

**In silico study on β -aminoketone derivatives as thyroid hormone receptor
inhibitors: a combined 3D-QSAR and molecular docking study**

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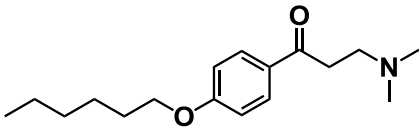
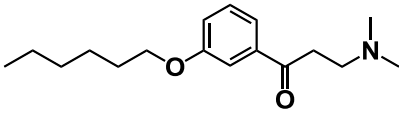
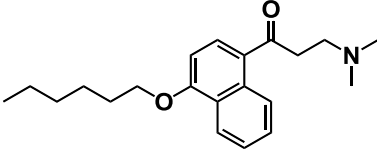
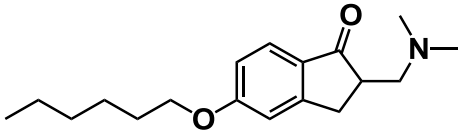
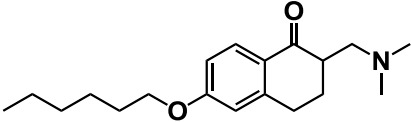
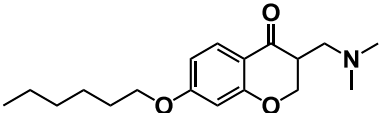
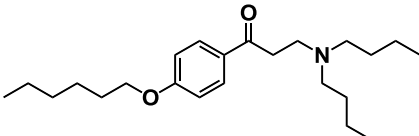
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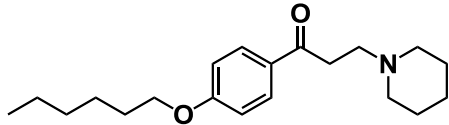
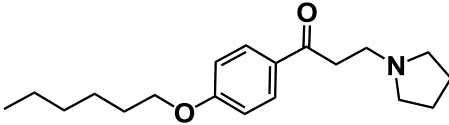
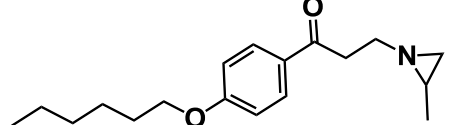
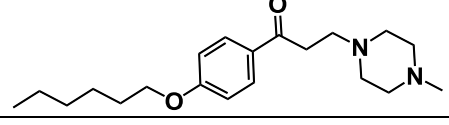
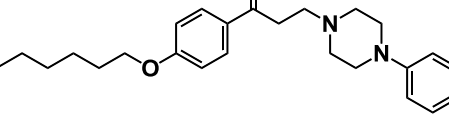
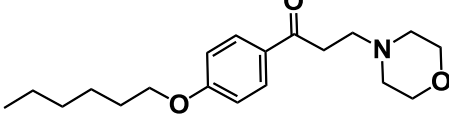
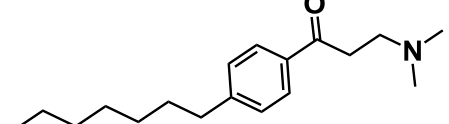
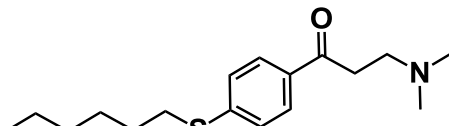
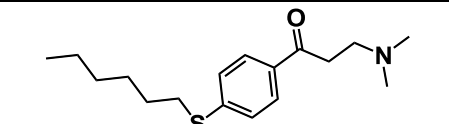
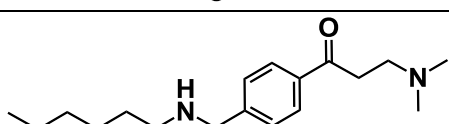
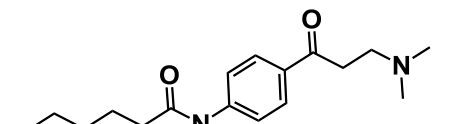
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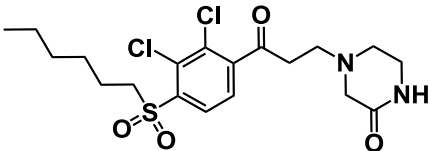
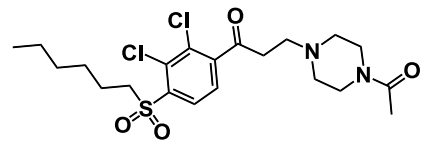
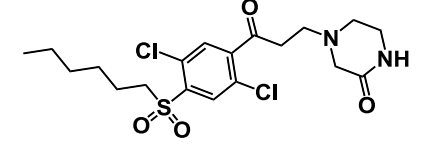
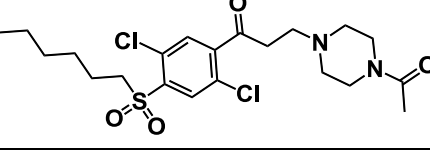
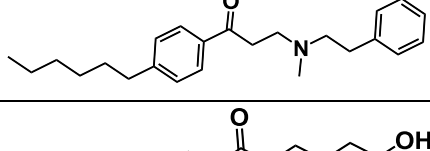
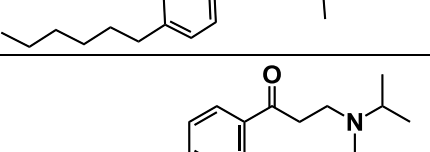
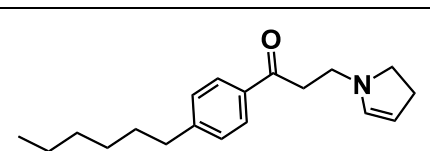
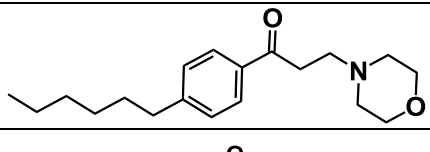
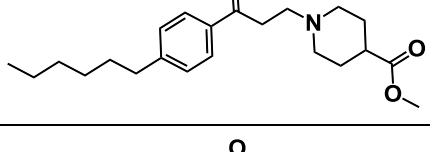
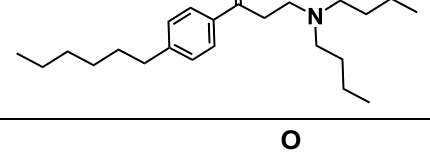
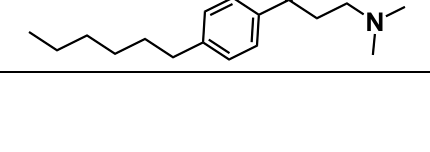

