Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supplementary Information

The Development of an Amber-compatible organosilane force field for drug-like molecules

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1. Supplementary Figures

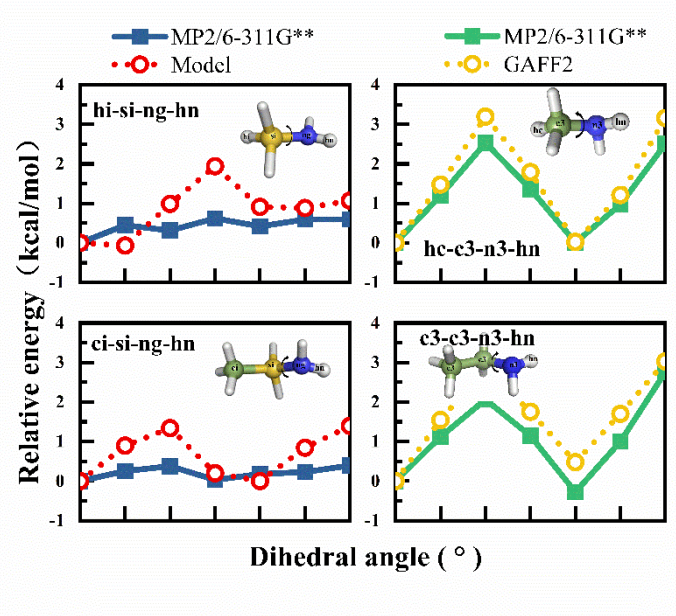
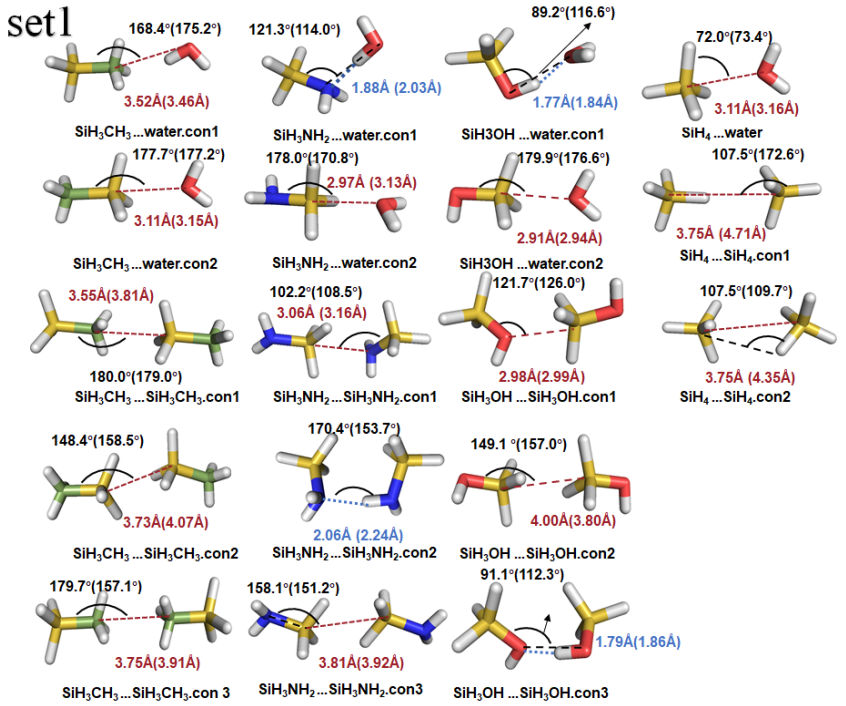


