Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Optical spectra and conformation pool of tyrosine kinase inhibitor PD153035 using robust quantum mechanical conformation search

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Supplementary Materials

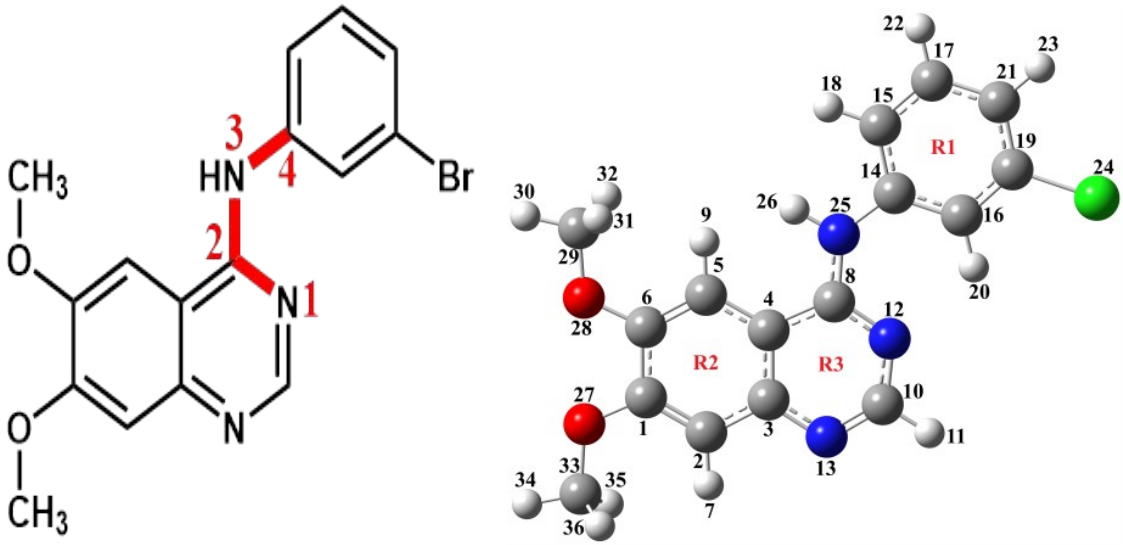
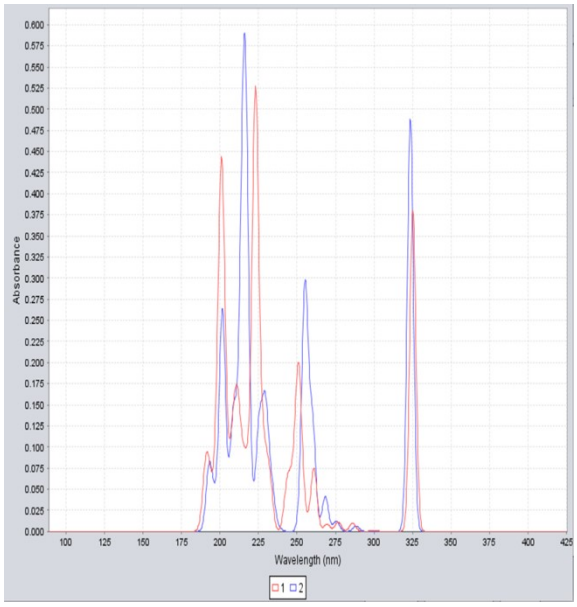
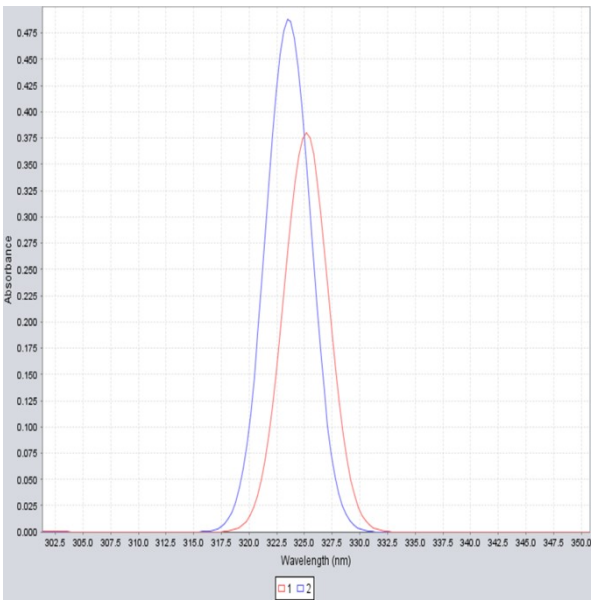


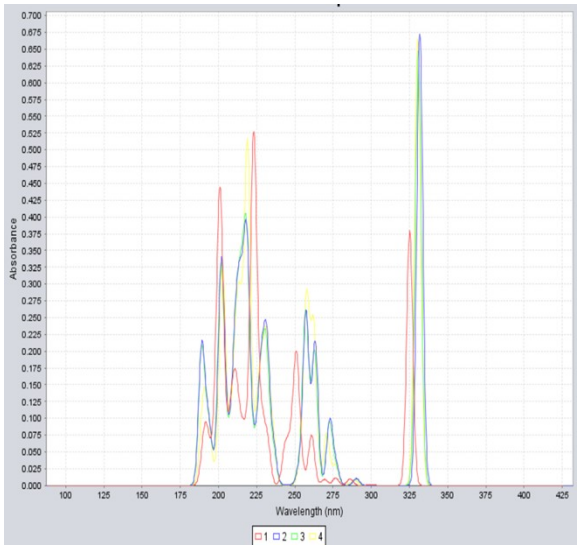
Fig. S1. Chemical structure of PD153035 (IUPAC name: 4-(3-bromoanilino)-6,7-dimethoxy quinazoline). Synonyms: AG1517, SU-5271, ZM-252868, K11-900B, and NSC 669364. The atomic labels on the structure on the right is not the IUPAC nomenclature but numbering form the Gaussian calculations for convenience. The halogen atom (Br) is atom 24.



