

Supplementary Materials

Modeling the aromatase inhibitor activity of indole-imidazole derivatives:
Quantitative structure activity relationship and molecular docking

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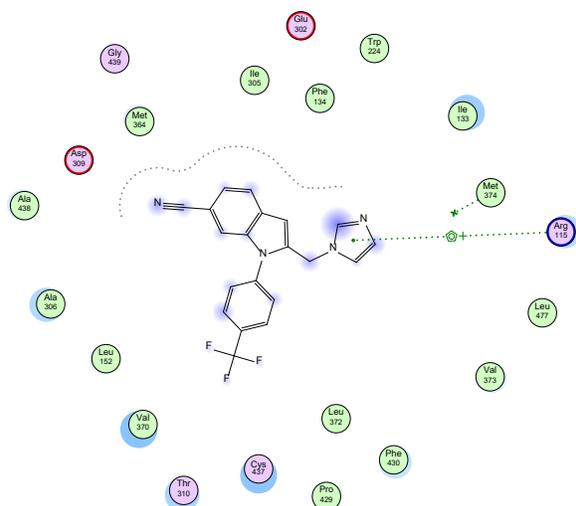


Figure S1. Interaction mode of compound 1 with the receptor 3EQM.

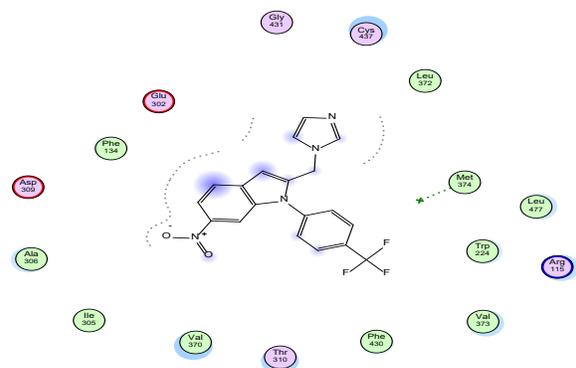


Figure S2. Interaction mode of compound 2 with the receptor 3EQM.

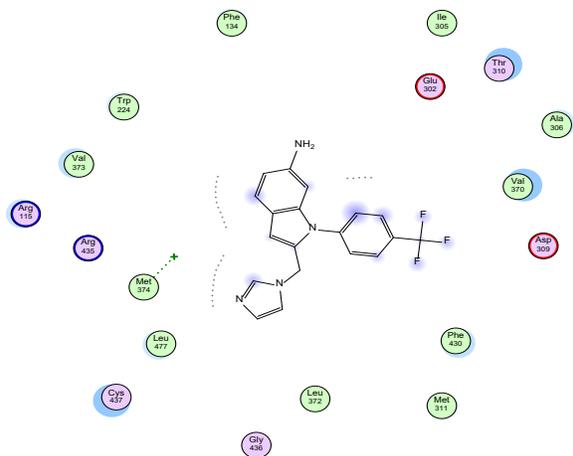


Figure S3. Interaction mode of compound 3 with the receptor 3EQM.

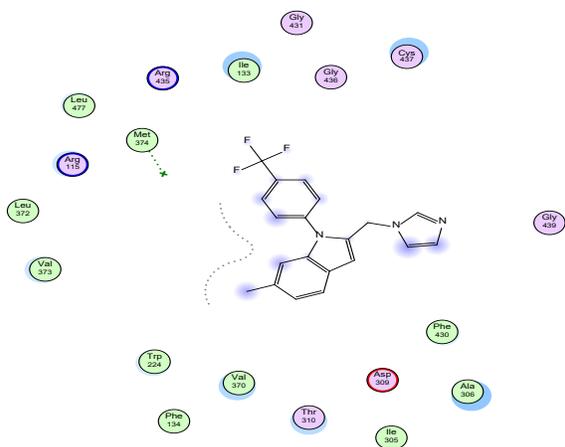


Figure S4. Interaction mode of compound 4 with the receptor 3EQM.

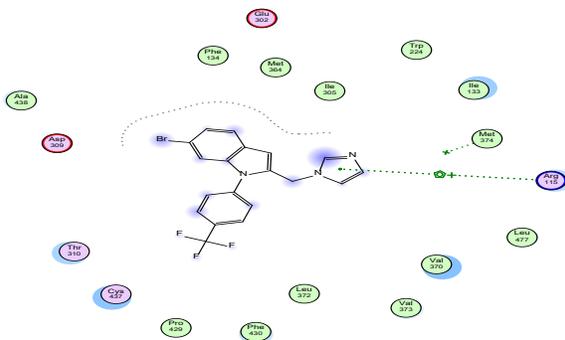


Figure S5. Interaction mode of compound 5 with the receptor 3EQM.

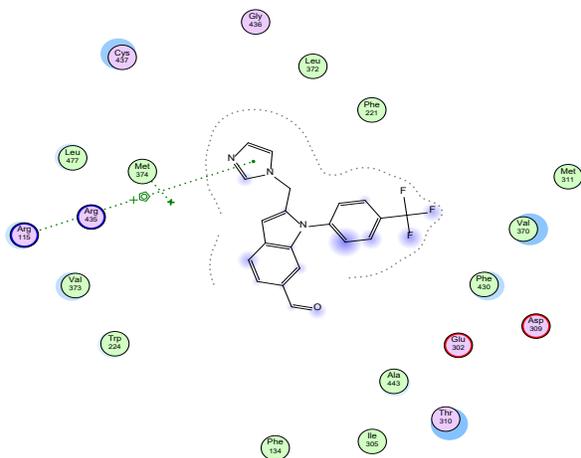


Figure S6. Interaction mode of compound 6 with the receptor 3EQM.

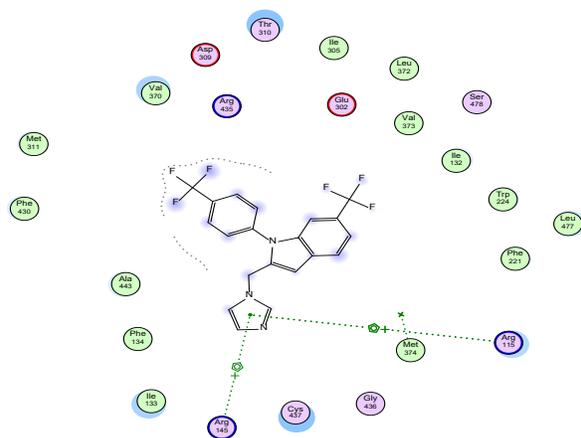


Figure S7. Interaction mode of compound 7 with the receptor 3EQM.

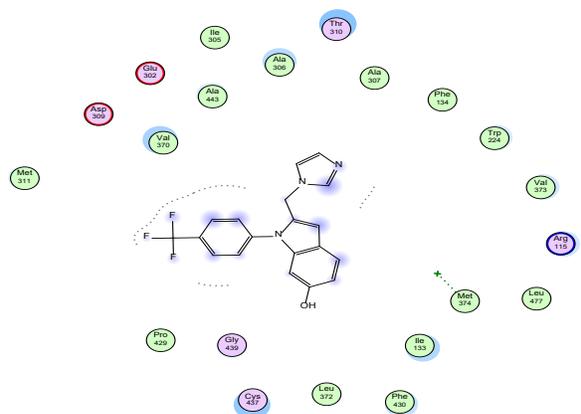


Figure S8. Interaction mode of compound 8 with the receptor 3EQM.

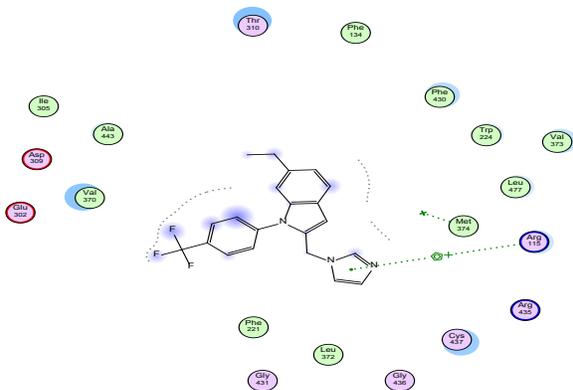


Figure S9. Interaction mode of compound 9 with the receptor 3EQM.

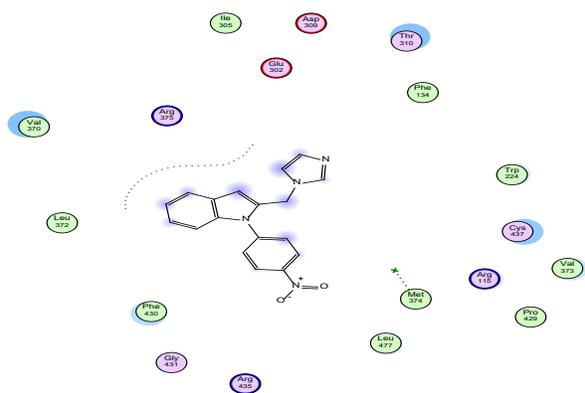


Figure S10. Interaction mode of compound 10 with the receptor 3EQM.

