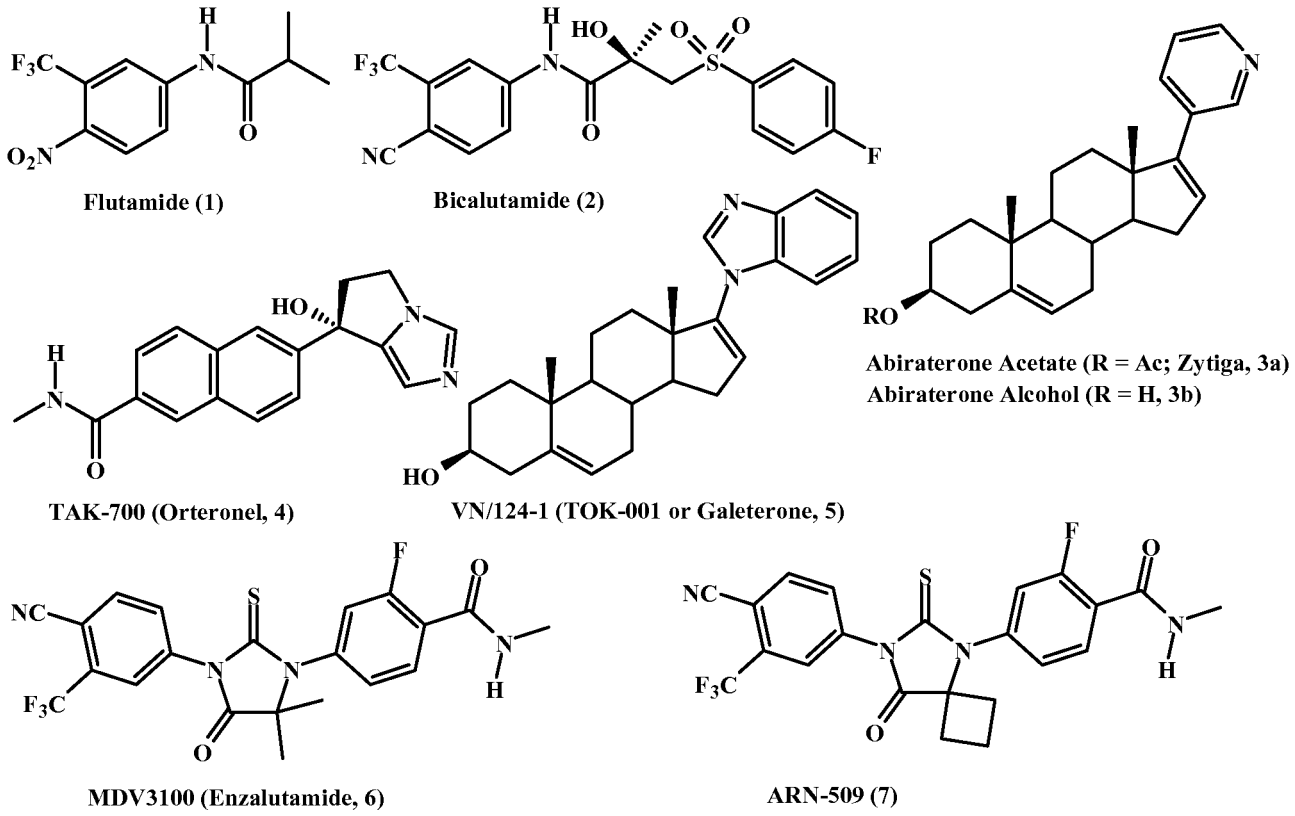
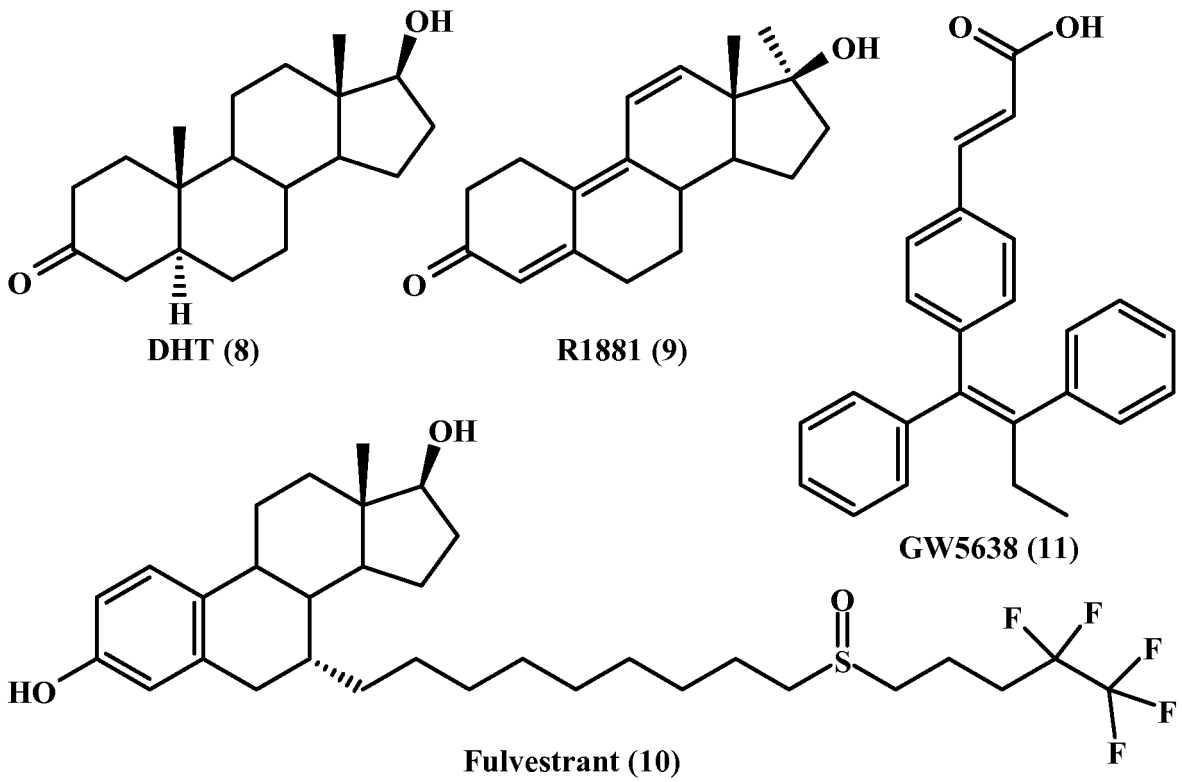

