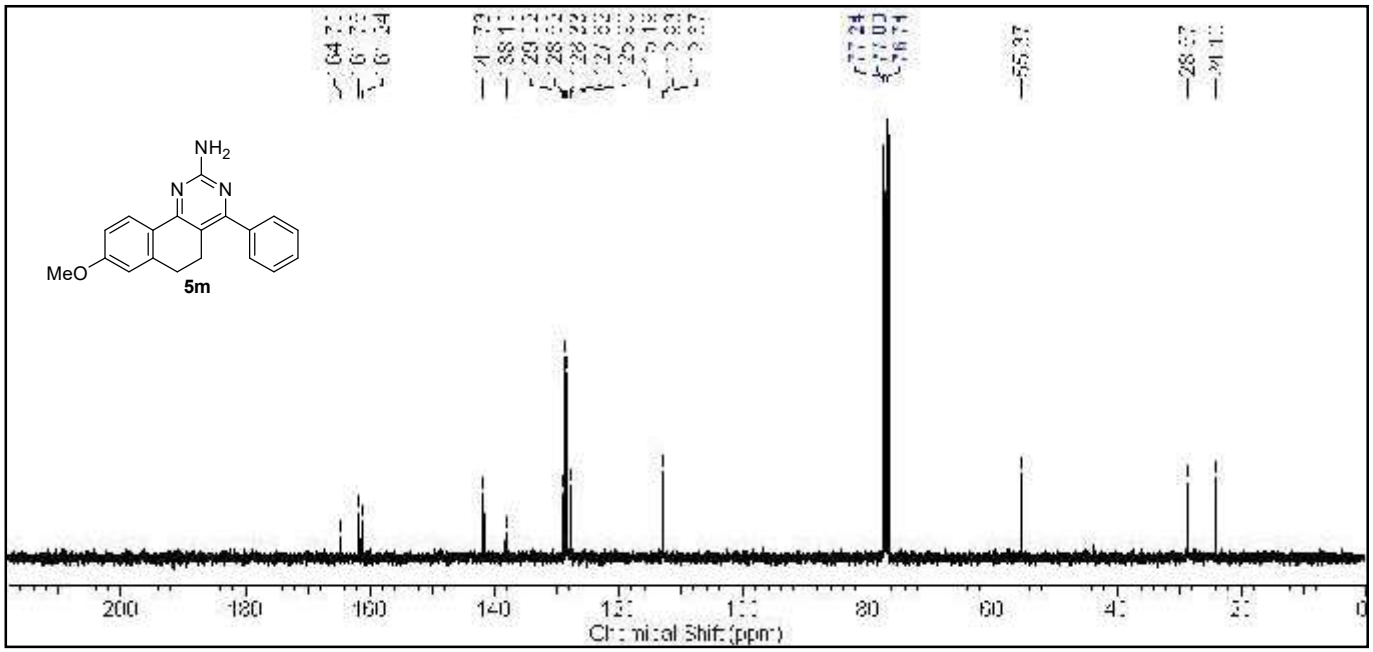
5m
Chemical Shift (ppm)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