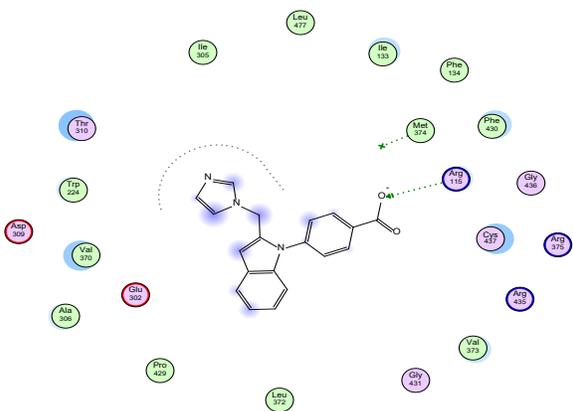


Figure S11. Interaction mode of compound 11 with the receptor 3EQM.

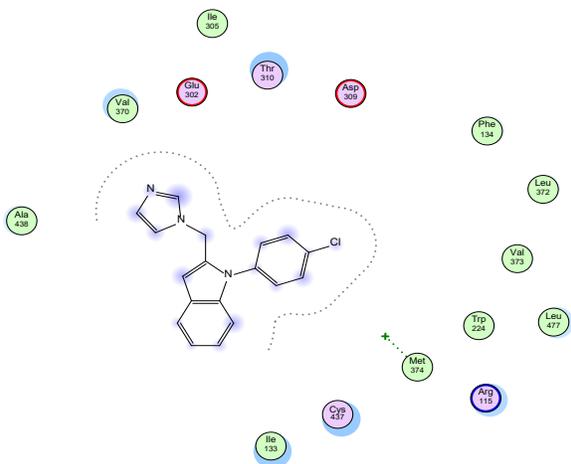


Figure S12. Interaction mode of compound 12 with the receptor 3EQM.

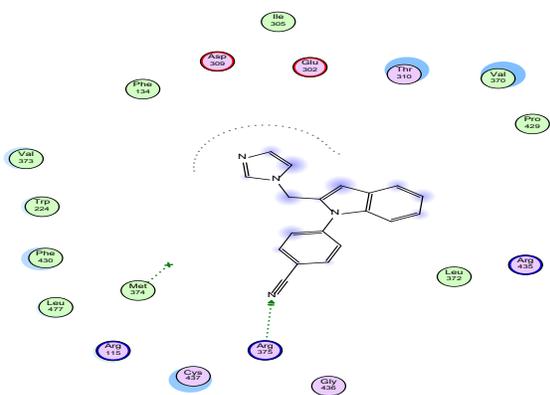


Figure S13. Interaction mode of compound 13 with the receptor 3EQM.

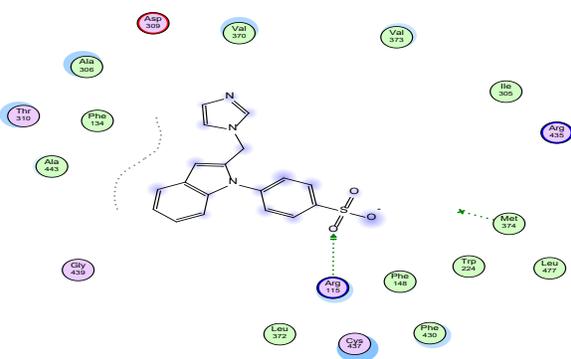


Figure S14. Interaction mode of compound 14 with the receptor 3EQM.

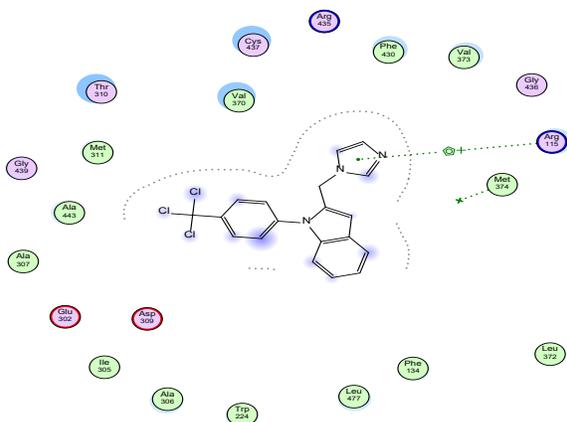


Figure S15. Interaction mode of compound 15 with the receptor 3EQM.

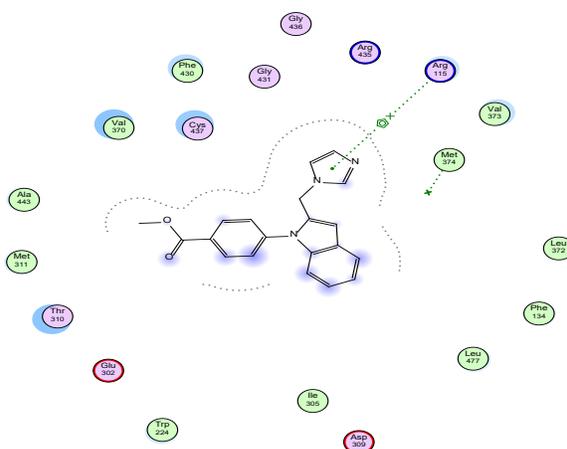


Figure S16. Interaction mode of compound 16 with the receptor 3EQM.

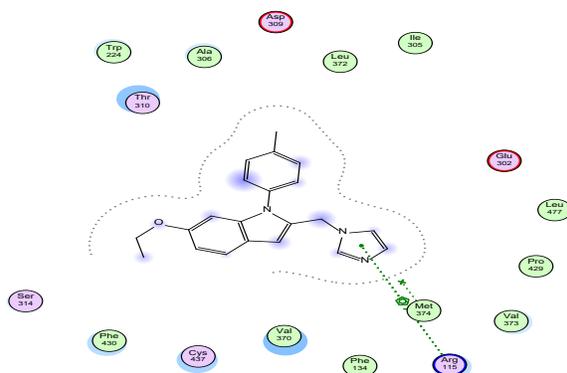


Figure S17. Interaction mode of compound 17 with the receptor 3EQM.

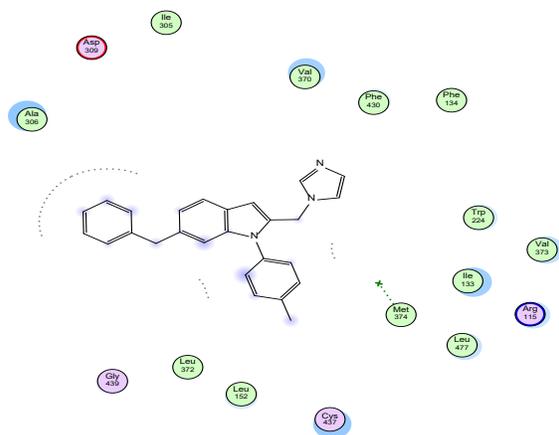


Figure S18. Interaction mode of compound 18 with the receptor 3EQM.

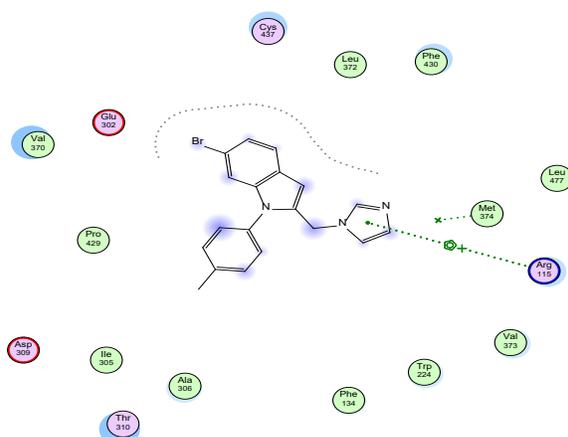


Figure S19. Interaction mode of compound 19 with the receptor 3EQM.

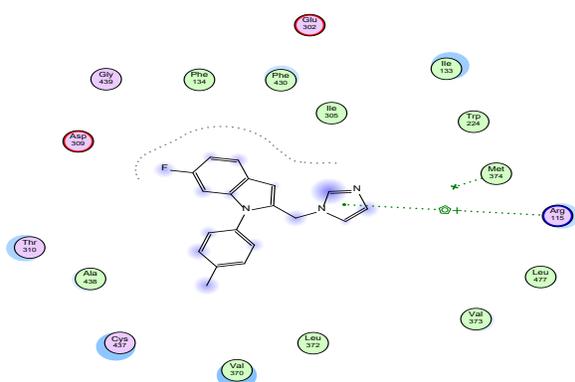


Figure S20. Interaction mode of compound 20 with the receptor 3EQM.

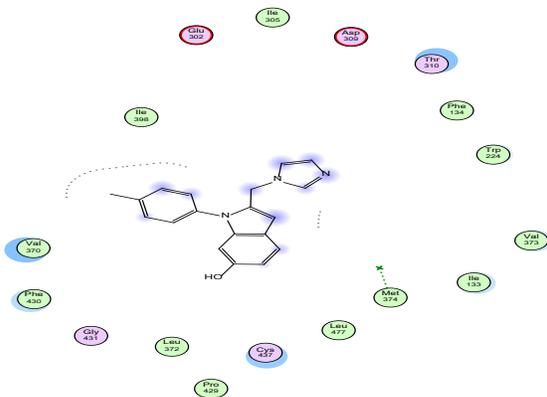


Figure S21. Interaction mode of compound 21 with the receptor 3EQM.