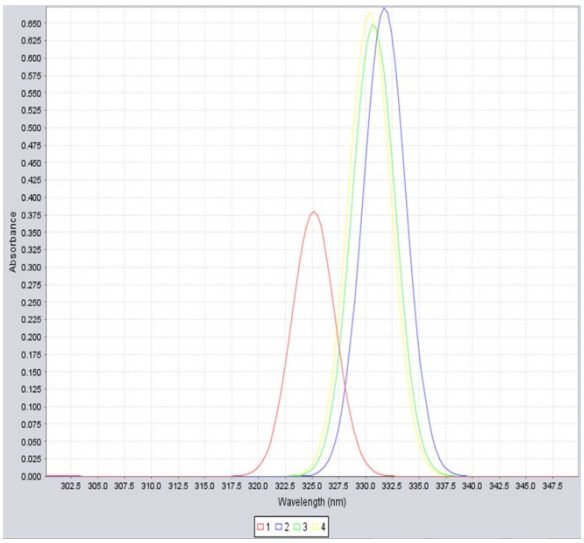
(a) ***Spectra in 180-330 nm.***



(b) Spectra above 300 nm.



(c) ***Spectra in solvent in 180-330 nm.***



(d) Spectra in solvent above 300 nm.

Fig. S2 UV-vis spectra of PD153035 were calculated for the conformer from the EGFR Database (spectrum 1, red) and the global minimum structure in gas phase (spectrum 2, blue) in (a) and (b)) using the TD-DFT method. The same UV-vis spectra in (c) and (d) for the conformer from the EGFR database (1 red) and the global minimum structures in DMSO (2 blue), MeOH (3 green), TOL (4 yellow) solvent, respectively.

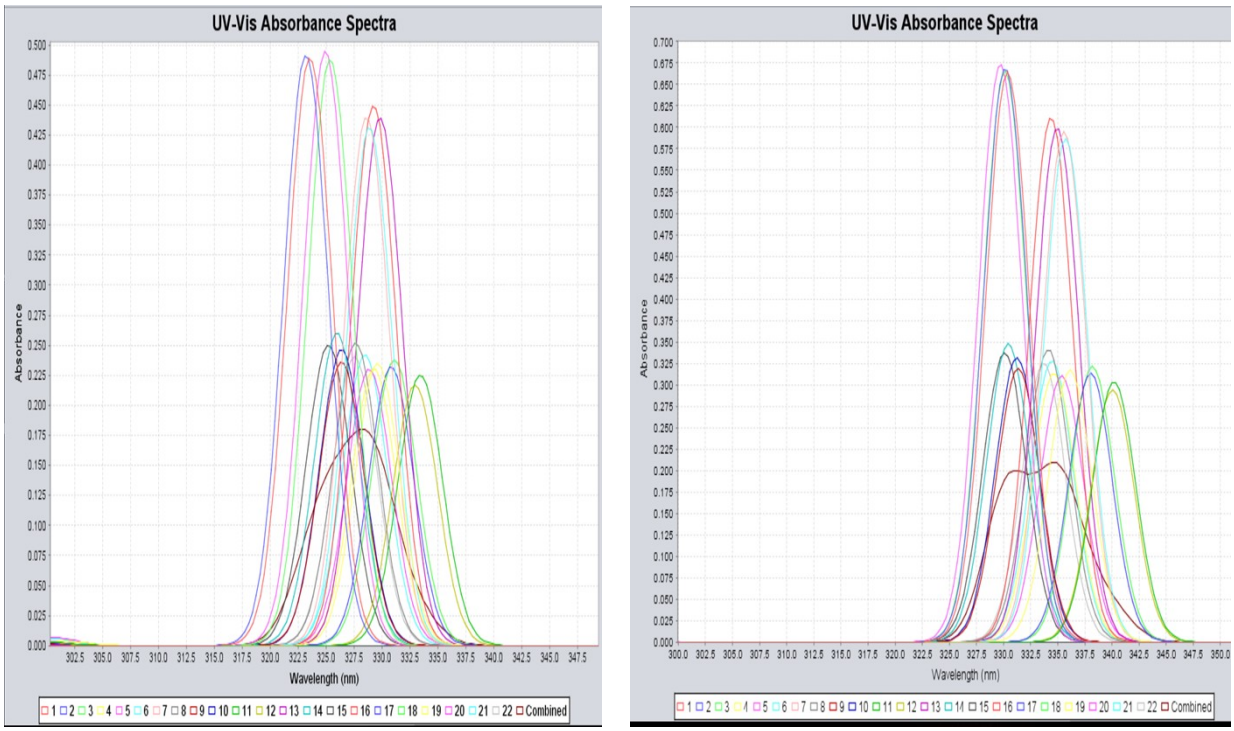


Fig. S3 UV-vis spectra of all 22 low-lying cluster conformers of PD153035 calculated using DFT B3LYP/6-311++G(d,p) in gas phase (x-axis nm) (left) and in Toluene (right).