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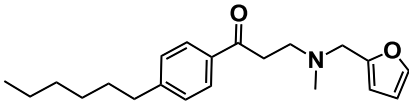
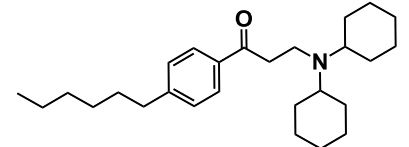
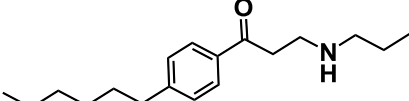
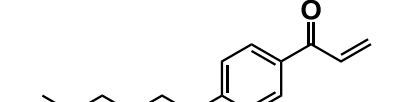
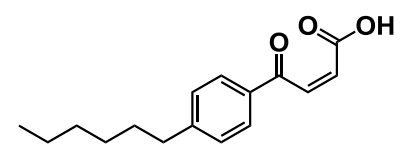
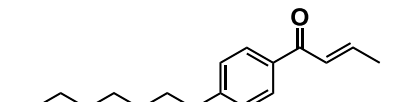
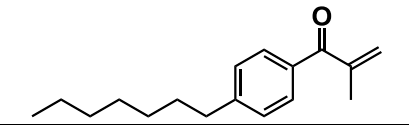
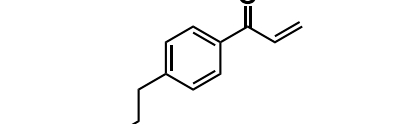
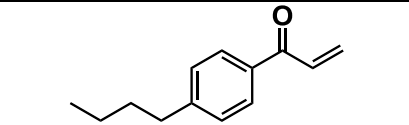
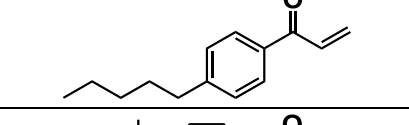
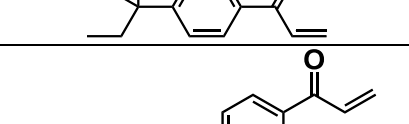
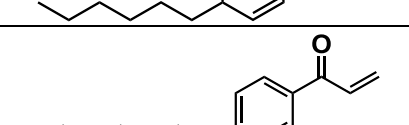
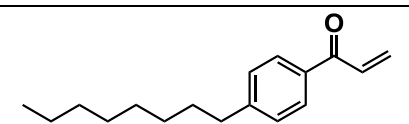

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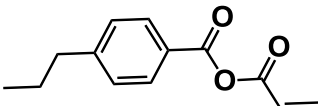
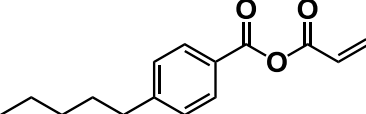
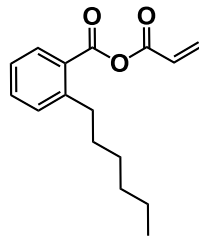
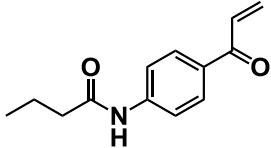
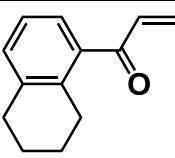
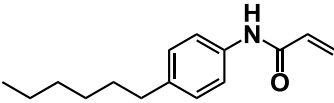
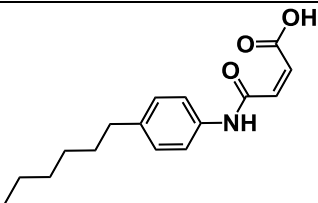
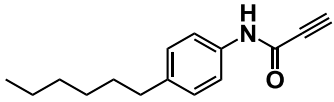
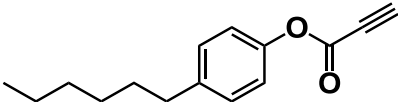
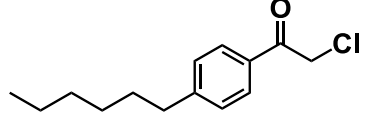
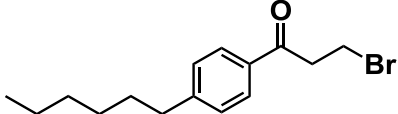
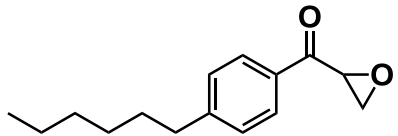
Table S1. Molecular structures of Indane Derivatives and their TR β binding affinity values (pIC₅₀).