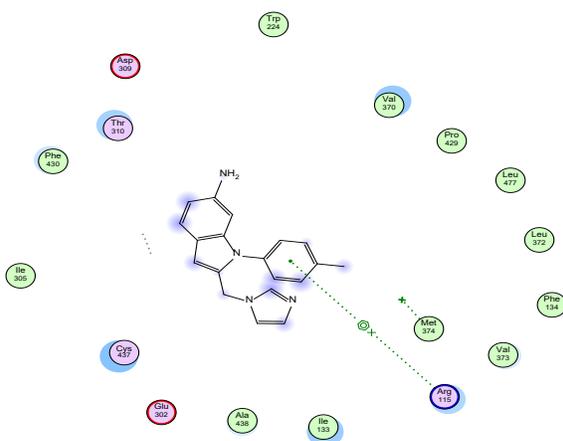


Figure S22. Interaction mode of compound 22 with the receptor 3EQM.

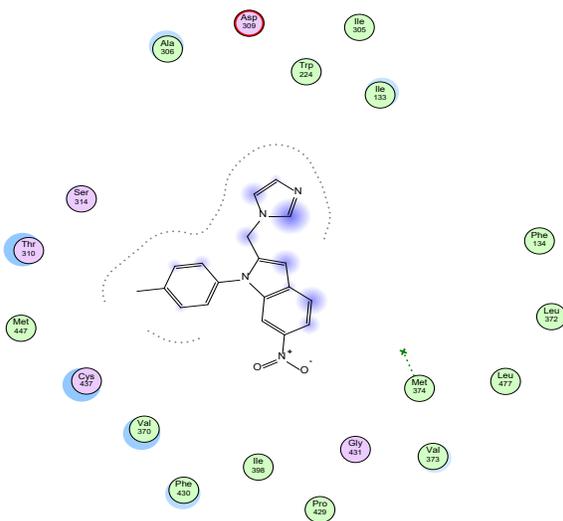


Figure S23. Interaction mode of compound 23 with the receptor 3EQM.

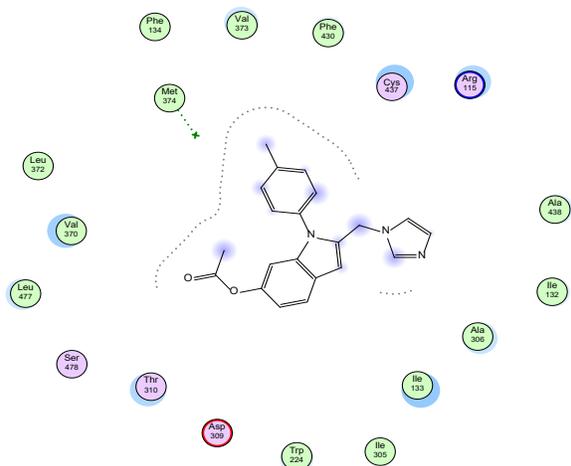


Figure S24. Interaction mode of compound 24 with the receptor 3EQM.

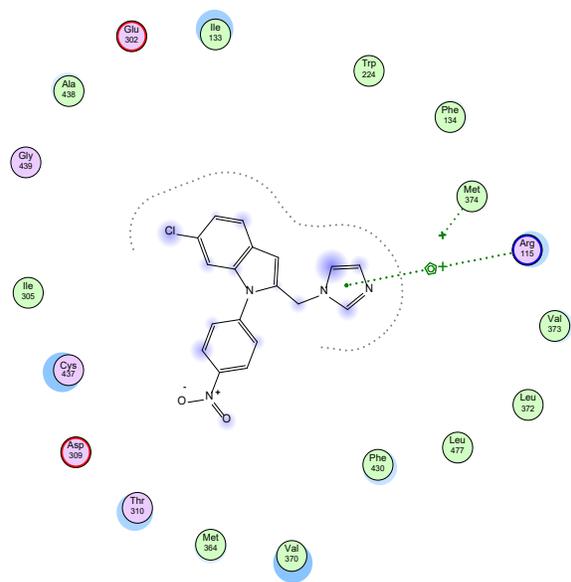


Figure S25. Interaction mode of compound 25 with the receptor 3EQM.

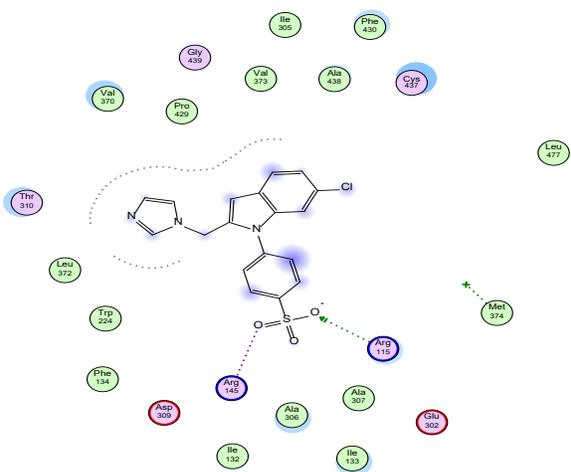


Figure S26 Interaction mode of compound 26 with the receptor 3EQM.

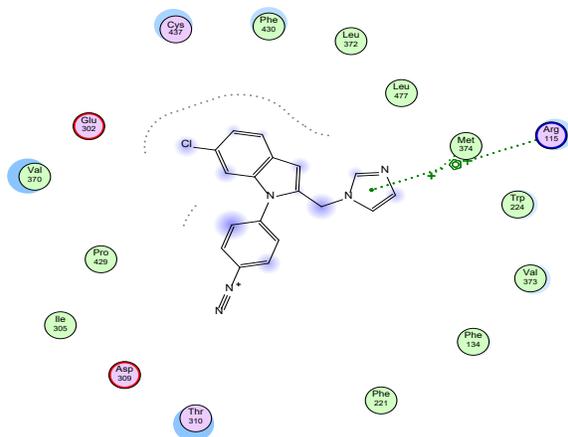


Figure S27. Interaction mode of compound 27 with the receptor 3EQM.

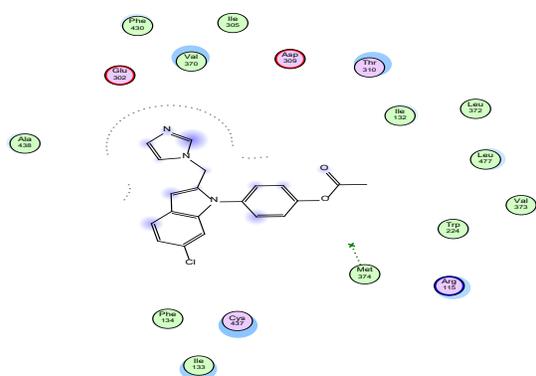


Figure S28. Interaction mode of compound 28 with the receptor 3EQM.

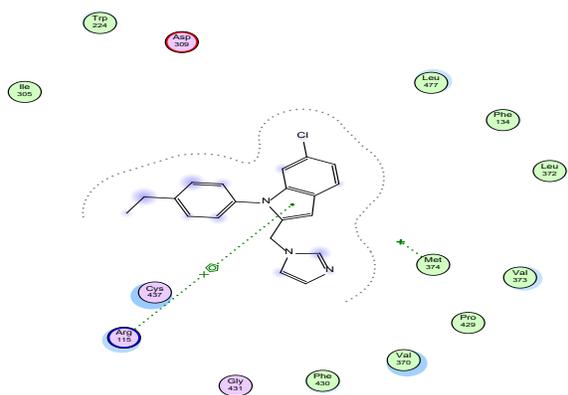


Figure S29. Interaction mode of compound 29 with the receptor 3EQM.

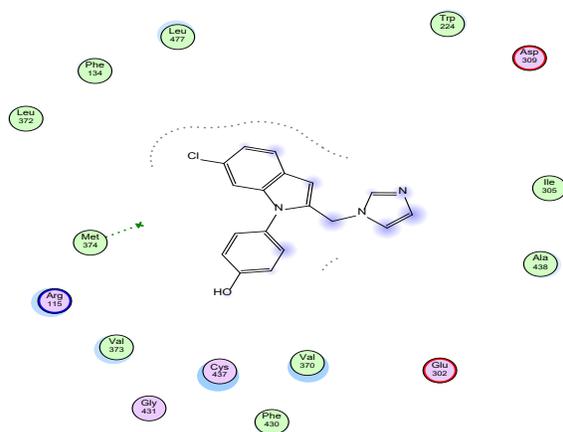


Figure S30. Interaction mode of compound 30 with the receptor 3EQM.

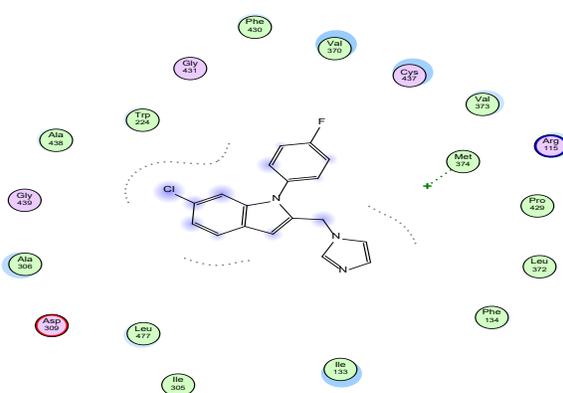


Figure S31. Interaction mode of compound 31 with the receptor 3EQM.