Figure S1. Comparison of the rotational energy surface of SiH_3NH_2 and $SiH_2CH_3NH_2$ with their carbon analogs, CH_3NH_2 and $C_2H_5NH_2$.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3.52Å(3.46Å)
SiH3CH3...water.con1
121.3°(114.0°)
1.88Å (2.03Å)
SiH3NH2...water.con1
89.2°(116.6°)
1.77Å(1.84Å)
SiH3OH ...water.con1
72.0°(73.4°)
3.11Å(3.16Å)
SiH4 ...water
177.7°(177.2°)
3.11Å(3.15Å)
SiH3CH3...water.con2
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2.97Å (3.13Å)
SiH3NH2...water.con2
179.9°(176.6°)
2.91Å(2.94Å)
SiH3OH ...water.con2
107.5°(172.6°)
3.75Å (4.71Å)
SiH4 ...SiH4.con1
3.55Å(3.81Å)
180.0°(179.0°)
SiH3CH3...SiH3CH3.con1
102.2°(108.5°)
3.06Å (3.16Å)
SiH3NH2...SiH3NH2.con1
121.7°(126.0°)
2.98Å(2.99Å)
SiH3OH ...SiH3OH.con1
107.5°(109.7°)
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SiH4 ...SiH4.con2
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170.4°(153.7°)
2.06Å (2.24Å)
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4.00Å(3.80Å)
SiH3OH ...SiH3OH.con2
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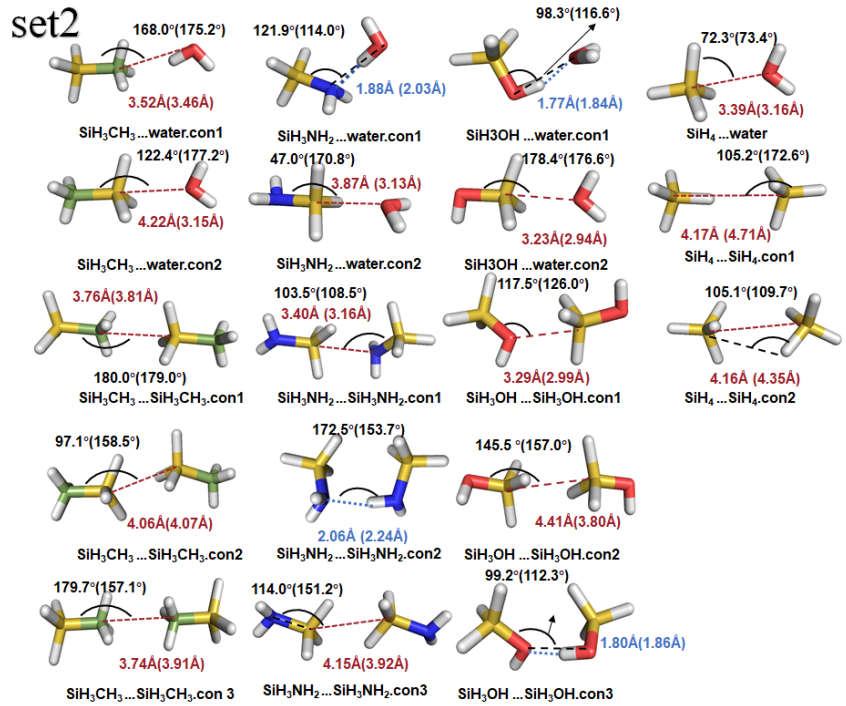
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SiH3NH2...water.con1
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1.77Å(1.84Å)
SiH3OH ...water.con1
72.3°(73.4°)
3.39Å(3.16Å)
SiH4 ...water
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SiH3OH ...water.con2
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4.17Å (4.71Å)
SiH4 ...SiH4.con1
3.76Å(3.81Å)
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SiH3CH3...SiH3CH3.con1
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SiH3NH2...SiH3NH2.con1
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SiH3OH ...SiH3OH.con1
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4.16Å (4.35Å)
SiH4 ...SiH4.con2
97.1°(158.5°)
4.06Å(4.07Å)
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4.15Å(3.92Å)
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1.80Å(1.86Å)
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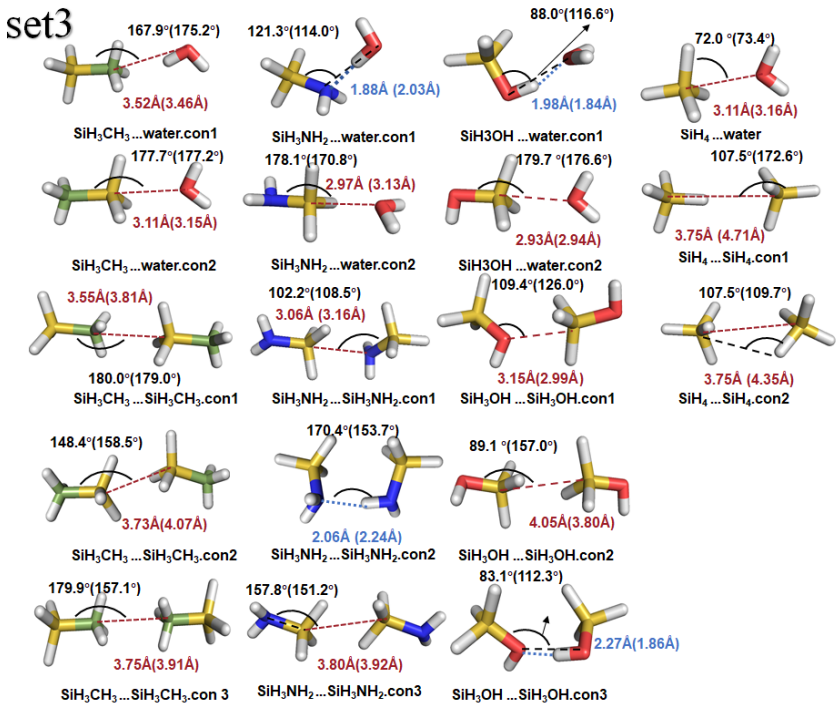


Figure S2. Comparison of the intermolecular distance and angle of the force field and QM (in the parenthesis, MP2/cc-pVTZ) optimized structures of 18 pairs. The results of three different vdW parameter sets (namely **set1**, **set2** and **set3** in the figures) were shown.