Compound	Structure	TR β 1 pK _i	TR α 1 pK _i
1		4.7825	-
2		5.1487	-
3		5.3979	-
4		5.7696	-
5		5.6383	-
6		5.7959	-
7		5.5686	-

8		5.041 ^a	-
9		4.7235	-
10		4.6576 ^a	-
11		5.2518	-
12		5.4202	-
13		5.3872 ^a	-
14		5.0177 ^a	-
15		5.2291	-
16		5.3098 ^a	-
17		5.0915 ^a	-
18		4.9066	-

19		6.0969	-
20		6.0000 ^a	-
21		6.2218	-
22		6.0969	-
23		5.8239	5.4437
24		5.7959	5.5229
25		5.6990	5.3872
26		5.5686 ^a	5.3665
27		5.5686	5.3872
28		5.4089	5.2007
29		5.3768 ^a	5.1612 ^a
30		5.3665	4.9747 ^a

31		4.9172 ^a	4.6459 ^a
32		4.8962	4.7825
33		4.8182	4.5884
34		5.8239 ^a	4.5513 ^a
35		4.7520	4.7167
36		5.1192	4.7235
37		4.6345 ^a	4.2765 ^a
38		4.0000	-
39		4.1805	4.1487
40		4.4698	4.2154
41		4.3615 ^a	4.1574 ^a
42		4.7305	4.3449
43		4.9788	4.6383
44		4.9431	4.6696

45		4.2147	-
46		4.2534	-
47		5.0862	4.4078
48		4.0660	-
49		4.1561	4.0691
50		4.6925 ^a	4.6655 ^a
51		4.7471	4.757
52		4.4547	4.1618
53		5.2076	4.7773
54		4.6364	4.3215
55		5.5229	5.3768
56		4.719	4.4789

^a represents the test set.

Table S2. Summary of QSAR results for TR β based on superimposition I .

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R ² _{cv}	0.604	0.387	0.395	0.481	0.054	0.259	0.495	0.444	0.396
R ² _{ncv}	0.922	0.770	0.871	0.984	0.318	0.741	0.921	0.986	0.942
SEE	0.174	0.291	0.230	0.084	0.515	0.317	0.178	0.080	0.162
F	108.852	65.197	39.326	225.05	4.317	26.406	83.886	221.474	57.473
R ² _{pred}	0.5580	0.6481	0.4691	0.5734	0.0722	0.1999	0.5486	0.5452	0.3009
SEP	0.392	0.475	0.499	0.483	0.606	0.536	0.449	0.508	0.521
N _C	4	2	6	9	4	4	5	10	9
Field contribution									
S	0.578	1.000	-	-	-	-	0.396	0.366	0.815
E	0.422	-	1.000	-	-	-	0.604	-	-
H	-	-	-	1.000	-	-	-	0.634	-
D	-	-	-	-	1.000	-	-	-	0.185
A	-	-	-	-	-	1.000	-	-	-
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R ² _{cv}	0.401	0.391	0.345	0.398	0.310	0.384	0.315	0.456	0.439
R ² _{ncv}	0.969	0.676	0.561	0.884	0.730	0.982	0.787	0.957	0.930
SEE	0.116	0.346	0.402	0.221	0.320	0.089	0.300	0.133	0.170
F	129.753	40.665	24.870	37.041	34.212	224.54	17.915	129.491	77.370
R ² _{pred}	0.4244	0.5139	0.4560	0.4653	0.4747	0.6302	0.0241	0.6069	0.4845
SEP	0.511	0.474	0.491	0.505	0.511	0.518	0.538	0.473	0.480
N _C	8	2	2	7	3	8	7	6	6
Field contribution									
S	0.499	-	-	-	-	-	-	0.249	0.360
E	-	0.620	0.648	0.565	-	-	-	0.413	0.514
H	-	0.380	-	-	0.568	0.561	-	0.338	-
D	-	-	0.352	-	0.432	-	0.240	-	0.125
A	0.501	-	-	0.435	-	0.439	0.760	-	-
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R ² _{cv}	0.478	0.393	0.395	0.381	0.392	0.403	0.361	0.358	0.426
R ² _{ncv}	0.943	0.809	0.984	0.930	0.798	0.919	0.752	0.838	0.842
SEE	0.154	0.269	0.083	0.172	0.276	0.180	0.306	0.250	0.245
F	95.668	53.597	254.416	64.221	50.029	81.512	38.419	48.007	67.443
R ² _{pred}	0.5717	0.6209	0.6125	0.1750	0.6114	0.7277	0.4138	0.3137	0.6680
SEP	0.463	0.479	0.513	0.511	0.480	0.488	0.492	0.499	0.466
N _C	6	3	8	7	3	5	3	4	3
Field contribution									