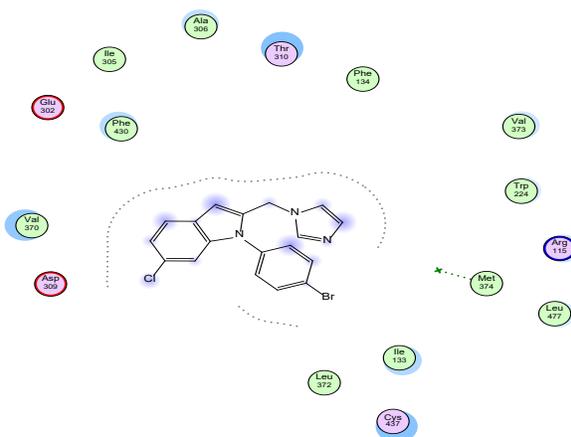


Figure S32. Interaction mode of compound 32 with the receptor 3EQM.

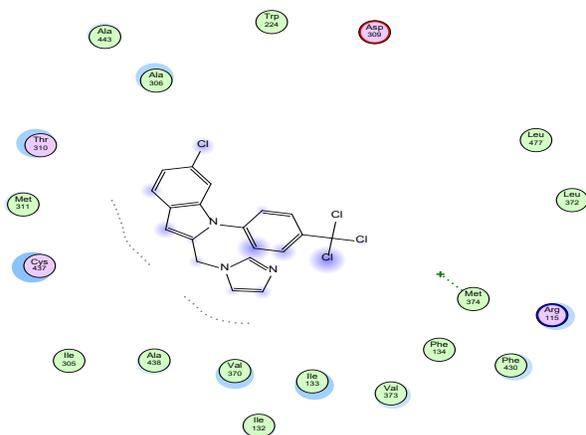


Figure S33. Interaction mode of compound 33 with the receptor 3EQM.

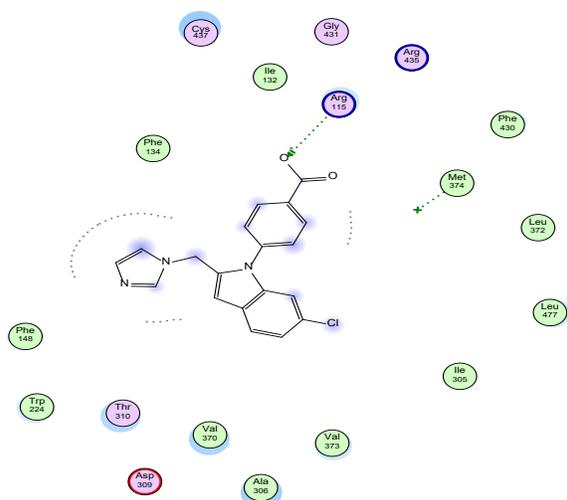


Figure S34. Interaction mode of compound 34 with the receptor 3EQM.

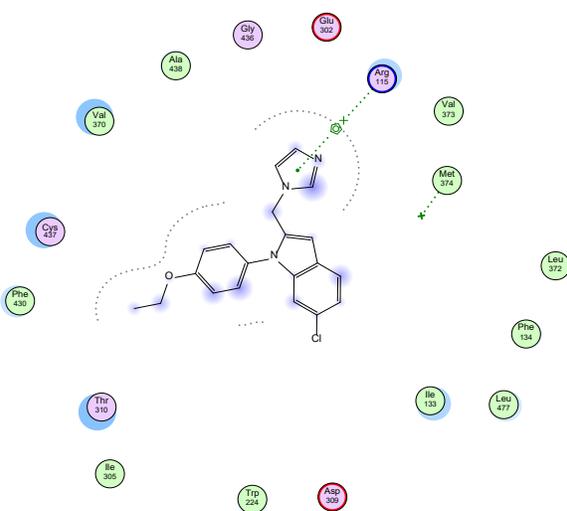


Figure S35. Interaction mode of compound 35 with the receptor 3EQM.

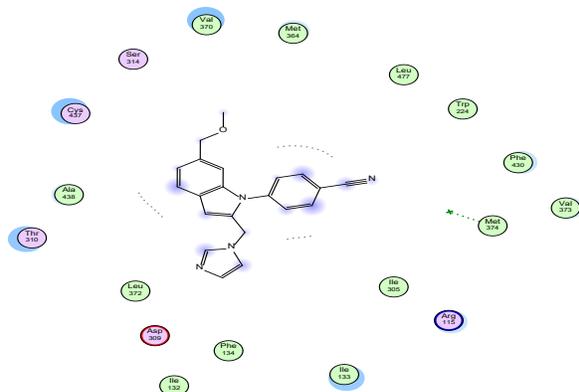


Figure S42. Interaction mode of compound 42 with the receptor 3EQM.

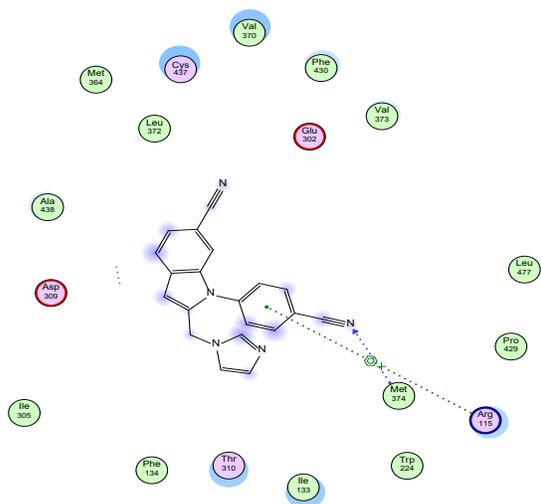


Figure S43. Interaction mode of compound 43 with the receptor 3EQM.

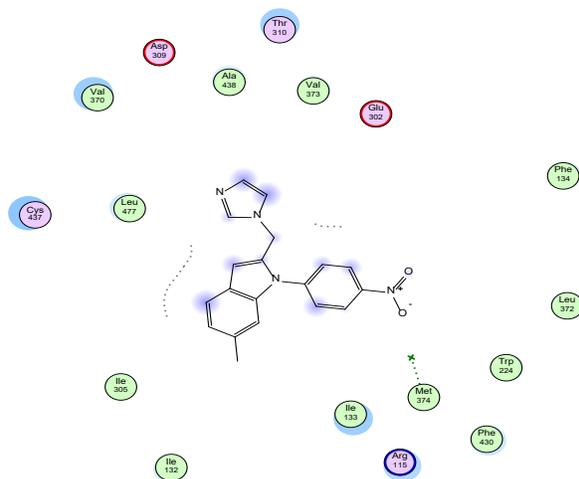


Figure S44. Interaction mode of compound 44 with the receptor 3EQM.

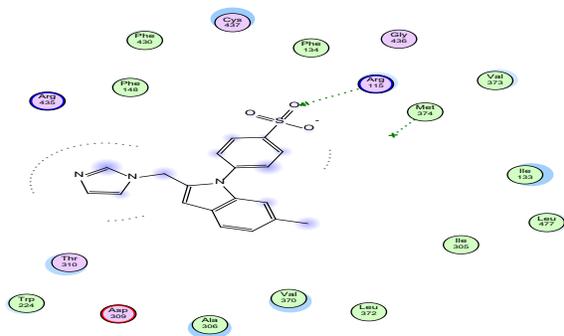


Figure S45. Interaction mode of compound 45 with the receptor 3EQM.

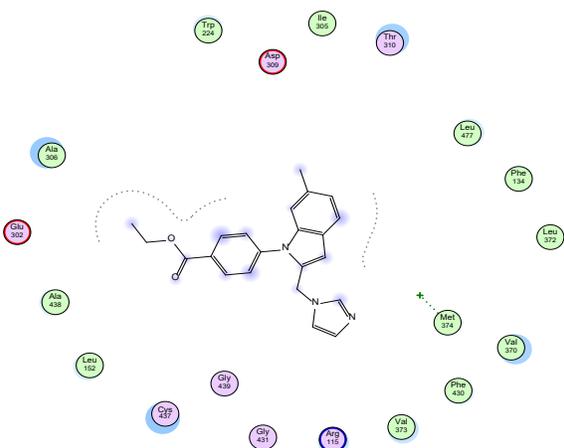


Figure S46. Interaction mode of compound 46 with the receptor 3EQM.

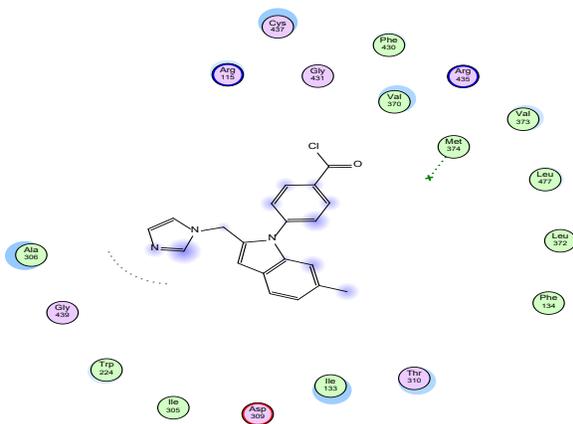


Figure S47. Interaction mode of compound 47 with the receptor 3EQM.