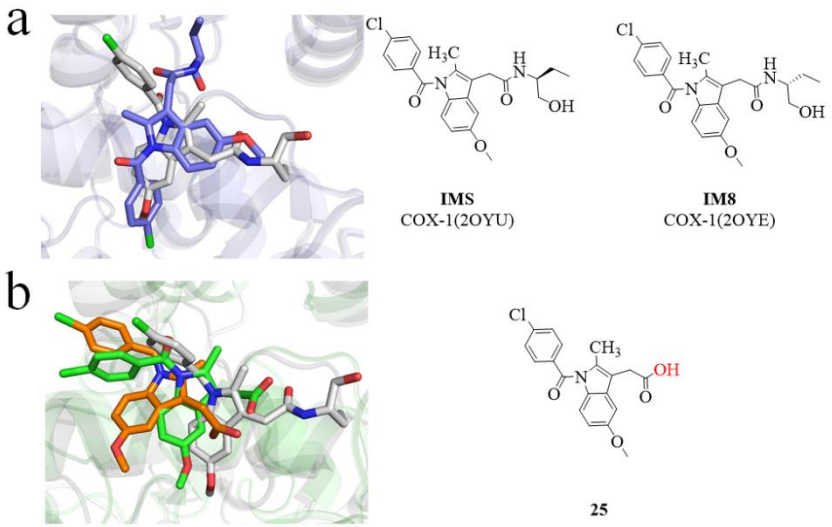


Figure S3. The binding pocket of COX proteins may have a large degree of binding flexibility for small molecule binders. Thus, ligand may have more than one binding conformations in COX proteins. a) Two different binding poses of the chiral molecules, **IMS** (2OYU, silver) and **IM8** (2YOE, blue), reported in crystal structures. b) The starting conformations of **25** in con1 (green) and con2 (orange) that have been used in TI calculations, compared with **IMS** (silver) in 2OYU.

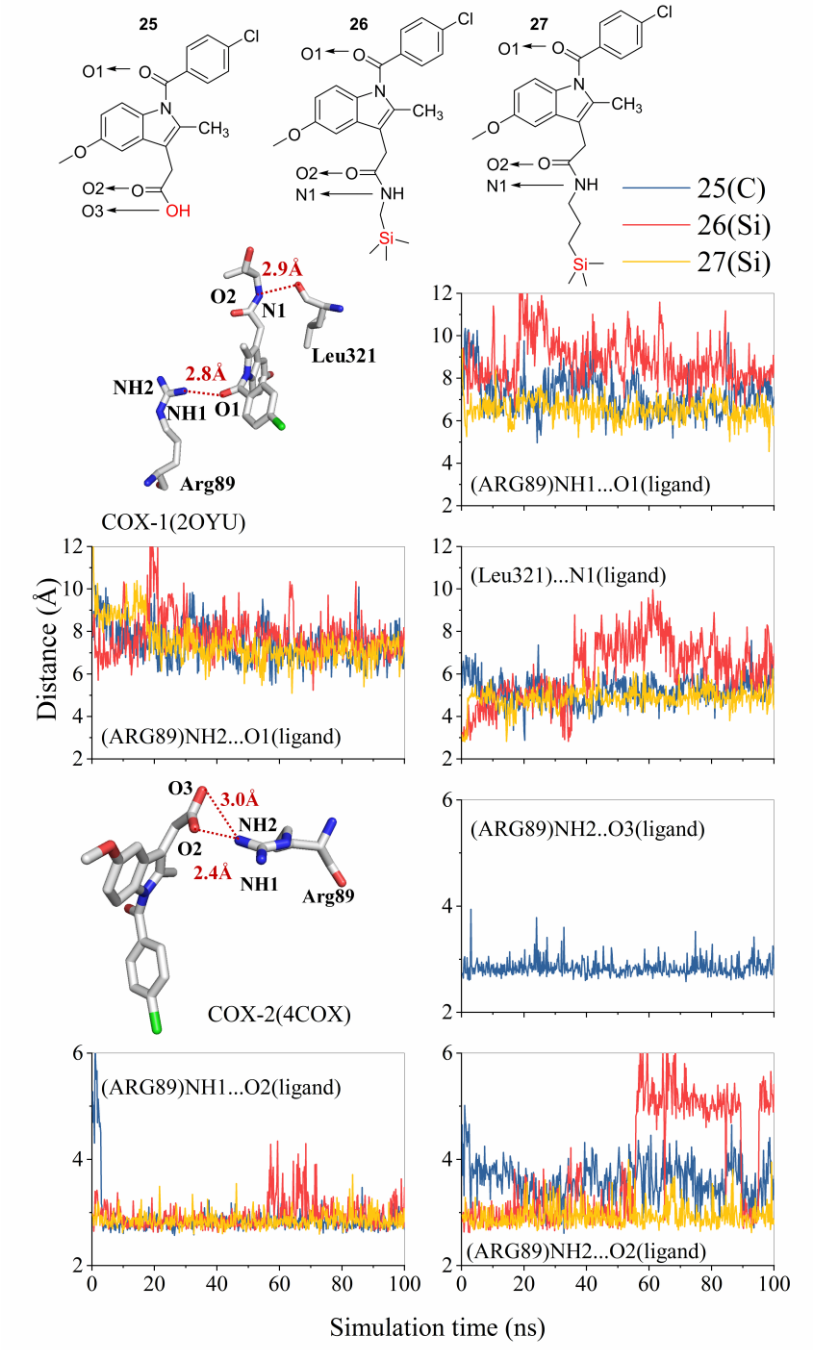


Figure S4. The hydrogen bonds between the COX protein (COX-1 in the upper panel and COX-2 in the lower) and ligand (**25**, **26** and **27**) in crystal structures (2OYU and 4COX) and during the 100 ns MD simulations.