S	0.283	0.256	0.253	0.399	-	-	-	-	0.188
E	0.412	-	-	-	0.373	0.355	0.404	-	0.306
H	-	0.404	0.393	-	0.353	0.343	-	0.391	0.276
D	-	0.340	-	0.181	0.274	-	0.271	0.261	0.230
A	0.305	-	0.354	0.420	-	0.302	0.325	0.348	-
CoMSIA									
	SEHA	SEDA	SHDA	EHDA	SEHDA				
R^2_{cv}	0.447	0.435	0.394	0.391	0.413				
R^2_{ncv}	0.969	0.897	0.870	0.846	0.832				
SEE	0.115	0.203	0.225	0.244	0.252				
F	151.282	62.523	61.959	50.871	62.786				
R^2_{pred}	0.6599	0.4685	0.3728	0.5946	0.6330				
SEP	0.484	0.475	0.485	0.486	0.471				
N_c	7	5	4	4	3				
Field contribution									
S	0.191	0.235	0.196	-	0.147				
E	0.301	0.355	-	0.285	0.245				
H	0.276	-	0.297	0.278	0.214				
D	-	0.141	0.233	0.198	0.198				
A	0.232	0.268	0.274	0.240	0.197				

Table S3. Summary of QSAR results for TR β based on superimposition II (the lowest binding energy).

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R^2_{cv}	0.649	0.657	0.611	0.611	0.619	0.609	0.666	0.623	0.629
R^2_{ncv}	0.994	0.787	0.654	0.650	0.660	0.651	0.922	0.920	0.882
SEE	0.051	0.280	0.352	0.355	0.349	0.354	0.172	0.174	0.215
F	925.504	72.216	75.758	74.349	77.654	74.566	149.043	144.835	68.825
R^2_{pred}	0.6081	0.6963	0.7666	0.7717	0.7690	0.7637	0.6219	0.7182	0.6680
SEP	0.380	0.356	0.374	0.374	0.370	0.375	0.356	0.378	0.380
N_c	6	2	1	1	1	1	3	3	4
Field contribution									
S	0.394	0.549	-	-	-	-	0.301	0.322	0.450
E	0.439	-	0.147	-	-	-	0.433	-	-
H	-	-	-	0.120	-	-	-	0.409	-
D	-	-	-	-	0.180	-	-	-	0.262
A	-	-	-	-	-	0.136	-	-	-
EEig06d	0.167	0.451	0.853	0.880	0.820	0.864	0.266	0.269	0.287
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R^2_{cv}	0.612	0.626	0.611	0.601	0.611	0.602	0.609	0.661	0.656
R^2_{ncv}	0.658	0.999	0.664	0.655	0.661	0.652	0.662	0.947	0.957

SEE	0.350	0.018	0.347	0.352	0.349	0.354	0.349	0.141	0.130
F	77.056	432.819	79.117	75.965	78.054	74.804	78.32	227.904	204.817
R ² _{pred}	0.7622	0.6267	0.7525	0.7473	0.7593	0.7530	0.7516	0.6131	0.4285
SEP	0.373	0.417	0.374	0.379	0.374	0.378	0.375	0.358	0.366
N _C	1	10	1	1	1	1	1	3	4
Field contribution									
S	0.063	-	-	-	-	-	-	0.197	0.232
E	-	0.420	0.123	0.129	-	-	-	0.329	0.365
H	-	0.360	-	-	0.101	0.105	-	0.229	-
D	-	-	0.158	-	0.162	-	0.160	-	0.193
A	0.127	-	-	0.118	-	0.121	0.114	-	-
EEig06d	0.810	0.220	0.719	0.753	0.737	0.773	0.726	0.245	0.210
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R ² _{cv}	0.615	0.613	0.604	0.611	0.603	0.603	0.600	0.602	0.642
R ² _{ncv}	0.931	0.668	0.659	0.669	0.665	0.999	0.665	0.662	0.967
SEE	0.162	0.345	0.350	0.345	0.347	0.024	0.347	0.348	0.114
F	170.357	80.549	77.176	80.879	79.369	248.559	79.35	78.506	269.218
R ² _{pred}	0.5820	0.7576	0.7516	0.7506	0.7438	0.5018	0.7352	0.7425	0.4759
SEP	0.381	0.373	0.377	0.374	0.378	0.429	0.379	0.378	0.383
N _C	3	1	1	1	1	10	1	1	4
Field contribution									
S	0.228	0.054	0.057	0.053	-	-	-	-	0.170
E	0.332	-	-	-	0.112	0.322	0.111	-	0.292
H	-	0.095	0.100	-	0.089	0.285	-	0.090	0.174
D	-	0.153	-	0.151	0.144	-	0.142	0.145	0.158
A	0.201	-	0.115	0.108	-	0.192	0.101	0.104	-
EEig06d	0.239	0.697	0.729	0.687	0.654	0.201	0.646	0.661	0.206
CoMSIA									
	SEHA	SEDA	SHDA	EHDA	SEHDA				
R ² _{cv}	0.621	0.602	0.603	0.592	0.594				
R ² _{ncv}	0.947	0.672	0.669	0.665	0.672				
SEE	0.142	0.343	0.345	0.347	0.343				
F	225.443	81.887	80.945	79.432	81.851				
R ² _{pred}	0.5873	0.7335	0.7414	0.7265	0.7254				
SEP	0.379	0.378	0.377	0.383	0.382				
N _C	3	1	1	1	1				
Field contribution									
S	0.164	0.048	0.049	-	0.044				
E	0.257	0.106	-	0.102	0.097				
H	0.192	-	0.086	0.081	0.077				
D	-	0.135	0.138	0.130	0.125				
A	0.156	0.097	0.099	0.093	0.089				