Flutamide (1)
Bicalutamide (2)
Abiraterone Acetate (R = Ac; Zytiga, 3a)
Abiraterone Alcohol (R = H, 3b)
TAK-700 (Orteronel, 4)
VN/124-1 (TOK-001 or Galeterone, 5)
MDV3100 (Enzalutamide, 6)
ARN-509 (7)

FIGURE 1



DHT (8) R1881 (9)

Fulvestrant (10)

FIGURE 2

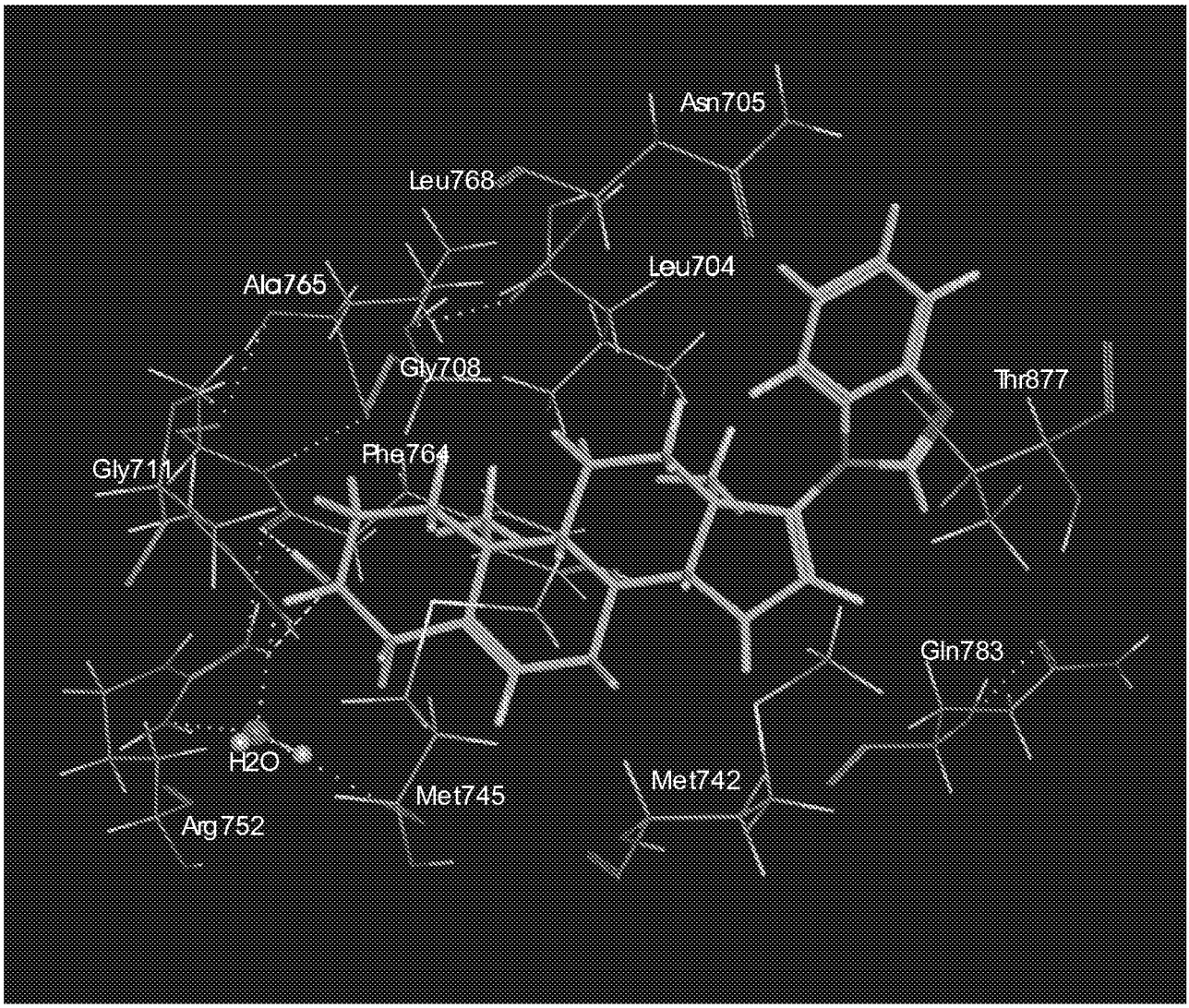

Asn705
Leu768
Leu704
Ala765
Gly708
Thr877
Phe764
Gly711
Gln783
H2O
Met745
Met742
Arg752

FIGURE 3

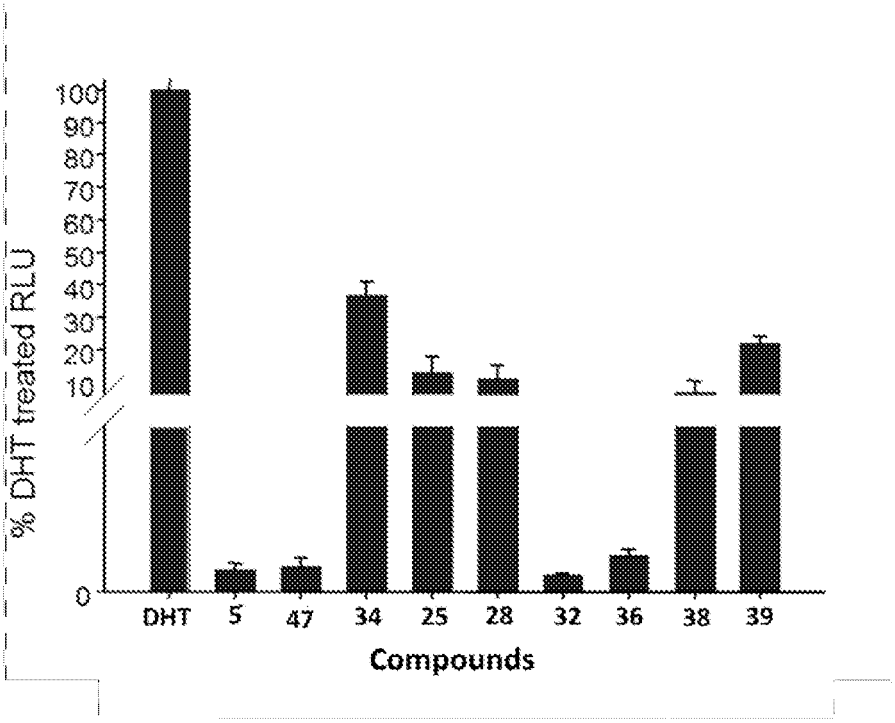

% DHT treated RLU
100
90
80
70
60
50
40
30
20
10
0
DHT
5
47
34
25
28
32
36
38
39
Compounds