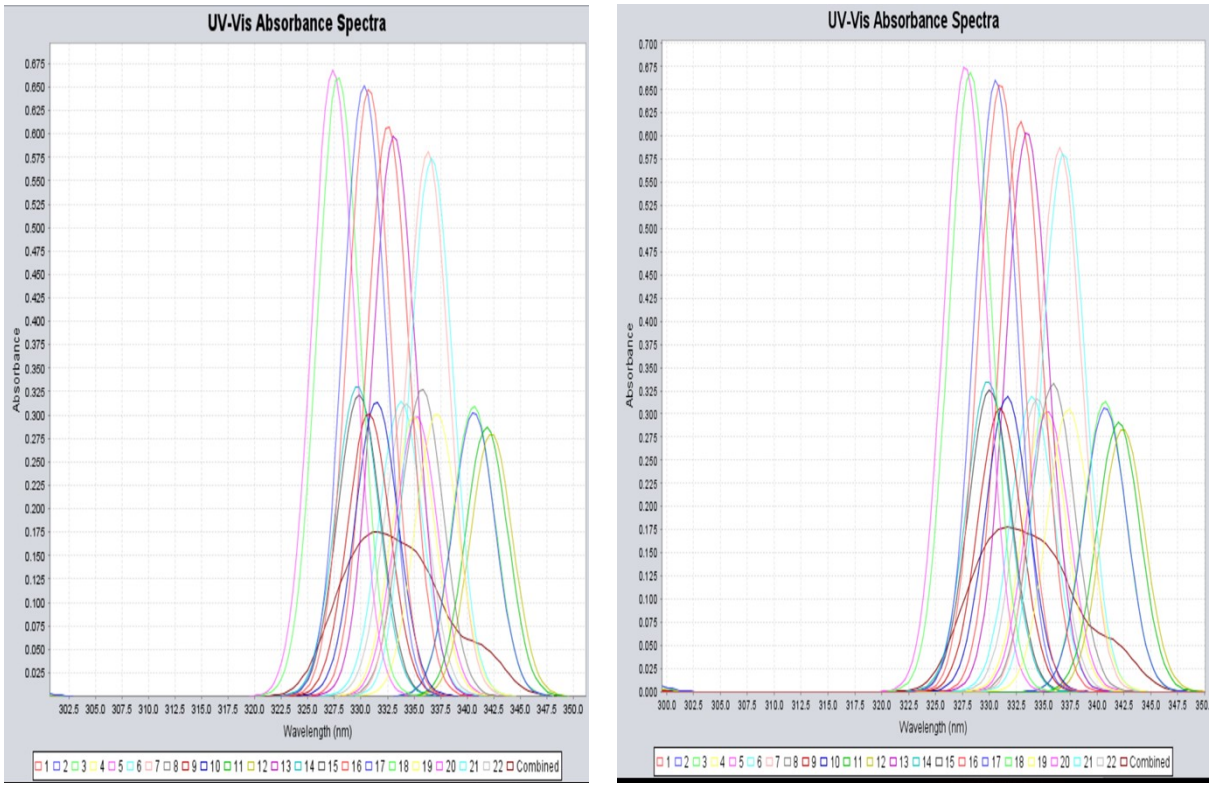


Fig. S4 UV-vis spectra of all 22 low-lying cluster conformers of PD153035 calculated using DFT B3LYP/6-311++G(d,p) in MeOH (x-axis nm) (left) and in EtOH (right).

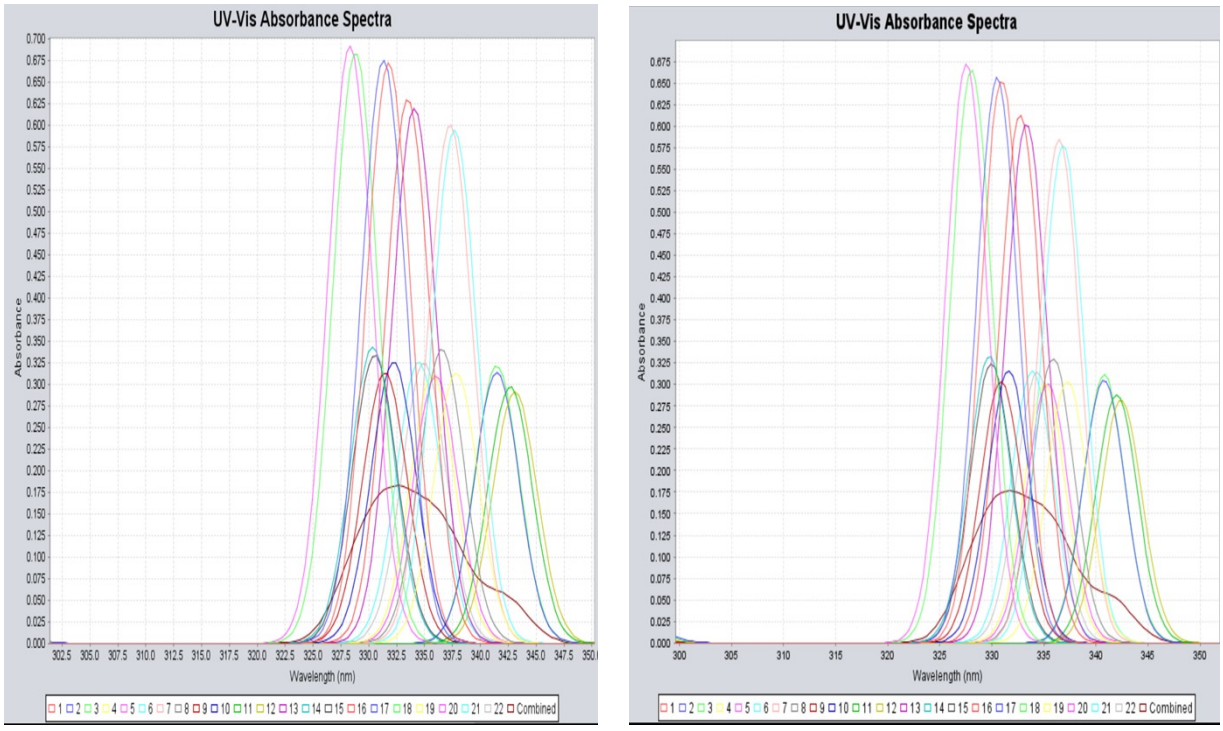
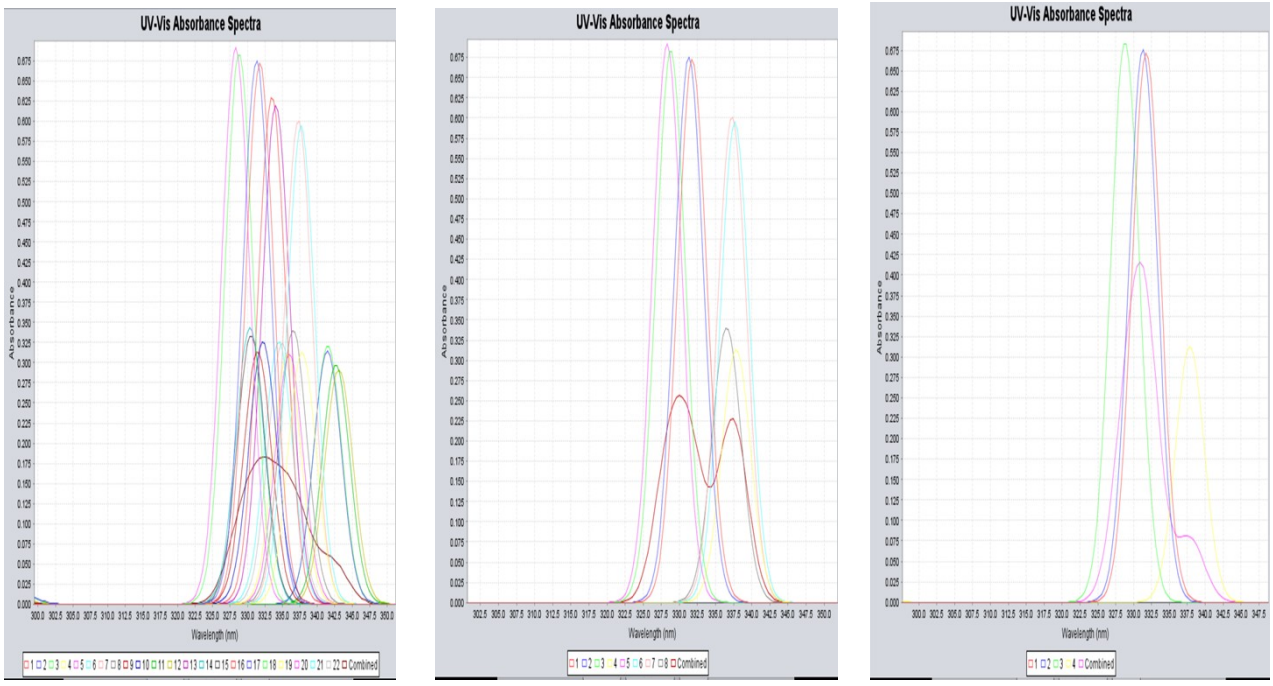