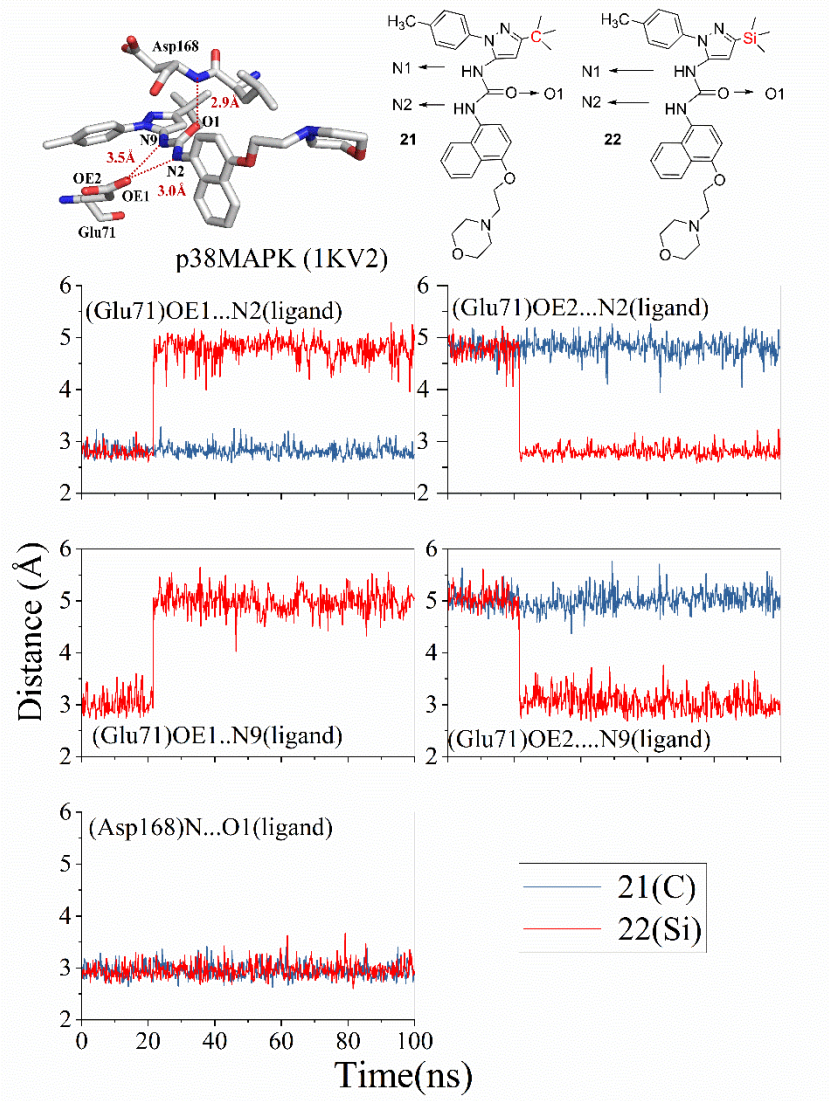


Figure S5. The hydrogen bonds between p38 MAPK and the ligand (**21** and **22**) in crystal structure (1KV2) and during the 100 ns MD simulations.

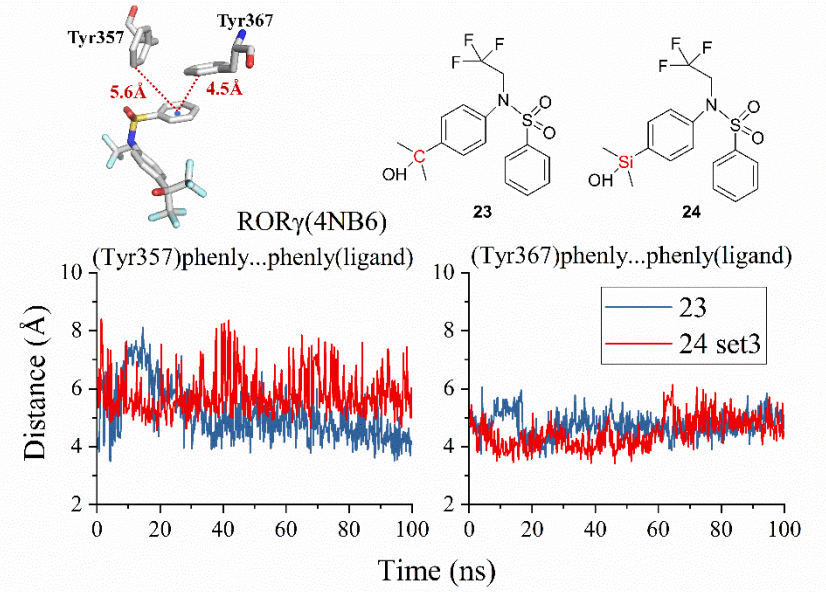


Figure S6. The intermolecular distances between RORγ and ligand (**23** and **24**) in crystal structure (4NB6) and during the 100 ns MD simulations.