EEig06d	0.232	0.615	0.629	0.593	0.567
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Table S4. Summary of QSAR results for TR β based on superimposition II (the optimal conformation).

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R ² _{cv}	0.651	0.659	0.612	0.697	0.616	0.609	0.668	0.687	0.631
R ² _{ncv}	0.676	0.668	0.656	0.938	0.658	0.651	0.674	0.934	0.677
SEE	0.341	0.345	0.352	0.156	0.350	0.354	0.342	0.160	0.341
F	83.626	80.581	76.165	139.11	77.109	74.550	82.728	144.835	83.734
R ² _{pred}	0.6090	0.6981	0.7657	0.7801	0.7692	0.7640	0.6222	0.7183	0.6682
SEP	0.365	0.363	0.373	0.343	0.371	0.375	0.366	0.349	0.364
N _C	2	1	1	4	1	1	1	4	1
Field contribution									
S	0.105	0.116	-	-	-	-	0.101	0.258	0.098
E	0.142	-	0.149	-	-	-	0.134	-	-
H	-	-	-	0.730	-	-	-	0.501	-
D	-	-	-	-	0.171	-	-	-	0.154
A	-	-	-	-	-	0.143	-	-	-
EEig06d	0.752	0.884	0.851	0.270	0.829	0.857	0.766	0.241	0.747
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R ² _{cv}	0.624	0.610	0.612	0.602	0.693	0.606	0.606	0.624	0.664
R ² _{ncv}	0.669	0.661	0.664	0.657	0.952	0.656	0.659	0.677	0.682
SEE	0.345	0.349	0.347	0.351	0.138	0.352	0.350	0.341	0.338
F	80.911	77.865	79.119	76.533	78.054	76.197	77.199	83.948	85.615
R ² _{pred}	0.7624	0.6269	0.7527	0.7469	0.7595	0.7541	0.7514	0.6017	0.5063
SEP	0.368	0.374	0.375	0.378	0.350	0.376	0.376	0.368	0.368
N _C	1	1	1	1	5	1	1	1	1
Field contribution									
S	0.101	-	-	-	-	-	-	0.090	0.087
E	-	0.131	0.126	0.130	-	-	-	0.119	0.115
H	-	0.118	-	-	0.601	0.118	-	0.107	-
D	-	-	0.149	-	0.185	-	0.150	-	0.136
A	0.128	-	-	0.124	-	0.126	0.121	-	-
EEig06d	0.770	0.751	0.724	0.746	0.214	0.756	0.728	0.684	0.661
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R ² _{cv}	0.617	0.672	0.620	0.620	0.606	0.599	0.602	0.603	0.620
R ² _{ncv}	0.674	0.936	0.672	0.676	0.669	0.661	0.664	0.664	0.685
SEE	0.342	0.157	0.343	0.341	0.345	0.349	0.346	0.348	0.336
F	82.774	135.866	82.099	83.480	80.952	78.090	79.38	78.986	86.993
R ² _{pred}	0.5831	0.7580	0.7518	0.7511	0.7439	0.5011	0.7354	0.7427	0.4752
SEP	0.371	0.357	0.369	0.369	0.376	0.379	0.370	0.378	0.370