FIGURE 4

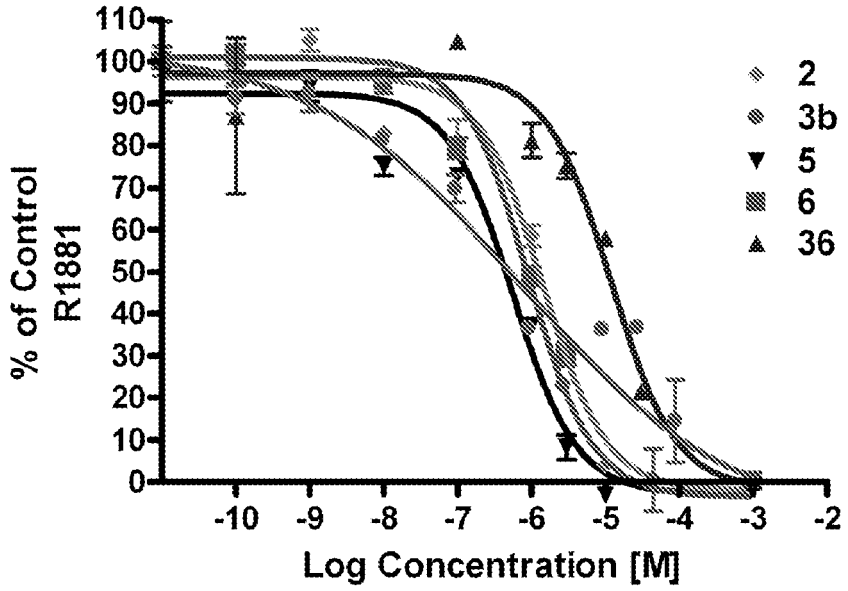


FIGURE 5A

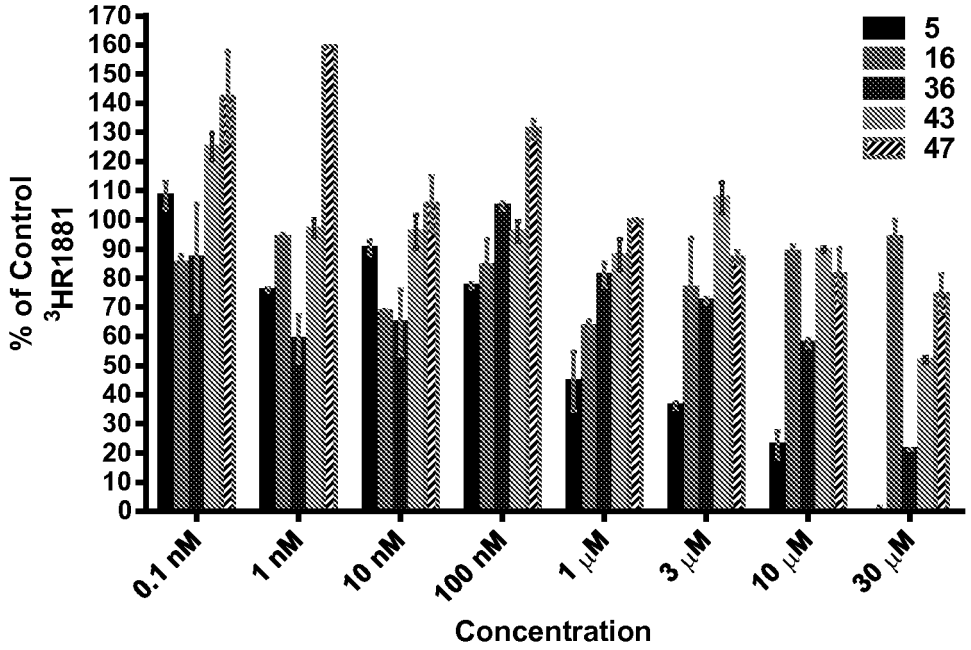


FIGURE 5B

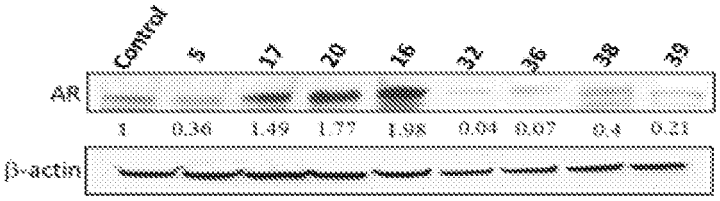