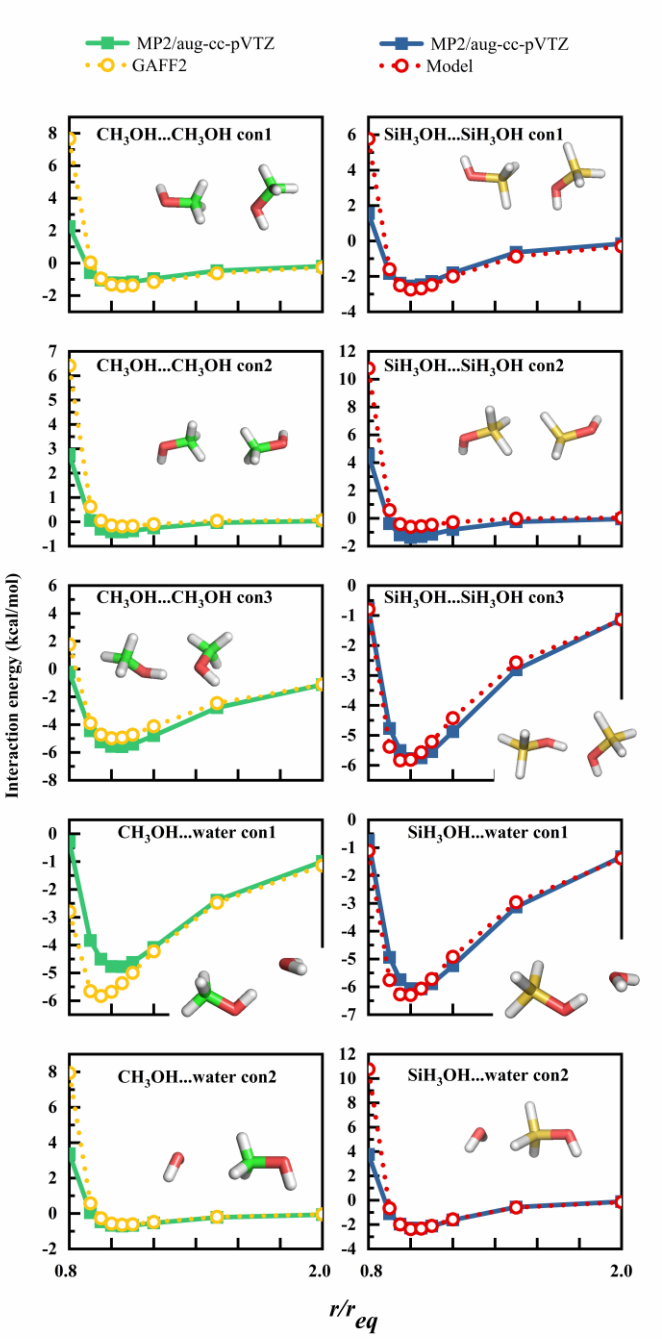


Figure S7. The potential energy surfaces of hydroxyl containing carbon (left panel) and silicon (right panel) compounds. The vdW parameters for *oh* (hydroxyl oxygen, 1.820 Å and 0.093 kcal/mol for r^* and ε) in GAFF2 was fitted to obtain a good condensed phase performance by sacrificing the accuracy in gas phase. This might be the reason of the poor performance of the gas phased fitted vdW for *oi* (1.990 Å and 0.032 kcal/mol for r^* and ε, hydroxyl oxygen directly bonded to silicon) in binding free energy calculation.

2. Supplementary Table

Table S1. The optimized force constant and equilibrium bond length involving the newly introduced atom types.

Bond	K_r(kcal/mol Å $^{-2}$)	r_{eq}(Å)
si-ci	223.29	1.884
si-ng	302.02	1.740
si-oi	301.70	1.674
si-hi	200.20	1.487
si-si	410.80	2.339
si-ca	42.34	1.885
si-cc	38.50	1.878
si-cd	38.50	1.878
ci-hc	375.92	1.097
ci-c3	232.52	1.538
ci-n3	261.19	1.465
ci-oh	293.40	1.423
ci-h1	375.92	1.097
ci-ca	250.32	1.516
oi-ho	569.60	0.973
ng-hn	511.28	1.019
n -ci	263.77	1.462

Table S2. The optimized force constant and equilibrium bond angle involving the newly introduced atom types.