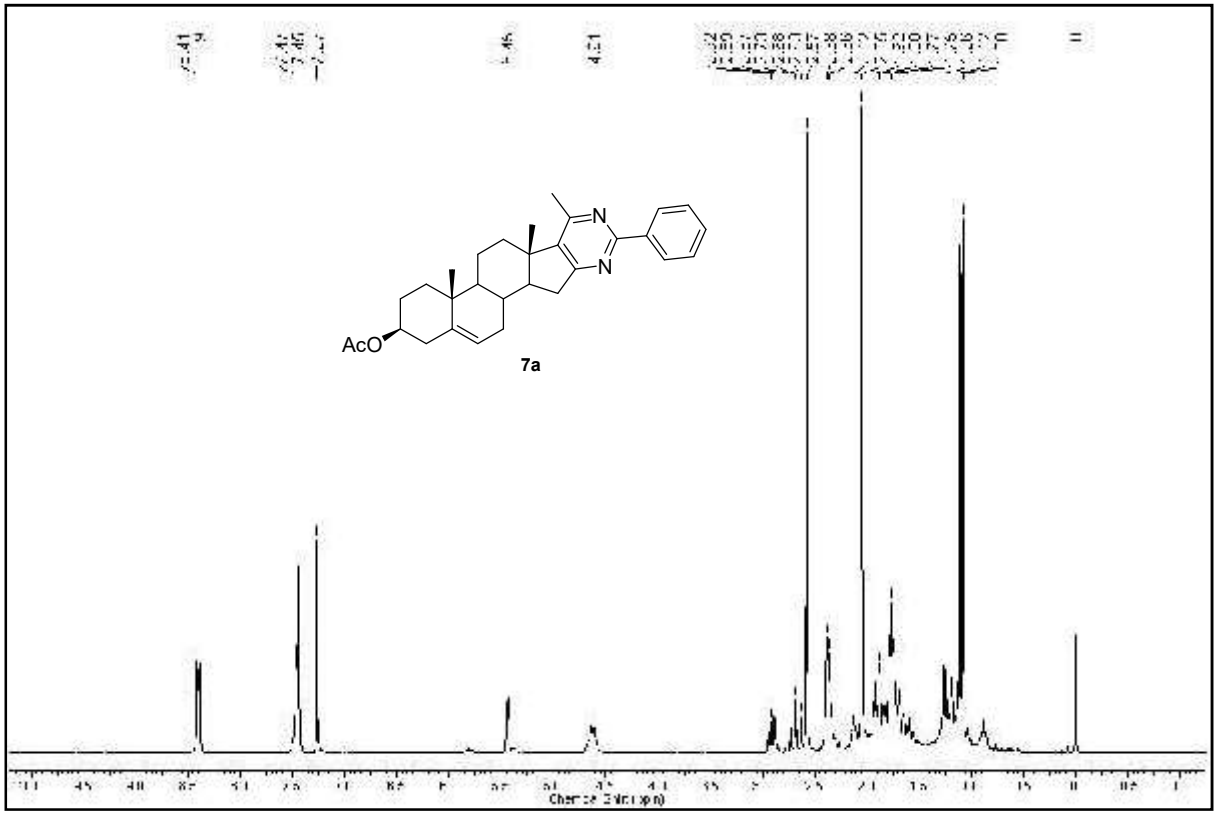
5m
Chemical Shift (ppm)



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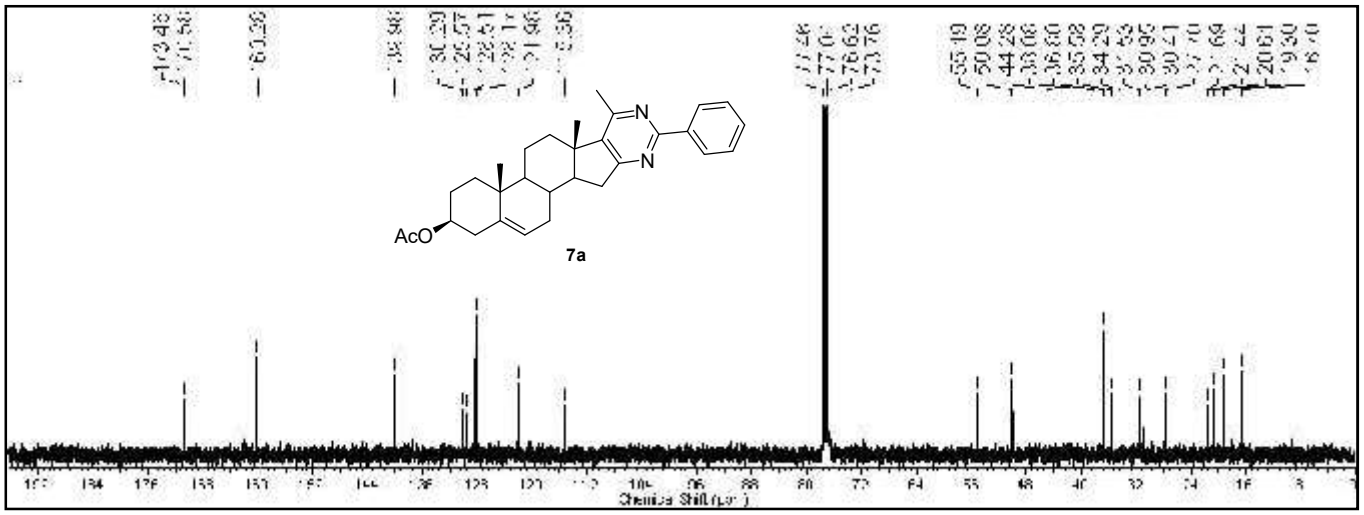