A	-	-	-	-	1.000	-	-	-	-
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R^2_{cv}	0.471	0.503	0.412	0.358	0.298	0.380	0.280	0.543	0.517
R^2_{ncv}	0.765	0.992	0.787	0.685	0.683	0.713	0.697	0.995	0.855
SEE	0.240	0.048	0.234	0.278	0.279	0.266	0.280	0.040	0.194
F	32.61	350.991	23.441	21.702	21.50 4	24.809	14.541	58.396	37.255
R^2_{pred}	0.8010	0.7264	0.3251	0.3827	0.722 1	0.7189	0.7552	0.7370	0.5754
SEP	0.360	0.391	0.390	0.397	0.415	0.390	0.431	0.375	0.353
N_C	2	6	3	2	2	2	3	6	3
Field contribution									
S	0.327	-	-	-	-	-	-	0.189	0.210
E	-	0.575	0.640	0.579	-	-	-	0.506	0.486
H	-	0.425	-	-	0.482	0.366	-	0.305	-
D	-	-	0.360	-	0.518	-	0.385	-	0.305
A	0.673	-	-	0.421	-	0.634	0.615	-	-
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R^2_{cv}	0.470	0.371	0.451	0.435	0.416	0.402	0.328	0.343	0.471
R^2_{ncv}	0.864	0.741	0.774	0.859	0.834	0.989	0.751	0.783	0.862
SEE	0.187	0.252	0.235	0.191	0.207	0.058	0.247	0.237	0.189
F	40.314	28.643	34.273	38.494	31.88 9	238.535	30.210	22.896	39.445
R^2_{pred}	0.6565	0.7880	0.7884	0.8380	0.529 3	0.7594	0.5042	0.7654	0.6534
SEP	0.370	0.393	0.367	0.382	0.388	0.428	0.406	0.412	0.370
N_C	3	2	2	3	3	6	2	3	3
Field contribution									
S	0.234	0.218	0.233	0.265	-	-	-	-	0.157
E	0.441	-	-	-	0.440	0.420	0.399	-	0.370
H	-	0.352	0.274	-	0.247	0.334	-	0.276	0.195
D	-	0.430	-	0.250	0.312	-	0.305	0.346	0.278
A	0.324	-	0.493	0.485	-	0.245	0.296	0.378	-
CoMSIA									
	SEHA	SEDA	SHDA	EHDA	SEHDA				
R^2_{cv}	0.463	0.445	0.413	0.391	0.448				
R^2_{ncv}	0.884	0.853	0.832	0.824	0.854				
SEE	0.173	0.195	0.208	0.213	0.194				
F	48.444	36.873	31.317	29.706	36.917				
R^2_{pred}	0.6977	0.6631	0.8158	0.5916	0.6799				
SEP	0.373	0.379	0.390	0.397	0.378				

N _C	3	3	3	3	3
Field contribution					
S	0.177	0.163	0.167	-	0.126
E	0.359	0.351	-	0.320	0.279
H	0.199	-	0.215	0.182	0.151
D	-	0.230	0.300	0.263	0.235
A	0.265	0.255	0.317	0.235	0.208

Table S6. Summary of QSAR results for TR α based on superimposition II (the lowest binding energy).

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R ² _{cv}	0.528	0.549	0.527	0.557	0.556	0.531	0.525	0.553	0.554
R ² _{ncv}	0.650	0.639	0.637	0.651	0.666	0.638	0.642	0.656	0.671
SEE	0.286	0.291	0.291	0.286	0.279	0.291	0.289	0.284	0.277
F	39.039	37.142	36.856	39.185	41.85	36.968	37.700	39.965	42.759
R ² _{pred}	0.5799	0.6049	0.5679	0.5857	0.5997	0.5816	0.5734	0.5909	0.6043
SEP	0.332	0.325	0.332	0.322	0.322	0.331	0.333	0.323	0.323
N _C	1	1	1	1	1	1	1	1	1
Field contribution									
S	0.117	0.098	-	-	-	-	0.083	0.088	0.086
E	0.147	-	0.161	-	-	-	0.147	-	-
H	-	-	-	0.108	-	-	-	0.098	-
D	-	-	-	-	0.133	-	-	-	0.121
A	-	-	-	-	-	0.126	-	-	-
H-051	0.736	0.902	0.839	0.892	0.867	0.874	0.769	0.814	0.793
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R ² _{cv}	0.529	0.531	0.532	0.505	0.561	0.535	0.536	0.528	0.529
R ² _{ncv}	0.643	0.654	0.666	0.640	0.681	0.654	0.668	0.658	0.671
SEE	0.289	0.285	0.279	0.290	0.273	0.284	0.279	0.283	0.277
F	37.845	39.617	41.927	37.391	44.886	39.752	42.279	40.342	42.776
R ² _{pred}	0.5878	0.5540	0.5682	0.5485	0.5857	0.5677	0.5818	0.5599	0.5734
SEP	0.332	0.331	0.331	0.340	0.320	0.330	0.329	0.332	0.332
N _C	1	1	1	1	1	1	1	1	1
Field contribution									
S	0.087	-	-	-	-	-	-	0.076	0.075
E	-	0.146	0.143	0.143	-	-	-	0.135	0.132
H	-	0.092	-	-	0.095	0.095	-	0.085	-
D	-	-	0.114	-	0.120	-	0.118	-	0.105
A	0.115	-	-	0.108	-	0.114	0.111	-	-
H-051	0.798	0.762	0.744	0.748	0.785	0.790	0.771	0.704	0.688
CoMSIA									