Angle	K_θ (kcal/mol radian^{-2})	θ_{eq} (°)
hi-si-hi	37.64	108.57
ci-si-hi	23.43	109.77
ci-si-ci	31.44	109.83
ci-si-ng	12.06	108.89
ci-si-oi	3.01	106.42
ci-si-ca	9.03	109.59
ci-si-cc	74.50	108.79
ci-si-cd	74.50	108.79
ng-si-hi	35.89	110.68
oi-si-hi	45.67	110.46
si-ci-hc	36.65	111.17
si-ci-c3	47.94	114.45
si-ci-n3	30.10	109.11
si-ci-n	30.10	112.105
si-ci-h1	12.72	110.34
si-ci-oh	58.82	105.76
si-ci-ca	48.16	111.84
si-ca-ca	9.92	121.38
si-ca-nb	5.72	116.08
si-cc-cc	7.20	130.41
si-cd-cd	7.20	130.41
si-cc-nc	3.00	119.51
si-cc-nd	3.00	119.51
si-cd-nc	3.00	119.51
si-cd-nd	3.00	119.51
si-ng-hn	31.84	118.89
si-oi-ho	20.78	116.37
si-si-hi	15.92	110.40
ng-si-ca	85.25	105.26
oi-si-ca	123.57	103.70
hc-ci-hc	38.96	107.58
hc-ci-c3	46.816	109.80
hc-ci-ca	47.281	110.47
hc-c3-ci	46.816	109.80
h1-ci-h1	38.802	108.46

h1-ci-n3	61.163	109.88
h1-ci-oh	62.54	110.26
ci-c3-hc	46.816	109.80
ci-n3-hn	47.782	109.29
ci-oh-ho	49.027	107.26
ci-ca-ca	65.583	120.77
hn-ng-hn	40.828	106.40
ci-n-hn	46.147	117.68
n -ci-h1	61.544	108.88
c -n -ci	65.252	120.69
c3-c3-ci	64.888	111.51

Table S3. The optimized dihedral parameters.

Dihedral	no. of paths[a]	$v_n/2$[b]	γ[c]	n[d]
X-si-si-X	9	0.579	0	3
X-si-ci-X	9	0.705	0	3
X-si-ng-X	6	0.699	0	3
X-si-oi-X	3	0.547	0	3
X-si-ca-X	6	0.000	0	2
X-si-cc-X	6	0.000	0	2
X-ci-c3-X	9	1.156	0	3
X-ci-n3-X	6	1.784	0	3
X-ci-n -X	6	0.000	0	2
X-ci-oh-X	3	0.295	0	3
X-ci-ca-X	6	0.000	0	2
si-ci-ca-ca	1	0.400	0	2
si-ci-n3-hn	1	1.000	0	1
si-ci-oh-ho	1	0.000	0	-3
	1	0.700	90	2
ci-si-ca-nb	1	0.200	0	3
ci-si-cc-nd	1	0.040	0	3
oi-si-ca-ca	1	-0.090	180	-2
	1	1.000	0	1
oi-si-ca-ca	1	2.0	180	-3
	1	0.2	180	2
si-ci-n -c	1	0.500	0	-3
	1	0.300	60	1

[a]Number of bond paths that the total $v_n/2$ is divided into. [b]Magnitude of torsion in kcal/mol. [c]Phase offset in the degree. [d]The periodicity of the torsion. A negative value is not used in the calculation but signifies more than one component around a given bond.

Table S4. Error of the relative rotational energy (kcal/mol) of the model compounds.

Molecule	MSE	MUE	RMSE
2	-0.01	0.01	0.02
3	-0.46	0.51	0.63
4	0.00	0.01	0.01
7	0.04	0.04	0.06
8	-0.39	0.54	0.66
9	-0.08	0.08	0.10
10	0.02	0.02	0.03
11	0.03	0.04	0.06
12	0.06	0.16	0.18
13	0.06	0.18	0.21
14	-0.01	0.08	0.09
15	-0.03	0.03	0.04
16	0.03	0.08	0.10
17	-0.06	0.06	0.10
18	0.03	0.04	0.05
19	-0.06	0.09	0.11
20	-0.41	0.33	0.45
Overall	-0.07	0.13	0.17

Table S5. Error of the interaction energy of three sets of vdW parameters at different distance ranges (0.8, 0.9, 0.95, 1.0, 1.05, 1.1, 1.2, 1.5 and 2.0 fold of the equilibrium distance) of 18 molecule pairs.

Distance		Energy(kcal/mol)		
		set1	**set2**	**set3**
0.8-0.9				
	MSE	-0.14	5.72	2.62
	MUE	0.83	6.09	3.29
	RMSE	1.08	11.49	7.71
0.95-1.2				
	MSE	0.10	0.35	0.24
	MUE	0.26	0.47	0.43
	RMSE	0.34	0.76	0.97
1.5-2.0				
	MSE	0.04	0.01	-0.01
	MUE	0.07	0.06	0.09
	RMSE	0.11	0.10	0.14

Table S6. The RMSD (Å) of protein (backbone atoms) and ligand (non-hydrogen atoms) during the 100 ns MD simulations.