Fig. S5 UV-vis spectra of all 22 low-lying cluster conformers of PD153035 calculated using DFT B3LYP/6-311++G(d,p) in ACN (x-axis nm) (left) and in DMSO (right).



(a) All 22 clusters of conformers (b) Lowest 8 clusters of conformers (c) Lowest 4 conformers

Fig. S6 UV-vis spectra of low-lying cluster conformers of PD153035 calculated using DFT B3LYP/6-311++G(d,p) in DMSO solvent (x-axis nm). (a) All 22 conformers with strain energy upto 10.459 kcal/mol, the eight low-lying conformers with strain energy cut-off at the strain energy of the crystal structure of 5.554 kcal/mol, and (c) the four low-lying conformers.

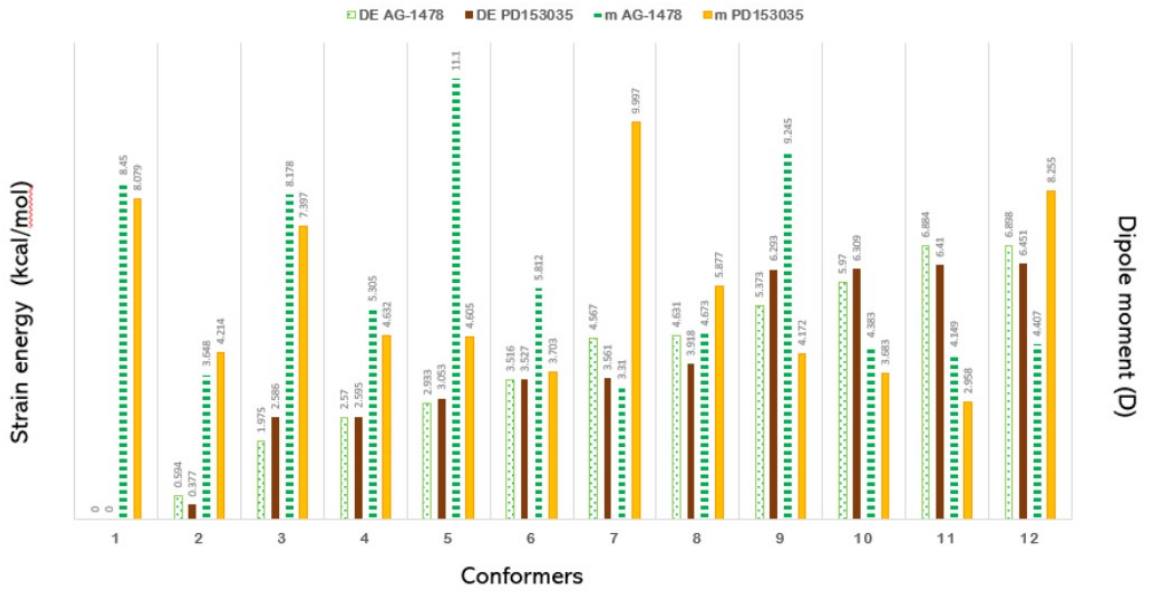


Fig. S7 Comparison of the strain energies and dipole moments of the first twelve low energy conformers of PD153035 (solid brown and yellow, λ_1 = 330 nm, λ_2=337.5 nm) and AG-1478 (pattern green, λ_1 = 329.5 nm, λ_2=337 nm) at the SE of 5.0 kcal/mol in DMSO obtained using B3LYP/6-311G++(d,p) method (refer to Table 4).

Table S1.1 The bond length of the four low-lying PD153035 conformers obtained from calculations and the EGFR structure from the database (Å).*