FIGURE 6A

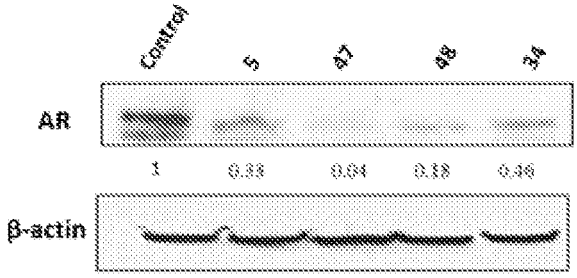


FIGURE 6B

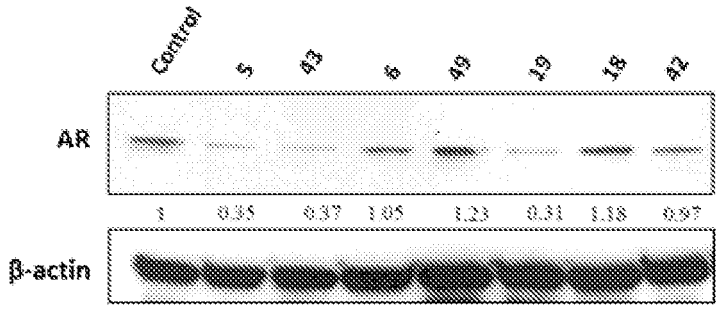


FIGURE 6C

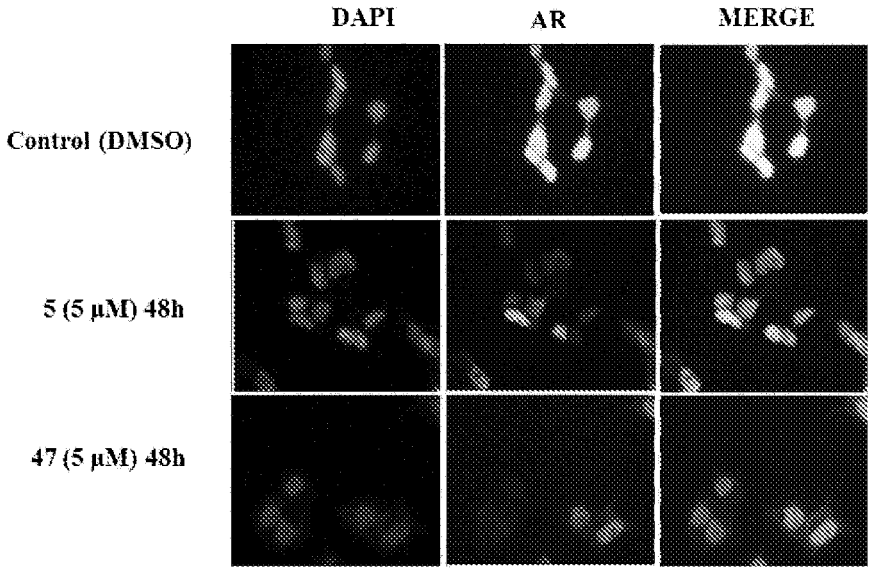