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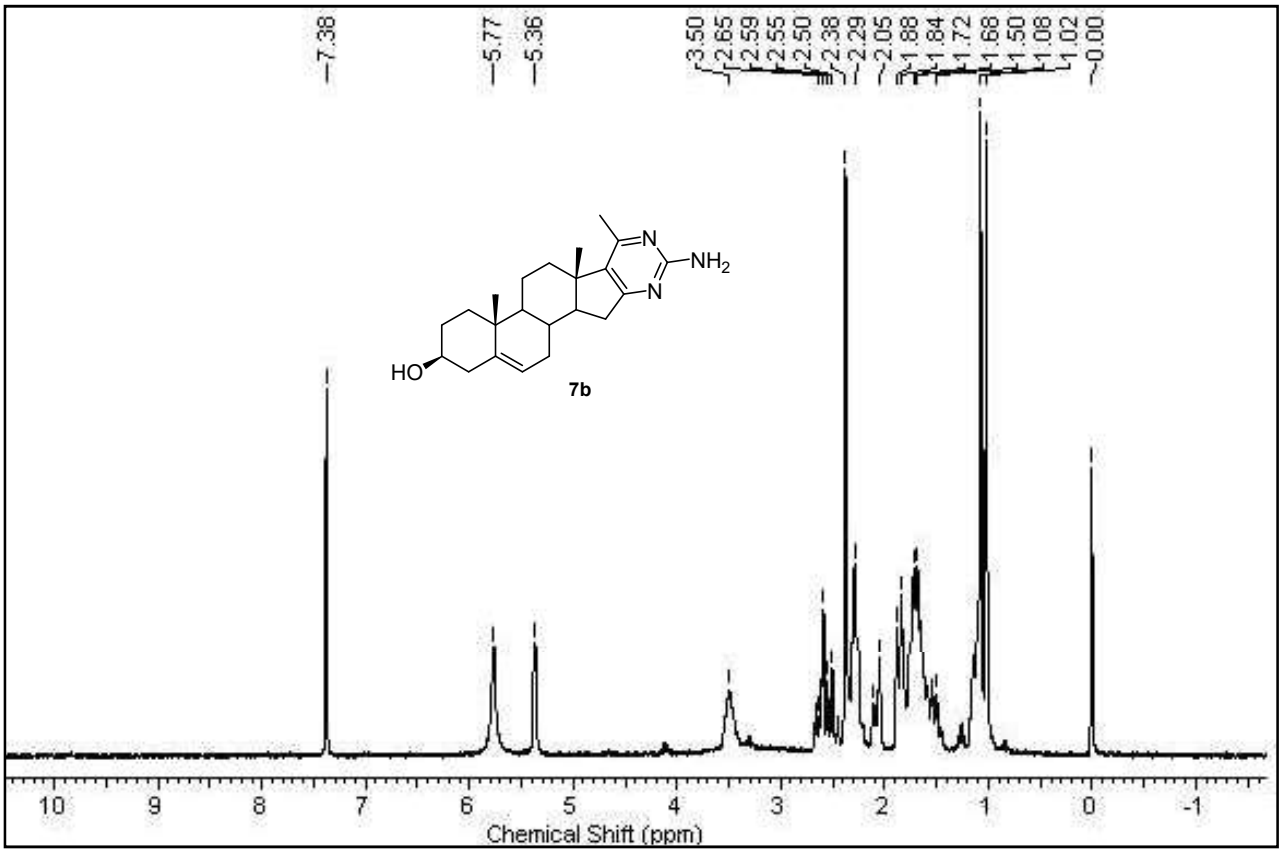