No	Bond		GAS1	GAS2	GAS3	GAS4	EGFR#
1	C(1) -	C(2)	1.374961	1.375499	1.378953	1.374574	1.406076
2	C(1) -	C(6)	1.436943	1.429076	1.431803	1.440443	1.411238
3	C(1) -	O(26)	1.35067	1.355441	1.355827	1.349655	1.368002
4	C(2) -	C(3)	1.416891	1.412946	1.414442	1.417712	1.405626
6	C(3) -	C(4)	1.416068	1.415517	1.418493	1.421591	1.423275
7	C(3) -	N(13)	1.366582	1.367603	1.368062	1.36251	1.355785
8	C(4) -	C(5)	1.420517	1.419523	1.414854	1.421015	1.418124
9	C(4) -	C(8)	1.438756	1.437208	1.440857	1.426598	1.422878
10	C(5) -	C(6)	1.376512	1.376408	1.37407	1.374152	1.410975
12	C(6) -	O(27)	1.355203	1.360233	1.367897	1.35333	1.369789
13	C(8) -	N(12)	1.323383	1.324422	1.32293	1.326674	1.361402
14	C(8) -	N(24)	1.376641	1.373009	1.373684	1.393538	1.368241
16	C(10) -	N(12)	1.351061	1.351141	1.352336	1.348355	1.353315
17	C(10) -	N(13)	1.310372	1.310643	1.30983	1.313944	1.350758
18	C(14) -	C(15)	1.405748	1.400659	1.405378	1.402224	1.414659
19	C(14) -	C(16)	1.40232	1.406843	1.402087	1.401314	1.419205
20	C(14) -	N(24)	1.405746	1.407514	1.406484	1.411469	1.370434
21	C(15) -	C(17)	1.387069	1.39273	1.387114	1.389335	1.406866
23	C(16) -	C(19)	1.390832	1.383072	1.390818	1.39037	1.408847
25	C(17) -	C(21)	1.394865	1.393176	1.394846	1.395036	1.404607
27	C(19) -	C(21)	1.389371	1.388238	1.389361	1.390435	1.405459
28	C(19) -	BR(36)	1.921133	1.922455	1.921074	1.920391	1.861498
31	O(26) -	C(32)	1.425091	1.436132	1.426534	1.424806	1.438359
32	O(27) -	C(28)	1.420638	1.433016	1.435632	1.423385	1.440611

*The nomenclature of PD153035 see Fig. S1.

#The EGFR database (http://crdd.osdd.net/raghava/egfrindb/, EGIN000762)

Table S1.2 The dihedral angles of the four low-lying PD153035 conformers obtained from calculations and the crystal structure (°).*

No	Dihedral	Angles		1	2	3	4	EGFR#
1	C(1) -	C(2) -	C(3) - C(4)	0	0	-0.25944	-2.05633	
2	C(1) -	C(2) -	C(3) - N(13)	180	-180	179.972	176.0014	
3	C(1) -	C(6) -	C(5) - C(4)	0	0	-0.58383	-0.10653	
5	C(1) -	C(6) -	O(27) - C(28)	180	180	68.99264	-178.943	84.99957
9	C(2) -	C(1) -	C(6) - C(5)	0.019782	0	1.470069	1.731218	
10	C(2) -	C(1) -	C(6) - O(27)	-179.972	-180	177.019	-178.021	
11	C(2) -	C(1) -	O(26) - C(32)	0	0	-2.19455	-0.75485	
12	C(2) -	C(3) -	C(4) - C(5)	0	0	1.135049	3.627038	
13	C(2) -	C(3) -	C(4) - C(8)	-180	180	-179.18	-178.996	
14	C(2) -	C(3) -	N(13) - C(10)	-180	-180	179.7474	-176.841	
15	C(3) -	C(2) -	C(1) - C(6)	-0.01978	0	-1.0438	-0.6215	
16	C(3) -	C(2) -	C(1) - O(26)	180	180	178.272	-179.739	
17	C(3) -	C(4) -	C(5) - C(6)	0	0	-0.71107	-2.56476	
19	C(3) -	C(4) -	C(8) - N(12)	0	0	-0.81996	-5.38802	
20	C(3) -	C(4) -	C(8) - N(24)	179.9802	-179.98	179.1909	179.5804	
22	C(3) -	N(13) -	C(10) - N(12)	0	0	-0.40348	-3.66736	
24	C(4) -	C(3) -	N(13) - C(10)	0	0	-0.02798	1.155552	
25	C(4) -	C(5) -	C(6) - O(27)	-180	-180	-176.242	179.6154	
26	C(4) -	C(8) -	N(12) - C(10)	0	0	0.48092	3.424284	
27	C(4) -	C(8) -	N(24) - C(14)	180	180	179.5335	-50.3081	
29	C(5) -	C(4) -	C(3) - N(13)	-180	180	-179.105	-174.356	
30	C(5) -	C(4) -	C(8) - N(12)	180	-179.972	178.8392	171.8009	
31	C(5) -	C(4) -	C(8) - N(24)	0	0	-1.15029	-3.23107	
32	C(5) -	C(6) -	C(1) - O(26)	-179.98	-179.98	-177.908	-179.066	
33	C(5) -	C(6) -	O(27) - C(28)	0	0	-115.427	1.320565	-97.2081
35	C(6) -	C(1) -	O(26) - C(32)	179.972	179.972	177.1469	-179.912	
36	C(6) -	C(5) -	C(4) - C(8)	180	180	179.639	-179.649	
42	C(8) -	C(4) -	C(3) - N(13)	0	-0.01978	0.580472	3.021613	
45	C(8) -	N(12) -	C(10) - N(13)	0	0	0.170174	1.406113	
46	C(8) -	N(24) -	C(14) - C(15)	-179.952	0	178.7633	168.3556	
47	C(8) -	N(24) -	C(14) - C(16)	0.048457	-180	-1.44442	-13.7845	
49	C(10) -	N(12) -	C(8) - N(24)	-180	180	-179.531	178.8693	
50	N(12) -	C(8) -	N(24) - C(14)	0	0	-0.45543	134.3467	
52	C(14) -	C(15) -	C(17) - C(21)	0	0	0	1.046424	
54	C(14) -	C(16) -	C(19) - C(21)	0	0	-0.03426	1.309255	
55	C(14) -	C(16) -	C(19) - BR(36)	180	-180	180	-179.627	
56	C(15) -	C(14) -	C(16) - C(19)	0	0	0.048457	-1.21885	
59	C(15) -	C(17) -	C(21) - C(19)	0.019782	0	0	-0.97317	
61	C(16) -	C(14) -	C(15) - C(17)	0	0	-0.02798	0.071326	
64	C(16) -	C(19) -	C(21) - C(17)	0	0	0	-0.21306	
66	C(17) -	C(15) -	C(14) - N(24)	-179.972	180	179.7702	178.0062	
67	C(17) -	C(21) -	C(19) - BR(36)	-180	180	180	-179.271	

71	C(19) -	C(16) -	C(14) -	N(24)	180	-179.972	-179.736	-179.054
78	O(26) -	C(1) -	C(6) -	O(27)	0.027976	0.027976	-2.35908	1.182337

*The nomenclature of PD153035 see Fig. S1.