FIGURE 6D

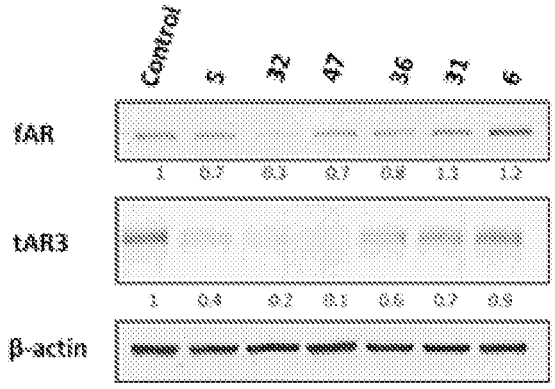


FIGURE 6E

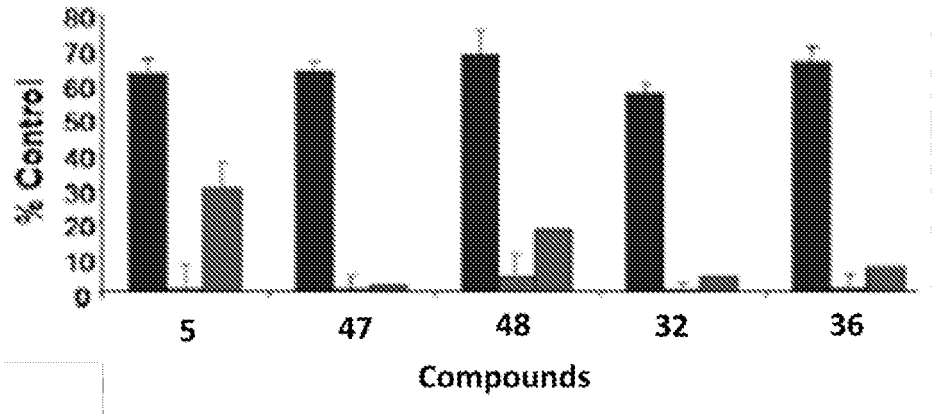


FIGURE 7

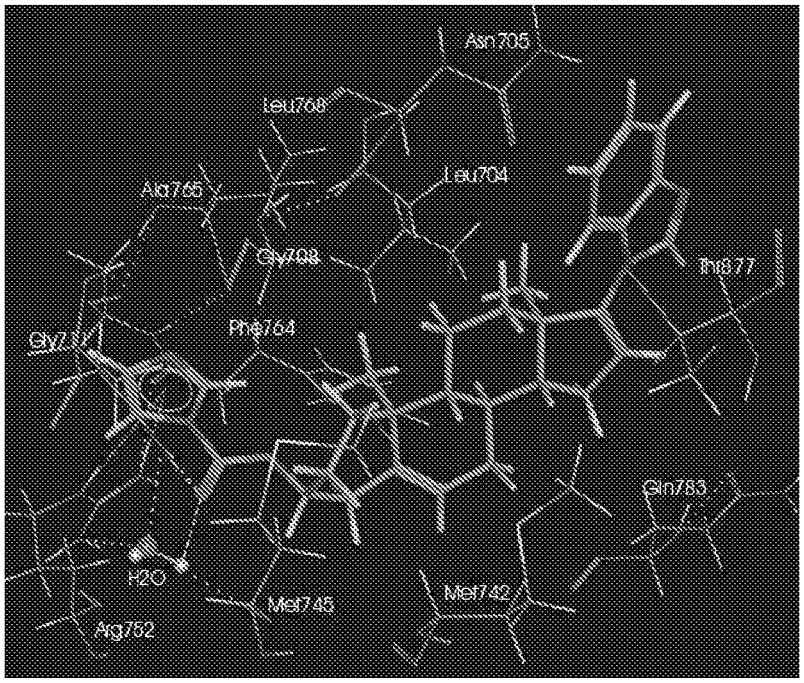