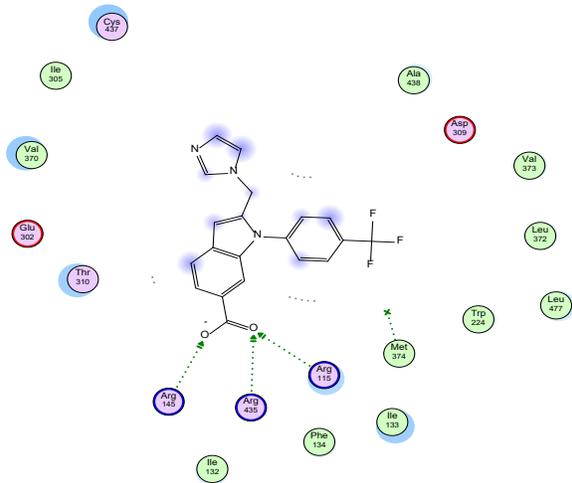


Figure S48. Interaction mode of compound 48 with the receptor 3EQM.

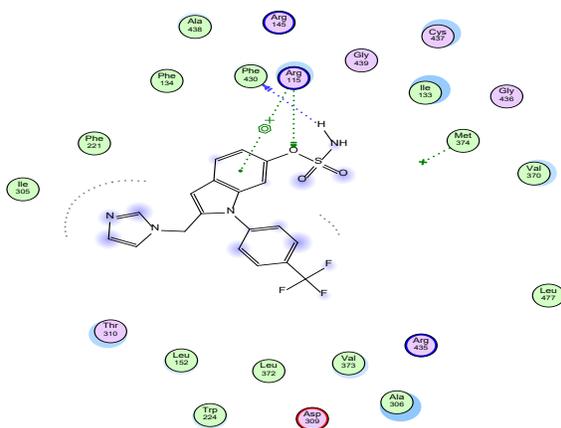


Figure S49. Interaction mode of compound 49 with the receptor 3EQM.

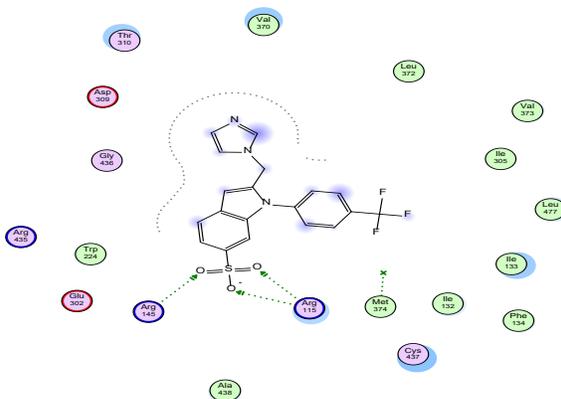


Figure S50. Interaction mode of compound 50 with the receptor 3EQM.

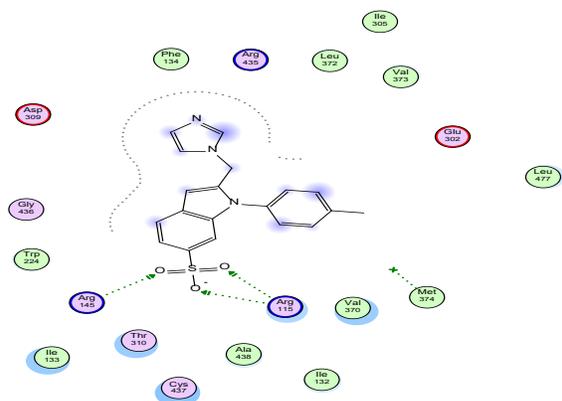


Figure S51. Interaction mode of compound 51 with the receptor 3EQM.

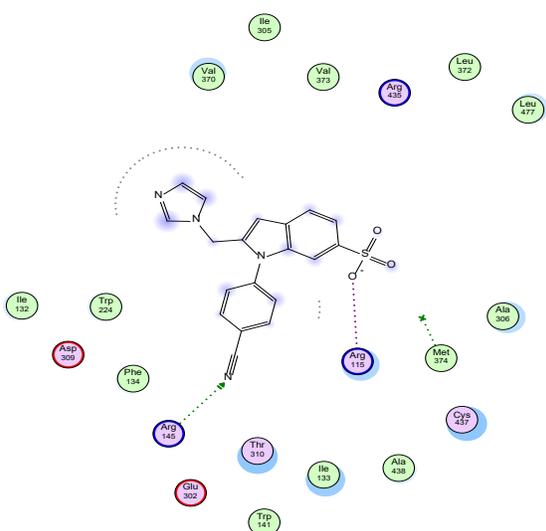


Figure S52. Interaction mode of compound 52 with the receptor 3EQM.

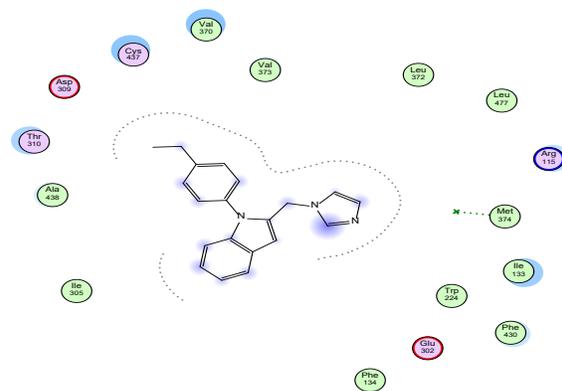


Figure S53. Interaction mode of compound 53 with the receptor 3EQM.

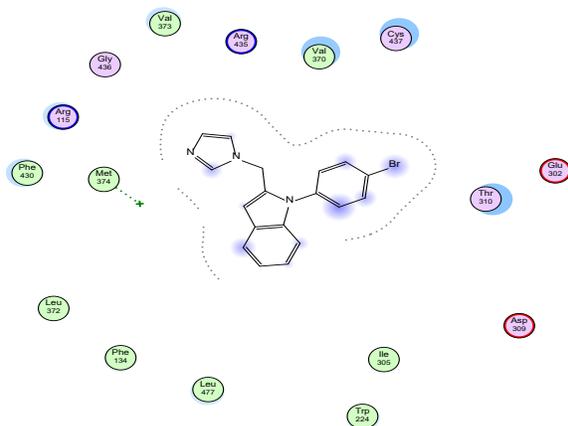


Figure S54. Interaction mode of compound 54 with the receptor 3EQM.

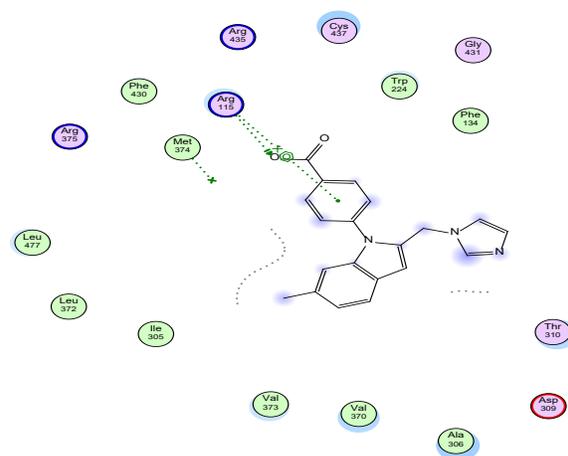


Figure S55. Interaction mode of compound 55 with the receptor 3EQM.

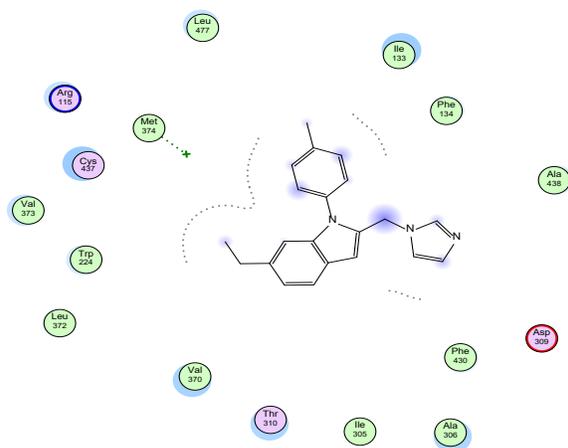


Figure S56. Interaction mode of compound 56 with the receptor 3EQM.

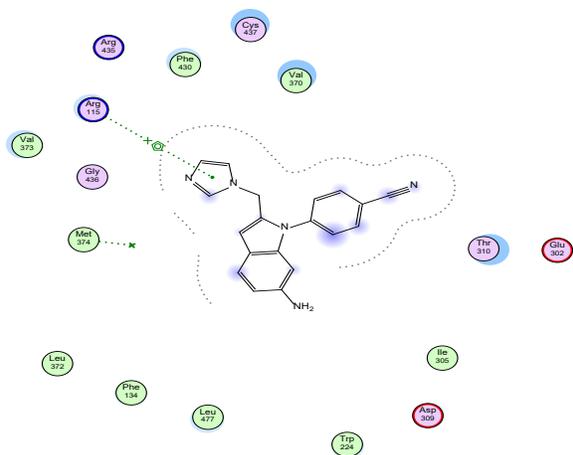


Figure S57. Interaction mode of compound 57 with the receptor 3EQM.