#The EGFR database (http://crdd.osdd.net/raghava/egfrindb/, EGIN000762)

Table S1.3 The dihedral angles of the crystal structure from the EGFR database.*

No	Dihedral Angle				EGFR#
1	C(1) -	C(3) -	C(5) -	C(6)	-1.75691
2	C(1) -	C(3) -	C(5) -	O(19)	-179.559
3	C(1) -	C(9) -	N(7) -	C(8)	0.459275
4	C(1) -	C(9) -	N(11) -	C(12)	-157.793
6	C(1) -	C(2) -	C(4) -	C(6)	-1.04755
8	C(1) -	C(2) -	N(10) -	C(8)	-1.35855
9	C(2) -	C(4) -	C(6) -	C(5)	-3.05966
10	C(2) -	C(4) -	C(6) -	O(20)	178.3095
11	C(2) -	N(10) -	C(8) -	N(7)	-1.54915
13	C(2) -	C(1) -	C(3) -	C(5)	-2.26071
15	C(2) -	C(1) -	C(9) -	N(7)	-3.2301
16	C(2) -	C(1) -	C(9) -	N(11)	175.098
17	C(3) -	C(1) -	C(9) -	N(7)	178.051
18	C(3) -	C(1) -	C(9) -	N(11)	-3.62104
19	C(3) -	C(1) -	C(2) -	C(4)	3.668424
20	C(3) -	C(1) -	C(2) -	N(10)	-177.485
21	C(3) -	C(5) -	C(6) -	C(4)	4.443516
22	C(3) -	C(5) -	C(6) -	O(20)	-176.939
23	C(3) -	C(5) -	O(19) -	C(21)	-97.2081
24	C(4) -	C(2) -	N(10) -	C(8)	177.5085
25	C(4) -	C(2) -	C(1) -	C(9)	-175.135
26	C(4) -	C(6) -	C(5) -	O(19)	-177.754
27	C(4) -	C(6) -	O(20) -	C(22)	-84.7553
28	C(5) -	C(3) -	C(1) -	C(9)	176.4439
30	C(5) -	C(6) -	O(20) -	C(22)	96.62187
34	C(6) -	C(4) -	C(2) -	N(10)	-179.912
35	C(6) -	C(5) -	C(3) -	H(23)	177.7595
36	C(6) -	C(5) -	O(19) -	C(21)	84.99957
40	N(7) -	C(9) -	N(11) -	C(12)	20.48827
42	C(8) -	N(7) -	C(9) -	N(11)	-177.855
43	C(9) -	N(7) -	C(8) -	N(10)	2.019067
46	C(9) -	C(1) -	C(2) -	N(10)	3.710668
47	C(9) -	N(11) -	C(12)	- C(16)	-33.6828
48	C(9) -	N(11) -	C(12)	- C(17)	146.0471
50	N(11) -	C(12) -	C(16)	- C(14)	177.5611
52	N(11) -	C(12) -	C(17)	- C(15)	-177.983
54	C(12) -	C(16) -	C(14)	- C(13)	1.38126
56	C(12) -	C(17) -	C(15)	- C(13)	-0.58784

60	C(14) -	C(13) -	C(15)	-	C(17)	-0.24469
62	C(14) -	C(16) -	C(12)	-	C(17)	-2.16211
63	C(15) -	C(13) -	C(14)	-	C(16)	-0.15195
65	C(15) -	C(17) -	C(12)	-	C(16)	1.769788
75	O(19) -	C(5) -	C(6) -		O(20)	0.862754

*The nomenclature of PD153035 see Fig. S1.
#The EGFR database (http://crdd.osdd.net/raghava/egfrindb/, EGIN000762)

Table S1.4 The nomenclature conversion between the calculated and the EGFR database in Table 1.3.

No	Atom1	Atom2	Atoms1-2
	Calculations		Crystal
1	C(3) -	C(1)	5,4
2	C(4) -	C(2)	2,3
3	C(5) -	C(3)	6,5
4	C(6) -	C(4)	1,2
5	C(6) -	C(5)	1,6
6	C(9) -	N(7)	8,12
7	N(10) -	C(8)	13,10
8	C(1) -	C(9)	4,8
9	C(2) -	N(10)	3,13
10	C(2) -	C(1)	3,4
11	C(8) -	N(7)	10,12
12	C(9) -	N(11)	8,24
13	N(11) -	C(12)	24,14
14	C(14) -	C(13)	19,21
15	C(15) -	C(13)	17,21
16	C(16) -	C(14)	16,19
17	C(17) -	C(15)	15,17
18	C(12) -	C(16)	14,16
19	C(12) -	C(17)	14,15
20	C(14) -	Br(18)	19,36
21	C(5) -	O(19)	6,27
22	C(6) -	O(20)	1,26
23	O(19) -	C(21)	27,28
24	O(20) -	C(22)	26,32

Table S2.1 The 22 clustered lowest lying PD153035 conformers calculated using DFT B3LYP/6-311++G(d,p) in gas phase.

Sorted clusters

#	Energy	RelativeEnergy (kcal/mol)	Dipole	File Name	Cluster Size	%
1	-3507.2195541	0.000	3.2556	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-02.log	1	47.802
2	-3507.2193768	0.111	5.8420	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-01.log	1	39.488
3	-3507.2173955	1.355	5.5328	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-03.log	1	4.668
4	-3507.2173938	1.356	3.9067	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-05.log	1	4.659
5	-3507.2162792	2.055	2.8600	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-08.log	1	1.402
6	-3507.2162673	2.062	3.0472	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-04.log	1	1.384
7	-3507.2146364	3.086	3.9857	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-07.log	1	0.239
8	-3507.2144194	3.222	6.9975	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-06.log	1	0.189
9	-3507.2127574	4.265	3.2646	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-14.log	1	0.031
10	-3507.2126927	4.306	2.0375	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-09.log	1	0.029
11	-3507.2124371	4.466	3.0344	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-10.log	1	0.022
12	-3507.2123526	4.519	3.7312	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-15.log	1	0.020
13	-3507.2123420	4.526	3.0196	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-16.log	1	0.020
14	-3507.2123328	4.531	5.7493	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-13.log	1	0.020
15	-3507.2114231	5.102	4.7455	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-12.log	1	0.007
16	-3507.2113024	5.178	4.0248	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-17.log	1	0.007
17	-3507.2112912	5.185	3.5527	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-18.log	1	0.006
18	-3507.2111928	5.247	5.2145	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-11.log	1	0.006
19	-3507.2076176	7.490	2.9118	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-21.log	1	0.000
20	-3507.2075100	7.558	3.5230	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-20.log	1	0.000
21	-3507.2075081	7.559	3.5035	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-19.log	1	0.000
22	-3507.2072306	7.733	2.7764	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Gas/min-22.log	1	0.000