Target		GAFF2		**set1**		**set2**		**set3**	
		Protein	Ligand	Protein	Ligand	Protein	Ligand	Protein	Ligand
p38 MAPK	**c1**	2.18±0.54	1.73±0.42	N/A	N/A	N/A	N/A	N/A	N/A
	c2	2.41±0.47	2.14±0.38	N/A	N/A	N/A	N/A	N/A	N/A
	21	1.90 ±0.21	2.17±0.39	N/A	N/A	N/A	N/A	N/A	N/A
	22	N/A	N/A	1.97 ±0.24	1.51±0.31	1.52 ±0.18	1.28±0.43	1.93±0.33	1.42±0.27
RORγ	**23**	2.54 ±0.23	2.60±0.43	N/A	N/A	N/A	N/A	N/A	N/A
	24	N/A	N/A	1.47 ±0.12	2.28±0.81	1.33 ±0.13	1.99±0.45	1.80±0.27	2.60±0.43
COX-1	**25**	1.80 ±0.27	2.98±0.31	N/A	N/A	N/A	N/A	N/A	N/A
	26	N/A	N/A	2.63 ±0.19	4.25±0.70	2.28 ±0.21	3.43±0.53	2.30±0.23	3.90±0.85
	27	N/A	N/A	2.41 ±0.23	5.37±1.11	2.48 ±0.21	6.97±0.97	2.49±0.21	4.24±0.44
COX-2	**25**	2.12 ±0.3	1.25±0.34	N/A	N/A	N/A	N/A	N/A	N/A
	26	N/A	N/A	2.11±0.19	2.18±0.27	2.28 ±0.18	2.25±0.29	2.12±0.26	2.19±0.27
	27	N/A	N/A	1.98±0.16	2.01±0.31	2.01 ±0.18	1.74±0.22	2.04±0.28	1.93±0.26
AChE	**31**	1.72 ±0.20	4.39±0.99	N/A	N/A	N/A	N/A	N/A	N/A
	32	N/A	N/A	1.44 ±0.25	2.71±0.94	1.17±0.09	4.42±2.51	1.65 ±0.17	3.39±0.79
	33	1.65±0.20	4.00±1.40	N/A	N/A	N/A	N/A	N/A	N/A
	34	N/A	N/A	1.36 ±0.16	4.03±1.52	1.60 ±0.16	5.79±2.14	1.32 ±0.09	5.44±1.85

Table S7. List of the literature reported experimental activity of the compounds.

Target	Ligand	Biological activity (M)
p38 MAPK	**21**(BIRB-796)[1]	$IC_{50}(9\times10^{-9})$
	22[1]	$IC_{50}(7\times10^{-9})$
	c1[2]	$IC_{50}(>7\times10^{-6})$
	c2[2]	$IC_{50}(3.3\times10^{-7})$
	c3[2]	$IC_{50}(1.3\times10^{-8})$
RORγ	**23**(T091317)[3]	$IC_{50}(>3\times10^{-5})$
	24[3]	$IC_{50}(1.1\times10^{-5})$
COX-1	**25**(indomethacin)[4]	$IC_{50}(4.7\times10^{-8})$
	26[4]	$IC_{50}(2.7\times10^{-6})$
	27[4]	$IC_{50}(>1.0\times10^{-5})$
	25(indomethacin)[5]	$IC_{50}(0.05\times10^{-6})$
	c4[5]	$IC_{50}(>6.6\times10^{-5})$
COX-2	**25** (indomethacin)[4]	$IC_{50}(5.9*10^{-7})$
	26[4]	$IC_{50}(3.9\times10^{-7})$
	27[4]	$IC_{50}(2.1*10^{-7})$
	25(indomethacin)[5]	$IC_{50}(0.75\times10^{-6})$
	c4[5]	$IC_{50}(0.05\times10^{-6})$
AChE	**31**[6]	Ki (2.9×10^{-8})
	32(MDL73105)[7]	Ki (6.8×10^{-9})
	33[8]	Ki (0.4×10^{-9})
	34(MDL73745)[7]	Ki (4.7×10^{-11})

Table S8. The binding free energy difference calculated using parameter **set1** and **set2**.

Protein Ligand **A**→**B**	Expt.[a]	Calculation			
		set1		**set2**	
p38 MAPK		con1	con2	con1	con2
21(C)→**22**(Si)	-0.15	-1.64±0.35	-2.03±0.19	-2.54±0.14	-1.92±0.22
RORγ					
23(C)→**24**(Si)	<-0.60	5.23±0.20	5.26±0.38	2.24±0.25	2.08±0.10
COX-1					
25(C)→**26**(Si)	2.41	5.95±0.49	-0.72±1.41	7.95±0.03	-7.37±0.26
26(Si)→**27**(Si)	>0.78	-0.24±0.11	0.09±0.24	-0.69±0.62	-5.74±0.54
COX-2					
25(C)→**26**(Si)	-0.25	0.27±0.83	-2.16±0.10	0.37±0.45	-2.50±0.47
26(Si)→**27**(Si)	-0.37	-0.79±0.01	-4.13±0.26	2.08±0.12	-1.36±0.10
AChE					
31(C)→**32**(Si)	-0.86	0.07±0.32	-0.52±0.14	-0.71±0.38	-0.39±0.54
33(C)→**34**(Si)	-1.28	0.37±0.16	-0.36±0.03	-0.27±0.09	-1.09±0.18
MSE[b]		0.54	-1.19	1.09	-2.25
MUE		1.27	1.65	2.06	3.08
RMSE		1.59	2.03	2.60	4.40