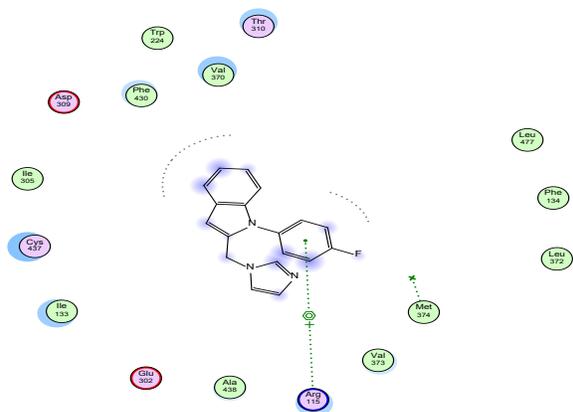


Figure S58. Interaction mode of compound 10 a with the receptor 3EQM.

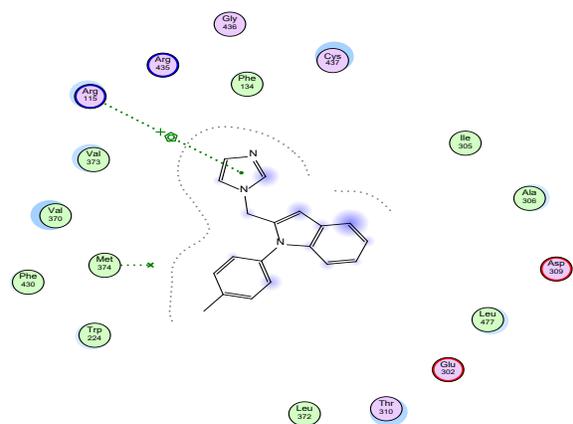


Figure S59. Interaction mode of compound 10 b with the receptor 3EQM.

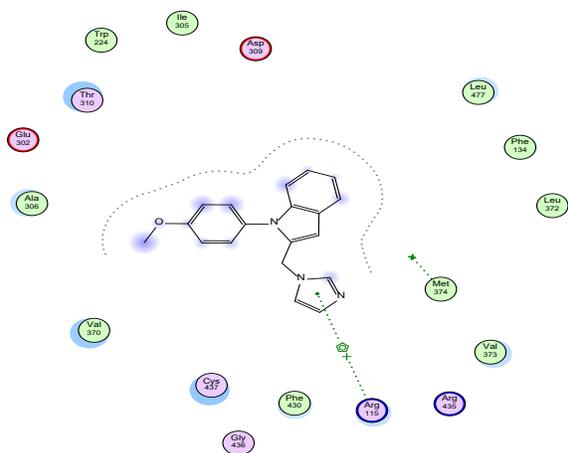


Figure S60. Interaction mode of compound 10 c with the receptor 3EQM.

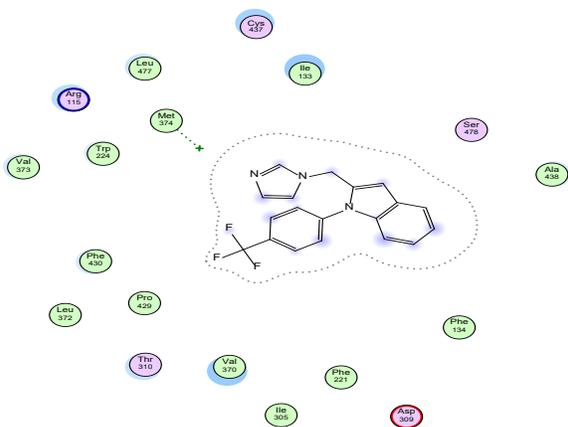


Figure S61. Interaction mode of compound 10 d with the receptor 3EQM.

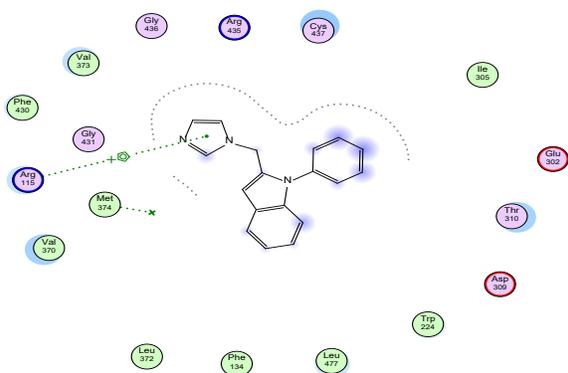


Figure S62. Interaction mode of compound 10 e with the receptor 3EQM.

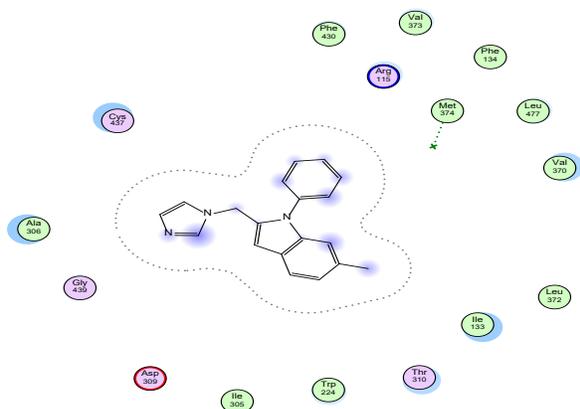


Figure S63. Interaction mode of compound 10 f with the receptor 3EQM.

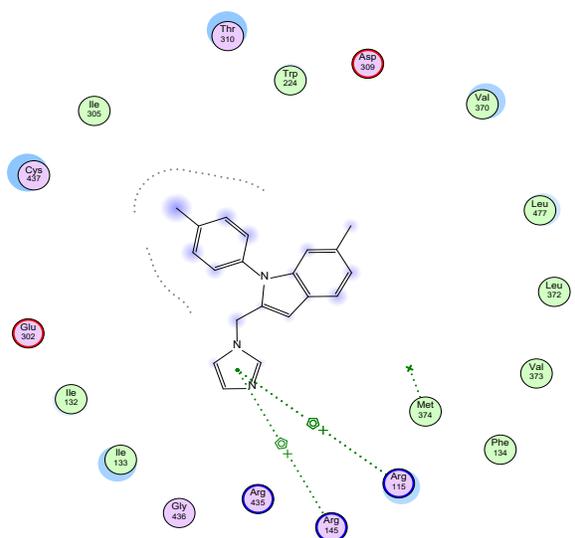


Figure S64. Interaction mode of compound 10 g with the receptor 3EQM.

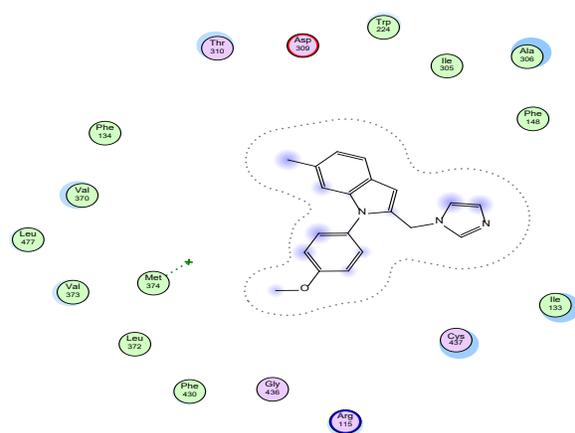


Figure S65. Interaction mode of compound 10 h with the receptor 3EQM.

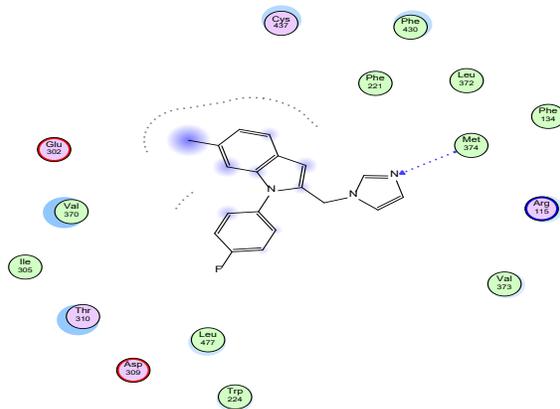


Figure S66. Interaction mode of compound 10 i with the receptor 3EQM.

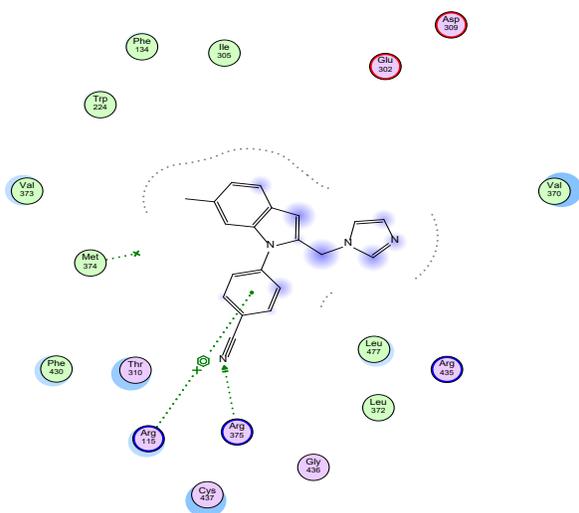


Figure S67. Interaction mode of compound 10 j with the receptor 3EQM.