	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R^2_{cv}	0.502	0.558	0.532	0.533	0.535	0.507	0.509	0.539	0.532
R^2_{ncv}	0.645	0.685	0.659	0.673	0.681	0.656	0.668	0.682	0.684
SEE	0.288	0.271	0.282	0.277	0.273	0.284	0.279	0.272	0.272
F	38.210	45.648	40.507	43.161	44.729	39.987	42.167	45.104	45.448
R^2_{pred}	0.5546	0.5904	0.5738	0.5878	0.5539	0.5345	0.5475	0.5679	0.5597
SEP	0.341	0.322	0.331	0.330	0.330	0.339	0.339	0.328	0.331
N_C	1	1	1	1	1	1	1	1	1
Field contribution									
S	0.075	0.079	0.079	0.077	-	-	-	-	0.069
E	0.133	-	-	-	0.131	0.131	0.129	-	0.122
H	-	0.087	0.088	-	0.082	0.083	-	0.085	0.077
D	-	0.111	-	0.109	0.104	-	0.103	0.108	0.097
A	0.100	-	0.105	0.103	-	0.099	0.097	0.102	-
H-051	0.692	0.724	0.728	0.711	0.683	0.686	0.672	0.705	0.636
CoMSIA									
	SEHA	SEDA	SHDA	EHDA			SEHDA		
R^2_{cv}	0.505	0.506	0.536	0.511			0.508		
R^2_{ncv}	0.660	0.672	0.686	0.681			0.684		
SEE	0.282	0.277	0.271	0.273			0.272		
F	40.696	42.998	45.851	44.773			45.486		
R^2_{pred}	0.5409	0.5545	0.5736	0.5341			0.5404		
SEP	0.340	0.340	0.329	0.338			0.339		
N_C	1	1	1	1			1		
Field contribution									
S	0.069	0.068	0.071	-			0.063		
E	0.122	0.120	-	0.119			0.111		
H	0.077	-	0.079	0.075			0.070		
D	-	0.096	0.100	0.095			0.089		
A	0.092	0.091	0.095	0.090			0.084		
H-051	0.639	0.626	0.655	0.621			0.582		

Table S7. Summary of QSAR results for TR α based on superimposition II (the optimal conformation).

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R^2_{cv}	0.544	0.551	0.553	0.547	0.558	0.586	0.551	0.545	0.557
R^2_{ncv}	0.649	0.642	0.650	0.643	0.669	0.884	0.657	0.651	0.677
SEE	0.287	0.289	0.286	0.289	0.278	0.173	0.283	0.285	0.275
F	38.787	37.693	39.078	37.902	42.395	48.349	40.302	39.242	43.941
R^2_{pred}	0.5802	0.6053	0.5800	0.5867	0.6003	0.5842	0.5745	0.5906	0.6112
SEP	0.327	0.324	0.323	0.325	0.321	0.327	0.324	0.326	0.322
N_C	1	1	1	1	1	3	1	1	1

Field contribution									
S	0.079	0.084	-	-	-	-	0.065	0.074	0.073
E	0.207	-	0.239	-	-	-	0.223	-	-
H	-	-	-	0.129	-	-	-	0.119	-
D	-	-	-	-	0.140	-	-	-	0.130
A	-	-	-	-	-	0.638	-	-	-
H-051	0.714	0.916	0.761	0.871	0.860	0.362	0.711	0.806	0.797
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R ² _{cv}	0.537	0.545	0.559	0.536	0.554	0.531	0.591	0.542	0.557
R ² _{ncv}	0.644	0.656	0.682	0.932	0.678	0.643	0.875	0.662	0.688
SEE	0.288	0.284	0.273	0.136	0.274	0.289	0.179	0.281	0.270
F	37.985	40.053	45.062	61.468	44.143	37.815	44.469	41.174	46.326
R ² _{pred}	0.5901	0.5545	0.5690	0.5505	0.5862	0.5669	0.5946	0.5601	0.5752
SEP	0.329	0.326	0.321	0.356	0.323	0.331	0.325	0.327	0.322
N _C	1	1	1	4	1	1	3	1	1
Field contribution									
S	0.069	-	-	-	-	-	-	0.059	0.059
E	-	0.215	0.213	0.402	-	-	-	0.202	0.200
H	-	0.101	-	-	0.113	0.106	-	0.095	-
D	-	-	0.110	-	0.124	-	0.283	-	0.104
A	0.184	-	-	0.312	-	0.177	0.350	-	-
H-051	0.747	0.684	0.677	0.286	0.763	0.717	0.368	0.644	0.637
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R ² _{cv}	0.531	0.552	0.528	0.543	0.552	0.524	0.563	0.537	0.549
R ² _{ncv}	0.652	0.684	0.649	0.676	0.686	0.650	0.933	0.675	0.692
SEE	0.285	0.272	0.286	0.275	0.271	0.286	0.136	0.276	0.268
F	39.409	45.539	38.905	43.810	45.976	38.955	62.223	43.548	47.118
R ² _{pred}	0.5552	0.5903	0.5733	0.5897	0.5548	0.5424	0.5553	0.5667	0.5660
SEP	0.331	0.324	0.332	0.327	0.324	0.334	0.345	0.329	0.325
N _C	1	1	1	1	1	1	4	1	1
Field contribution									
S	0.056	0.066	0.07962	0.061	-	-	-	-	0.054
E	0.190	-	-	-	0.193	0.184	0.290	-	0.183
H	-	0.105	0.100	-	0.091	0.087	-	0.095	0.086
D	-	0.116	-	0.109	0.100	-	0.199	0.105	0.095
A	0.149	-	0.166	0.164	-	0.144	0.231	0.158	-
H-051	0.605	0.713	0.673	0.666	0.615	0.585	0.281	0.642	0.582
CoMSIA									
	SEHA	SEDA	SHDA	EHDA	SEHDA				
R ² _{cv}	0.521	0.537	0.534	0.530	0.527				
R ² _{ncv}	0.655	0.681	0.680	0.678	0.683				