Table S2.2 The 22 clustered lowest lying PD153035 conformers calculated using DFT B3LYP/6-311++G(d,p) in Toluene solvent.

Sorted clusters

#	Energy	RelativeEnergy (kcal/mol)	Dipole	File Name	Cluster Size	%
1	-3507.2267308	0.000	6.8248	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-01.log	1	49.378
2	-3507.2266315	0.062	3.6844	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-02.log	1	44.367
3	-3507.2239178	1.765	6.3786	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-03.log	1	2.382
4	-3507.2237269	1.885	4.2869	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-05.log	1	1.939
5	-3507.2229087	2.398	3.2611	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-08.log	1	0.803
6	-3507.2228781	2.418	3.6826	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-04.log	1	0.777
7	-3507.2213671	3.366	8.2622	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-06.log	1	0.152
8	-3507.2213090	3.402	4.7342	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-07.log	1	0.143
9	-3507.2189864	4.860	3.5360	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-14.log	1	0.012
10	-3507.2188627	4.937	2.4584	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-09.log	1	0.010
11	-3507.2187408	5.014	3.5321	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-10.log	1	0.009
12	-3507.2186094	5.096	4.1797	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-15.log	1	0.008
13	-3507.2183857	5.237	6.7994	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-13.log	1	0.006
14	-3507.2181753	5.369	3.5279	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-16.log	1	0.005
15	-3507.2175535	5.759	5.7375	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-12.log	1	0.003
16	-3507.2174413	5.829	4.7937	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-17.log	1	0.002
17	-3507.2174171	5.844	4.2193	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-18.log	1	0.002
18	-3507.2172937	5.922	6.2527	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-11.log	1	0.002
19	-3507.2132799	8.440	3.4398	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-21.log	1	0.000
20	-3507.2132101	8.484	4.2607	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-20.log	1	0.000
21	-3507.2130900	8.560	4.2819	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-19.log	1	0.000
22	-3507.2129125	8.671	3.3014	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-Toluene/min-22.log	1	0.000

Table S2.3 The 22 clustered lowest lying PD153035 conformers calculated using DFT B3LYP/6-311++G(d,p) in ethanol solvent.

Sorted clusters

#	Energy	RelativeEnergy (kcal/mol)	Dipole	File Name	Cluster Size	%
1	-3507.2356315	0.000	7.9964	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-01.log	1	63.511
2	-3507.2350687	0.353	4.1774	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-02.log	1	34.628
3	-3507.2316011	2.529	7.3316	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-03.log	1	0.825
4	-3507.2310415	2.880	4.6106	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-05.log	1	0.451
5	-3507.2301882	3.416	4.5346	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-04.log	1	0.180
6	-3507.2301587	3.434	3.6758	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-08.log	1	0.174
7	-3507.2299675	3.554	9.8794	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-06.log	1	0.142
8	-3507.2294349	3.888	5.7961	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-07.log	1	0.080
9	-3507.2257604	6.194	4.1293	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-10.log	1	0.002
10	-3507.2257590	6.195	3.6797	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-14.log	1	0.002
11	-3507.2255992	6.295	2.9297	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-09.log	1	0.001
12	-3507.2255060	6.354	4.7178	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-15.log	1	0.001
13	-3507.2254875	6.365	8.1556	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-13.log	1	0.001
14	-3507.2249005	6.734	4.2448	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-16.log	1	0.001
15	-3507.2243805	7.060	6.9818	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-12.log	1	0.000
16	-3507.2242944	7.114	5.8035	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-17.log	1	0.000
17	-3507.2241715	7.191	7.6062	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-11.log	1	0.000
18	-3507.2241493	7.205	5.0393	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-18.log	1	0.000
19	-3507.2194630	10.146	5.2213	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-20.log	1	0.000
20	-3507.2194227	10.171	4.0466	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-21.log	1	0.000
21	-3507.2191227	10.359	5.2322	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-19.log	1	0.000
22	-3507.2190744	10.390	3.9839	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-EtOH/min-22.log	1	0.000

Table S2.4 The 22 clustered lowest lying PD153035 conformers calculated using DFT B3LYP/6-311++G(d,p) in MeOH solvent.

Sorted clusters

#	Energy	RelativeEnergy (kcal/mol)	Dipole	File Name	Cluster Size	%
1	-3507.2359428	0.000	8.0380	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-01.log	1	64.017
2	-3507.2353613	0.365	4.1954	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-02.log	1	34.208
3	-3507.2318667	2.558	7.3642	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-03.log	1	0.792
4	-3507.2312897	2.920	4.6213	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-05.log	1	0.425
5	-3507.2304298	3.459	4.5700	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-04.log	1	0.168
6	-3507.2303962	3.481	3.6896	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-08.log	1	0.162
7	-3507.2302728	3.558	9.9383	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-06.log	1	0.142
8	-3507.2297221	3.904	5.8369	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-07.log	1	0.078
9	-3507.2259934	6.243	4.1506	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-10.log	1	0.001
10	-3507.2259796	6.252	3.6815	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-14.log	1	0.001
11	-3507.2258191	6.353	2.9442	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-09.log	1	0.001
12	-3507.2257337	6.406	4.7382	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-15.log	1	0.001
13	-3507.2257304	6.408	8.2054	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-13.log	1	0.001
14	-3507.2251279	6.786	4.2730	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-16.log	1	0.001
15	-3507.2246080	7.113	7.0270	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-12.log	1	0.000
16	-3507.2245240	7.165	5.8420	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-17.log	1	0.000
17	-3507.2244032	7.241	7.6584	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-11.log	1	0.000
18	-3507.2243714	7.261	5.0686	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-18.log	1	0.000
19	-3507.2196679	10.213	5.2535	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-20.log	1	0.000
20	-3507.2196227	10.241	4.0662	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-21.log	1	0.000
21	-3507.2193176	10.432	5.2650	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-19.log	1	0.000
22	-3507.2192745	10.459	4.0096	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-MeOH/min-22.log	1	0.000

Table S2.5 The 22 clustered lowest lying PD153035 conformers calculated using DFT B3LYP/6-311++G(d,p) in ACN solvent.