FIGURE 8A

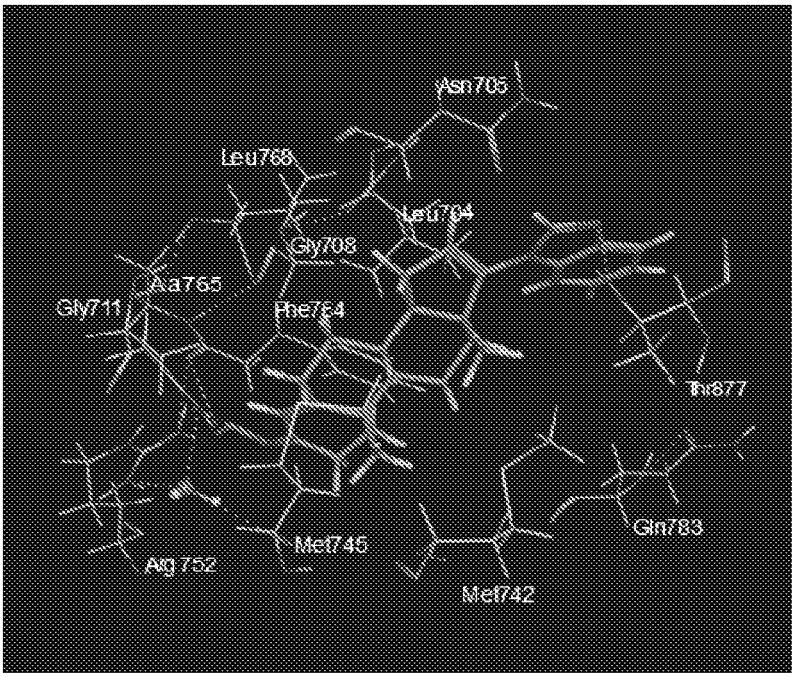
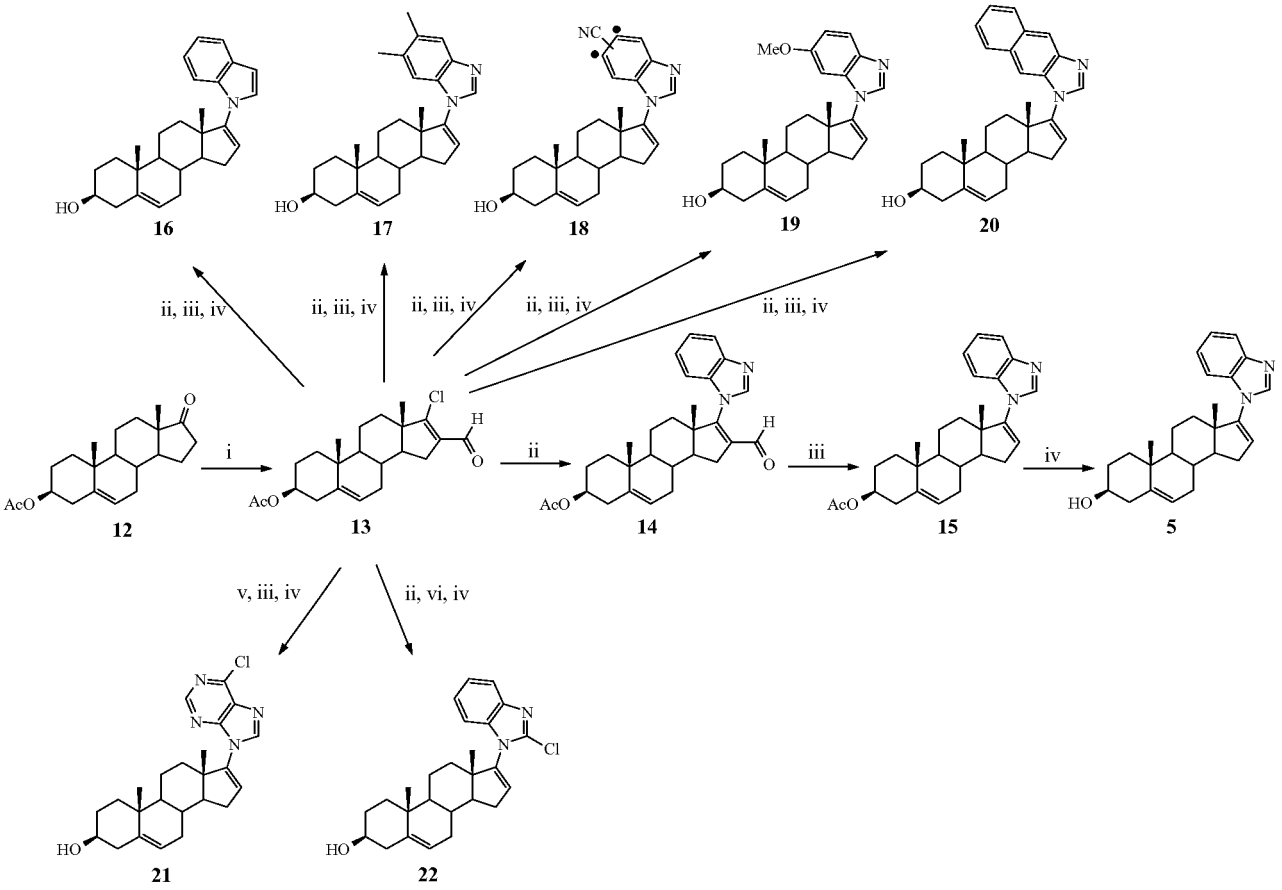
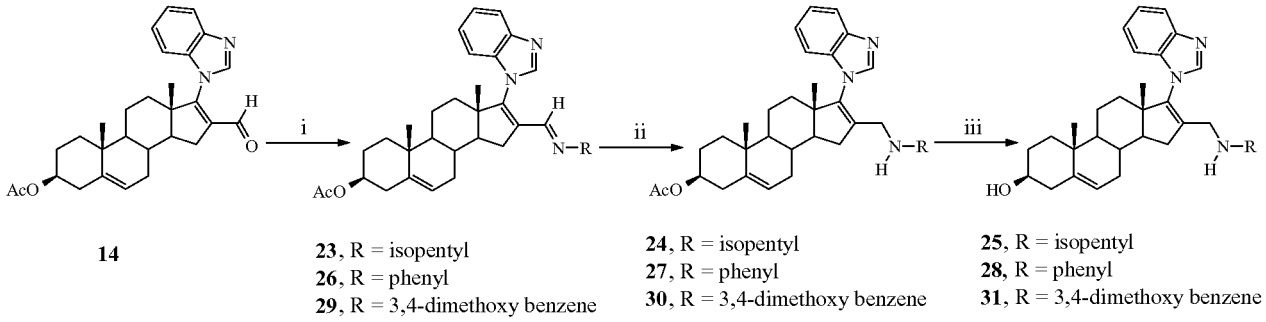