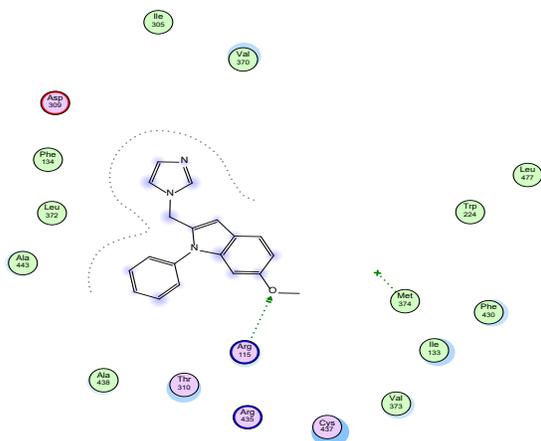


Figure S68. Interaction mode of compound 10 k with the receptor 3EQM.

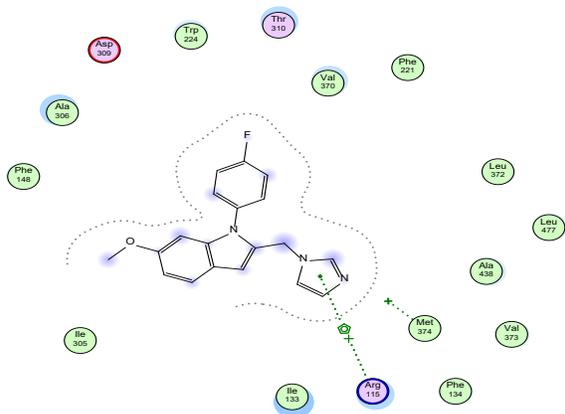


Figure S69. Interaction mode of compound 10 l with the receptor 3EQM.

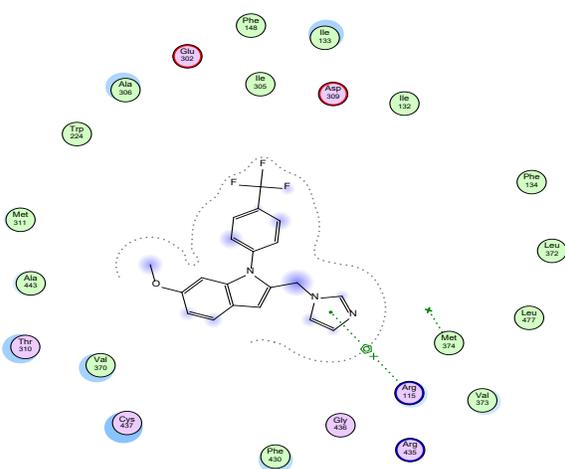


Figure S70. Interaction mode of compound 10 m with the receptor 3EQM.

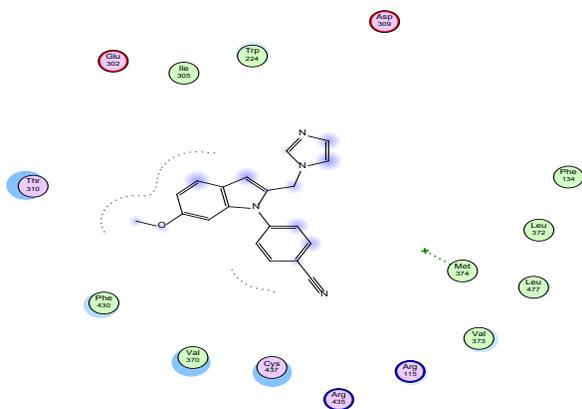


Figure S71. Interaction mode of compound 10 n with the receptor 3EQM.

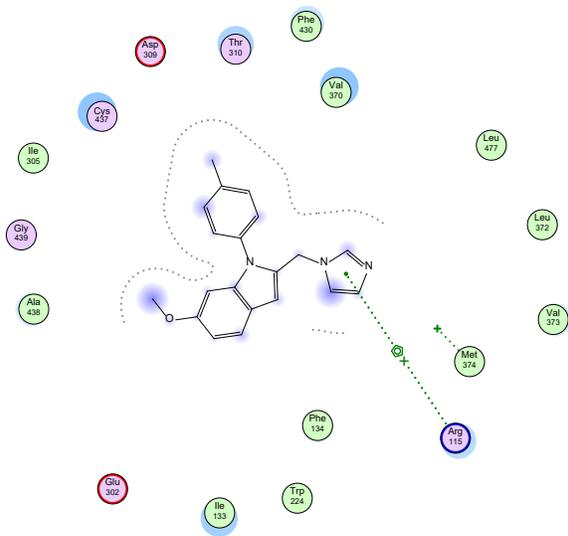


Figure S72. Interaction mode of compound 10 o with the receptor 3EQM.

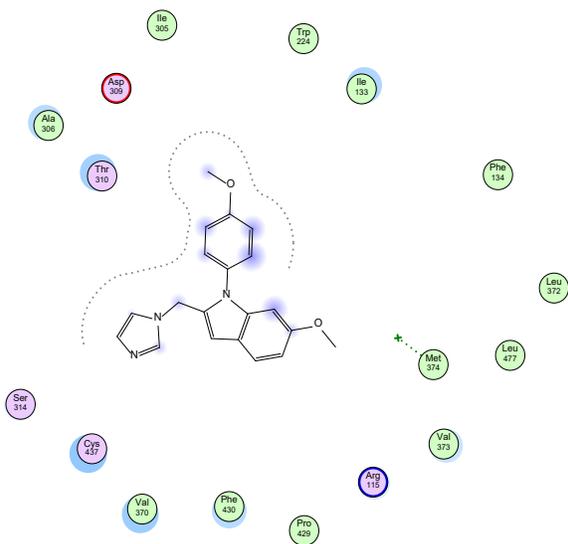


Figure S73. Interaction mode of compound 10 p with the receptor 3EQM.

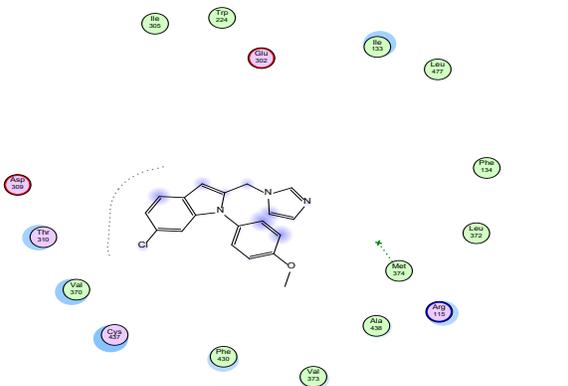


Figure S74. Interaction mode of compound 10 q with the receptor 3EQM.

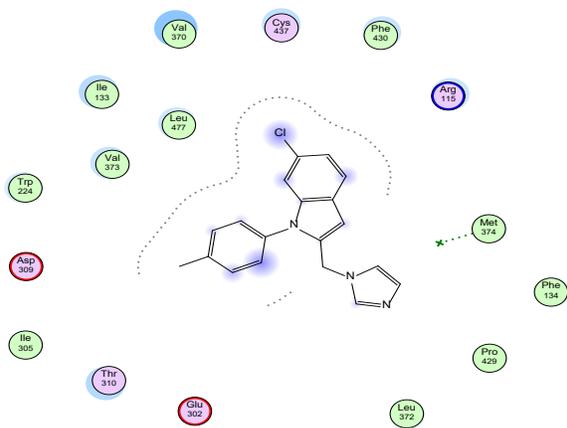


Figure S75. Interaction mode of compound 10 r with the receptor 3EQM.

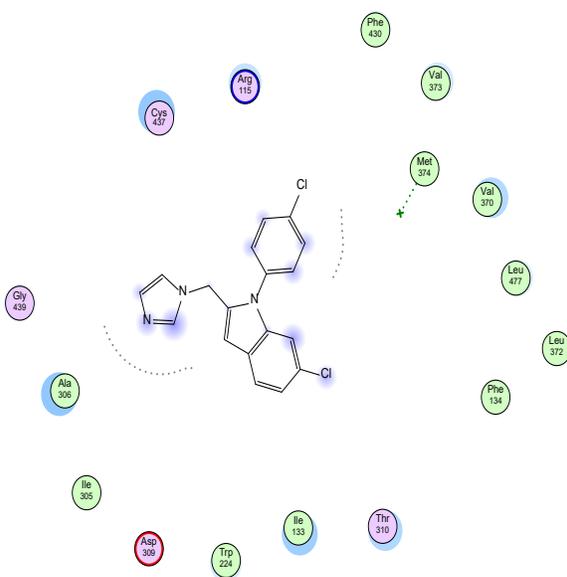
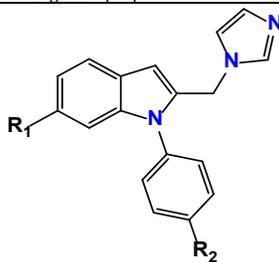
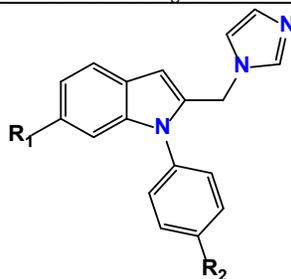


Figure S76. Interaction mode of compound 10 s with the receptor 3EQM.