Sorted clusters

#	Energy	RelativeEnergy (kcal/mol)	Dipole	File Name	Cluster Size	%
1	-3507.2360298	0.000	8.0497	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-01.log	1	64.159
2	-3507.2354430	0.368	4.2006	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-02.log	1	34.089
3	-3507.2319408	2.566	7.3731	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-03.log	1	0.782
4	-3507.2313590	2.931	4.6243	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-05.log	1	0.418
5	-3507.2304971	3.472	4.5800	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-04.log	1	0.165
6	-3507.2304623	3.494	3.6934	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-08.log	1	0.159
7	-3507.2303582	3.559	9.9549	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-06.log	1	0.142
8	-3507.2298024	3.908	5.8483	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-07.log	1	0.078
9	-3507.2260583	6.257	4.1567	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-10.log	1	0.001
10	-3507.2260410	6.268	3.6820	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-14.log	1	0.001
11	-3507.2258804	6.369	2.9482	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-09.log	1	0.001
12	-3507.2257982	6.420	8.2193	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-13.log	1	0.001
13	-3507.2257972	6.421	4.7439	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-15.log	1	0.001
14	-3507.2251914	6.801	4.2810	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-16.log	1	0.001
15	-3507.2246715	7.127	7.0396	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-12.log	1	0.000
16	-3507.2245881	7.180	5.8528	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-17.log	1	0.000
17	-3507.2244679	7.255	7.6731	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-11.log	1	0.000
18	-3507.2244333	7.277	5.0768	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-18.log	1	0.000
19	-3507.2197250	10.231	5.2625	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-20.log	1	0.000
20	-3507.2196784	10.261	4.0716	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-21.log	1	0.000
21	-3507.2193719	10.453	5.2741	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-19.log	1	0.000
22	-3507.2193302	10.479	4.0168	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-ACN/min-22.log	1	0.000

Table S2.6 The 22 clustered lowest lying PD153035 conformers calculated using DFT B3LYP/6-311++G(d,p) in DMSO solvent.

Sorted clusters

#	Energy	RelativeEnergy (kcal/mol)	Dipole	File Name	Cluster Size	%
1	-3507.2362515	0.000	8.0794	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-01.log	1	64.518
2	-3507.2356513	0.377	4.2142	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-02.log	1	33.788
3	-3507.2321299	2.586	7.3965	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-03.log	1	0.760
4	-3507.2315354	2.959	4.6320	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-05.log	1	0.400
5	-3507.2306686	3.503	4.6055	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-04.log	1	0.157
6	-3507.2306306	3.527	3.7032	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-08.log	1	0.151
7	-3507.2305760	3.561	9.9971	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-06.log	1	0.142
8	-3507.2300072	3.918	5.8769	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-07.log	1	0.077
9	-3507.2262236	6.293	4.1723	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-10.log	1	0.001
10	-3507.2261972	6.309	3.6831	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-14.log	1	0.001
11	-3507.2260362	6.410	2.9584	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-09.log	1	0.001
12	-3507.2259709	6.451	8.2549	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-13.log	1	0.001
13	-3507.2259587	6.459	4.7586	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-15.log	1	0.001
14	-3507.2253529	6.839	4.3013	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-16.log	1	0.001
15	-3507.2248330	7.165	7.0719	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-12.log	1	0.000
16	-3507.2247513	7.216	5.8805	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-17.log	1	0.000
17	-3507.2246326	7.291	7.7101	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-11.log	1	0.000
18	-3507.2245908	7.317	5.0978	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-18.log	1	0.000
19	-3507.2198703	10.279	5.2853	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-20.log	1	0.000
20	-3507.2198201	10.311	4.0854	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-21.log	1	0.000
21	-3507.2195098	10.505	5.2974	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-19.log	1	0.000
22	-3507.2194719	10.529	4.0353	/home/wv900/Amber/EGFR/AG-1478/Br-Feng/All-DMSO/min-22.log	1	0.000

Table S3 Comparison of the top AG-1478 and PD15035 conformers in DMSO.

	AG - 1478*				PD153035			
Cluster (conformer)	**ΔE Kcal/mol**	**μ Debye**	**Cluster Size[#]**	**Weight (%)**	**ΔE Kcal/mol**	**μ Debye**	**Cluster Size[$]**	**Weight (%)**
1	0.000	8.450	10	67.646	0.000	8.079	2	64.518
2	0.594	3.648	11	26.819	0.377	4.214	5	33.788
3	1.975	8.178	17	3.871	2.586	7.397	9	0.760
4	2.570	5.305	11	0.900	2.595	4.632	9	0.400
5	2.933	11.100	9	0.395	3.053	4.605	3	0.157
6	3.516	5.812	19	0.306	3.527	3.703	9	0.151
7	4.567	3.310	12	0.032	3.561	9.997	6	0.142
8	4.631	4.673	10	0.024	3.918	5.877	2	0.077
9	5.373	9.245	5	0.003	6.293	4.172	2	0.001
10	5.970	4.383	5	0.001	6.309	3.683	1	0.001
11	6.884	4.149	6	0.000	6.410	2.958	9	0.001
12	6.898	4.407	14	0.001	6.451	8.255	8	0.001

* Wang and Vasilyev, Int. J. Quan. Chem. (2021, 10.1002/qua.26765).

[#]The total number of AG-1478 (Cl) conformers in the lowest 12 clusters is 129.

[$]The total number of PD153035 (Br) conformers in the lowest 12 clusters is 65.