FIGURE 8B



[a]**Reagents and conditions:** (i) $POCl_3$-DMF, $CHCl_3$, Ar, reflux; (ii) benzimidazole or indole-3-carbaldehyde or 5,6-dimethylbenzimidazole or 5(6)-cyanobenzimidazole or 5(6)-methoxybenzimidazole or naphtho{2,3-d}imidazole, or 2-chlorobenzimidazole, K_2CO_3, DMF, Ar, 80° C (iii) 10% Pd on activated charcoal, PhCN, reflux; (iv) 10% methanolic KOH, Ar, rt (2 - 3 h). (v) 6-chloropurine, TBAF, THF, Ar, 50° C; (vi) chlorotri(triphenylphosphine)rhodium[I], $PhCH_3$, Ar, reflux.

FIGURE 9



14

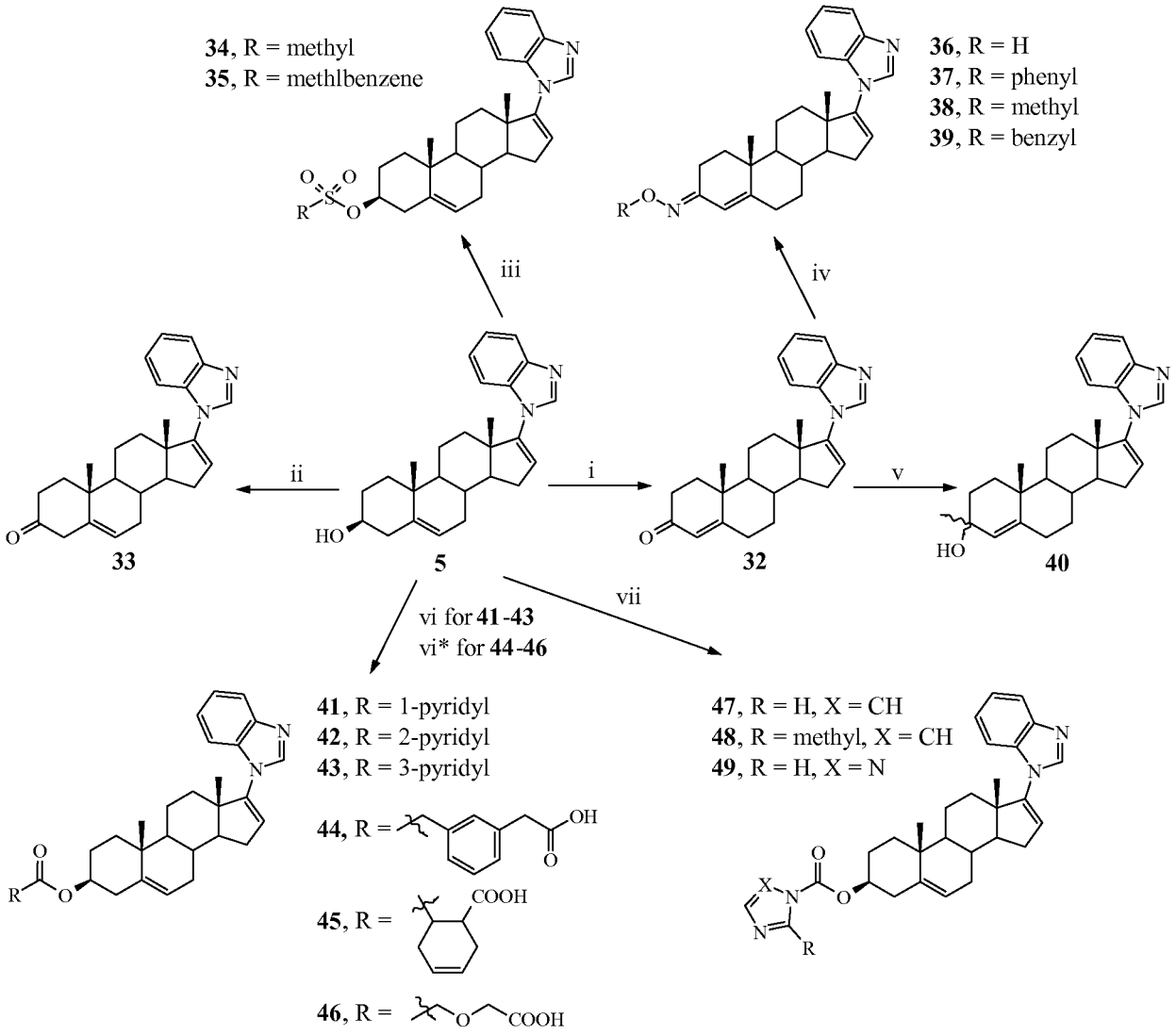
23, R = isopentyl
26, R = phenyl
29, R = 3,4-dimethoxy benzene

24, R = isopentyl
27, R = phenyl
30, R = 3,4-dimethoxy benzene

25, R = isopentyl
28, R = phenyl
31, R = 3,4-dimethoxy benzene

[a]**Reagents and conditions**: (i) substituted amines, molecular sieves, EtOH, Ar, reflux (3 - 7 h); (ii) MeOH, $NaBH_4$, ice cold (2 h), rt (3 h); (iii) MeOH, 10% methanolic-KOH, Ar, rt (2 - 3 h);

FIGURE 10



[a]**Reagents and conditions**: (i) $Al(i\text{-}PrO)_3$, 1-methyl-4-piperidone, toluene, reflux; (ii) Dess-Martin periodinane, MDC, 0° C, rt (5 h); (iii) Mesyl chloride or Tosyl chloride, Pyridine, ice cold (5 h), rt (5 h); (iv) substituted hydroxylamine HCl, sodium acetate, MeOH, EtOH, Ar, reflux (2 - 3 h); (v) MeLi, THF, Ar, -60° C (1 h) rt (2 h); (vi) pyridine-carboxylic acid, 2-methyl-6-nitobenzoic anhydride, DMAP, TEA, THF, rt (1 h); (vi*) acid anhydride, DMAP, pyridine, reflux; (vii) 1,1'-carbonylbisimidazole or 1,1'-carbonylbis(2-methylimidazole) or 1,1'-carbonyl-di-(1,2,4-triazole), CH_3CN, Ar, rt/reflux.

FIGURE 11