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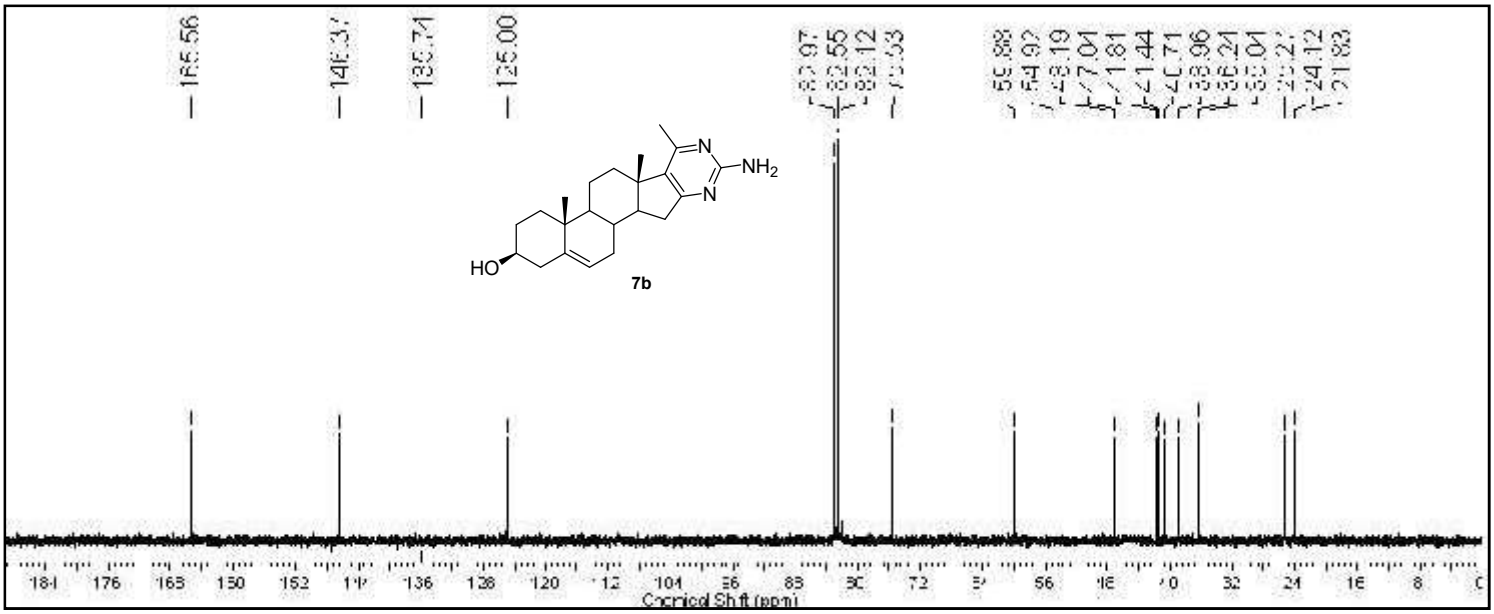
-1
Chemical Shift (ppm)


165.56
135.71
125.00
N
NH2
N
HO
7b