SEE	0.284	0.273	0.273	0.274	0.272
F	39.885	44.836	44.659	44.247	45.181
R^2_{pred}	0.5431	0.5556	0.5734	0.5346	0.5432
SEP	0.335	0.329	0.330	0.331	0.333
N_C	1	1	1	1	1
Field contribution					
S	0.051	0.051	0.056	-	0.047
E	0.174	0.173	-	0.168	0.160
H	0.082	-	0.090	0.079	0.075
D	-	0.090	0.099	0.087	0.083
A	0.137	0.136	0.150	0.132	0.126
H-051	0.555	0.551	0.606	0.534	0.509

R^2_{cv} = cross-validated correlation coefficient using the leave-one-out methods;

R^2_{ncv} = Non-cross-validated correlation coefficient; SEE = Standard error of estimate; F= Ratio of R^2_{ncv} explained to unexplained = $R^2_{\text{ncv}}/(1-R^2_{\text{ncv}})$;

R^2_{pred} = Predicted correlation coefficient for the test set of compounds; SEP= Standard error of prediction; N_C = Optimal number of principal components; S=steric, E=electrostatic, H=hydrophobic, D=H-bond donor, A= H-bond acceptor.

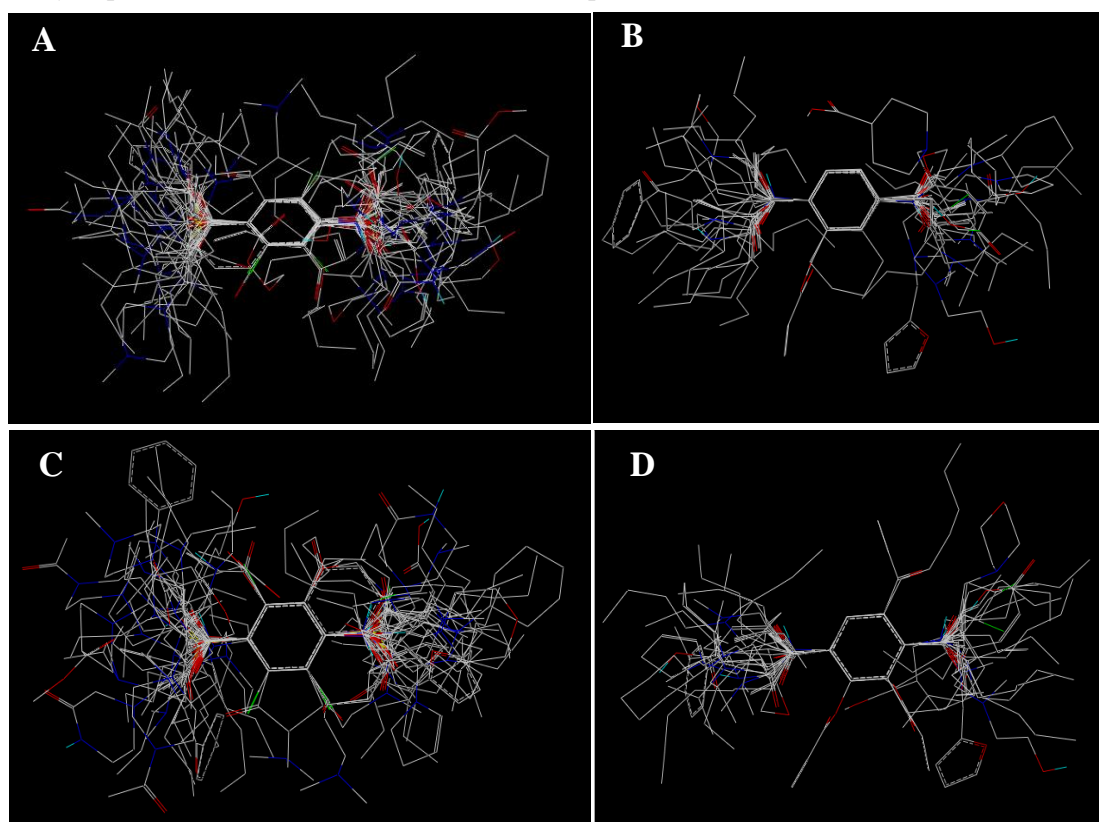


Figure S1 (A) Present the alignments for TR β from the superimposition II based on the lowest binding energy; (B) Present the alignments for TR α from the superimposition II based on the

lowest binding energy; (C) Present the alignments for TR β from the superimposition II based on the optimal conformation; (D) Present the alignments for TR α from the superimposition II based on the optimal conformation.