Table S1. Docking study of indole imidazole derivatives from Wang *et al.* [21].

Compound	R ₁	R ₂	Bond energy (kcal/mole)	RMSD	Amino acid	Group of interaction	Type of interaction	Bond length
10a	H	F	-23.62	3.8	Arg115	Substituted Ph ring	π -cation	-
10b	H	CH ₃	-21.22	2.4	Arg115	Imidazole ring	π -cation	-
10c	H	OCH ₃	-21.68	1.2	Arg115	Imidazole ring	π -cation	-
10d	H	CF ₃	-19.50	1.8	No Interaction			
10e	H	H	-19.74	3.0	Arg115	Imidazole ring	π -cation	-
10f	CH ₃	H	-22.80	3.9	No interaction			
10g	CH ₃	CH ₃	-20.63	2.0	Arg115/ Arg145	Imidazole ring	π -cation	
10h	CH ₃	OCH ₃	-23.67	5.0	No interaction			
10i	CH ₃	F	-21.43	0.8	Met374	Imidazole ring	H-bond acceptor	2.09
10j	CH ₃	CN	-19.11	1.6	Ar115	Substituted Ph ring	π -cation	-
10j	CH ₃	CN	-19.11	1.6	Arg375	CN	H-bond acceptor	1.97
10k	OCH ₃	H	-21.05	2.8	Arg115	OCH ₃	H-bond acceptor	2.17
10l	OCH ₃	F	-22.90	3.0	Arg115	Imidazole ring	π -cation	-
10m	OCH ₃	CF ₃	-24.58	2.5	Arg115	Imidazole ring	π -cation	-
10n	OCH ₃	CN	-22.47	2.7	No interaction			-
10o	OCH ₃	CH ₃	-24.75	1.6	Arg115	Imidazole ring	π -cation	-
10p	OCH ₃	OCH ₃	-21.45	2.2	No interaction			
10q	Cl	OCH ₃	-23.16	1.7	No interaction			
10r	Cl	CH ₃	-19.37	1.0	No interaction			
10s	Cl	Cl	-23.95	4.4	No interaction			
Letrozole	-	-	-20.18	1.6	Arg115	Phenyl ring	π -cation	-

Table S2. Binding affinity, bond of interaction, and amino acid interaction of designed indole imidazole derivatives with the active site of aromatase.



Compound	R ₁	R ₂	RMSD	Bond energy	Amino acid	Group of interaction	Type of interaction	Bond length
1	CN	CF ₃	2.6	-22.80	Arg115	Imidazole ring	π-cation	-
2	NO ₂	CF ₃	4.6	-23.69	No interaction			
3	NH ₂	CF ₃	2.6	-20.92	No interaction			
4	CH ₃	CF ₃	2.0	-22.92	No interaction			
5	Br	CF ₃	1.8	-24.37	Arg115	Imidazole ring	π-cation	-
6	COH	CF ₃	4.6	-21.76	Arg115	Imidazole ring	π-cation	-
7	CF ₃	CF ₃	3.5	-22.00	Arg115	Imidazole ring	π-cation	-
8	OH	CF ₃	3.8	-20.19	No interaction			
9	CH ₂ CH ₃	CF ₃	3.0	-21.67	Arg115	Imidazole ring	π-cation	-
10	H	NO ₂	3.2	-23.63	No interaction	-	-	-
11	H	COOH	2.4	-24.80	Arg115	COOH	H-bond acceptor	1.99
12	H	Cl	2.7	-21.38	Arg115	Imidazole ring	π-cation	-
13	H	CN	2.6	-19.81	Arg375	CN	H-bond acceptor	2.18
14	H	SO ₃ H	2.9	-21.59	Arg115	SO ₃ H	H-bond acceptor	1.94
15	H	CCl ₃	2.1	-20.06	Arg115	Imidazole ring	π-cation	-
16	H	COOCH ₃	1.5	-22.66	Arg115	Imidazole ring	π-cation	-
17	OCH ₂ CH ₃	CH ₃	4.1	-21.64	Arg115	Imidazole ring	π-cation	-
18	CH ₂ Ph	CH ₃	3.2	-24.74	No interaction			
19	Br	CH ₃	1.8	-20.24	Arg115	Imidazole ring	π-cation	-
20	F	CH ₃	2.1	-22.27	No interaction			
21	OH	CH ₃	5.0	-25.09	No interaction			
22	NH ₂	CH ₃	5.4	-24.94	Arg115	Substituted Ph ring	π-cation	-
23	NO ₂	CH ₃	2.0	-19.55	No interaction			
24	OCOCH ₃	CH ₃	2.0	-23.18	No interaction			
25	Cl	NO ₂	2.4	-25.15	Arg115	Substituted Ph ring	π-cation	-
26	Cl	SO ₃ H	3.2	-22.73	Arg115	SO ₃ H	H-bond acceptor	1.68
					Arg145	SO ₃ H	H-bond acceptor	3.12
27	Cl	N ₂	1.0	-11.50	Ar115	Imidazole ring	π-cation	-
28	Cl	OCOCH ₃	1.7	-19.95	No interaction			
29	Cl	CH ₂ CH ₃	2.2	-22.48	Arg115	Indole ring	π-cation	-
30	Cl	OH	1.4	-20.20	No interaction			
31	Cl	F	2.8	-18.03	No interaction			
32	Cl	Br	3.6	-20.67	No interaction			
33	Cl	CCl ₃	2.5	-22.55	No interaction			
34	Cl	COOH	3.2	-25.44	Arg115	COOH	H-bond acceptor	1.93
35	Cl	OCH ₂ CH ₃	2.8	-23.78	Arg115	Imidazole ring	π-cation	-
36	Cl	COH	1.2	-22.61	No interaction			
37	Cl	COCH ₃	2.3	-24.87	No interaction			
38	Cl	CH ₂ OCH ₃	1.5	-24.67	Arg115	CH ₂ OCH ₃	H-bond acceptor	2.22
					Arg115	Substituted Ph ring on indole	π-cation	-
39	CCl ₃	CN	2.9	-18.85	No interaction			
40	COCl	CN	1.3	-23.71	Arg115	Substituted Ph ring	π-cation	-
					Met374	H-bond acceptor	COCL	2.11
					Ar375	H-bond acceptor	CN	1.91
41	CF ₃	CN	1.6	-19.22	Arg375	CN	H-bond acceptor	1.96
					Arg115	Substituted Ph ring on indole	π-cation	-
42	CH ₂ OCH ₃	CN	3.5	-23.27	No interaction			
43	CN	CN	1.5	-25.09	Met374	CN	H-bond acceptor	2.29
					Arg115	Substituted Ph ring on indole	π-cation	-
44	CH ₃	NO ₂	1.6	-20.83	No interaction			
45	CH ₃	SO ₃ H	3.5	-17.72	Arg115	SO ₃ H	H-bond acceptor	1.91
46	CH ₃	COOCH ₂ CH ₃	2.5	-23.99	No interaction			
47	CH ₃	COCl	2.5	-24.80	No interaction			
48	COOH	CF ₃	1.5	-27.69	Arg435	COOH	H-bond acceptor	2.29
					Arg145	COOH	H-bond acceptor	2.19
					Arg115		H-bond acceptor	1.84
49	OSO ₂ NH ₂	CF ₃	2.6	-18.35	Arg115	Imidazole ring	π-cation	-
					Arg115	OSO ₂ NH ₂	H-bond acceptor	2.43
					Phe430	OSO ₂ NH ₂	H-bond donor	2.17
50	SO ₃ H	CF ₃	2.3	-18.30	Arg115	SO ₃ H	H-bond acceptor	2.33
					Arg115	SO ₃ H	H-bond acceptor	1.87

51	SO ₃ H	CH ₃	1.4	-17.77	Arg145	SO ₃ H	H-bond acceptor	1.94
					Arg115	SO ₃ H	H-bond acceptor	2.33
					Arg115	SO ₃ H	H-bond acceptor	1.85
52	SO ₃ H	CN	2.0	-21.32	Arg145	SO ₃ H	H-bond acceptor	1.94
					Arg115	SO ₃ H	H-bond acceptor	3.15
					Arg145	CN	H-bond acceptor	2.28
53	H	CH ₂ CH ₃	3.0	-23.84	No interaction			
54	H	Br	1.9	-21.92	No interaction			
55	CH ₃	COOH	2.5	-25.33	Arg115	COOH	H-bond acceptor	2.02
					Arg115	Substituted Ph ring on indole	π-cation	-
56	CH ₂ CH ₃	CH ₃	1.4	-23.97	No interaction			
57	NH ₂	CN	2.9	-20.68	Arg115	Substituted Ph ring on indole	π-cation	-