[a]The experimental free energy values were obtained based on the IC_{50} or K_i values reported in the same study for each protein system(see Table S7 for details and references), to minimize the potential error due to different experiment conditions. [b]As some experimental values are not definitive, the actual errors would be larger than the listed.

Table S9. The convergence of the TI calculation using parameter **set3**.

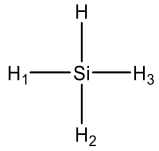
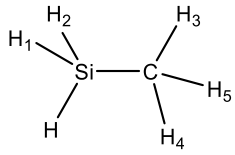
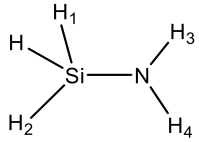
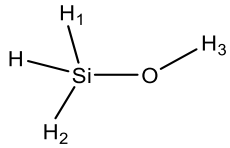
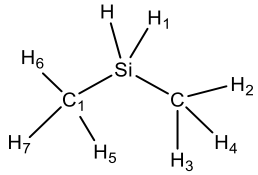
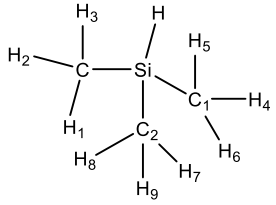
Protein	Ligand **A**→**B**	Expt.	Calculation									
			1st ns	2rd ns	3th ns	4th ns	5th ns	6th ns	7th ns	8th ns	Change in the last two cumulative averagesf	S.D. of each ns
			con1									
p38MAPK	**21**(C)→**22**(Si)	-0.15	-1.69	-1.80	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.05
	difference[a]			0.11	N/A	N/A	N/A	N/A	N/A	N/A		
	c1(C)→**c2**(C)	<-1.82	-3.80	-3.14	-3.06	-2.99	N/A	N/A	N/A	N/A	0.09	0.32
	difference			0.66	0.08	0.07	N/A	N/A	N/A	N/A		
	c2(C)→**c3**(C)	-1.93	-0.97	-1.03	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0.06
	difference			-0.06	N/A	N/A	N/A	N/A	N/A	N/A		
	c1(C)→**c3**(C)	<-3.75	-4.69	-4.52	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.16
	difference			0.16	N/A	N/A	N/A	N/A	N/A	N/A		
RORγ	**23**(C)→**24**(Si)	<-0.60	0.51	0.52	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.01
	difference			0.02	0.01	-0.06	N/A	N/A	N/A	N/A		
COX-1	**25**(C)→**26**(Si)	2.41	3.65	3.59	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0.06
	difference			-0.06	N/A	N/A	N/A	N/A	N/A	N/A		
	26(Si)→**27**(Si)	>0.78	-1.04	-1.56	-0.64	-1.91	-1.86	-1.86	N/A	N/A	-0.08	0.48
	difference			-0.52	0.92	-1.28	0.06	0.00	N/A	N/A		
	25(C)→**27**(Si)	>3.19	5.05	3.76	2.55	2.83	N/A	N/A	N/A	N/A	-0.24	0.98
	difference			-1.29	-1.21	0.28	N/A	N/A	N/A	N/A		
	25(C)→**c4**(C)	>4.28	0.99	1.57	3.23	1.38	1.01	N/A	N/A	N/A	-0.16	0.83
	difference			0.58	1.66	-1.85	-0.37	N/A	N/A	N/A		

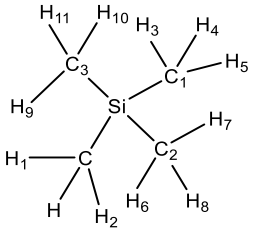
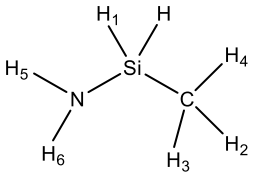
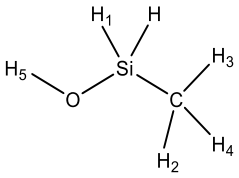
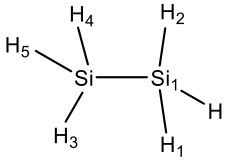
COX-2												
	25(C)→**26**(Si)	-0.25	-0.03	0.82	1.47	-0.39	-0.21	-1.19	0.27	0.04	-0.01	0.75
	difference			0.85	0.66	-1.87	0.18	-0.97	1.46	-0.24		
	26(Si)→**27**(Si)	-0.37	1.00	1.13	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.13
	difference			0.13	N/A	N/A	N/A	N/A	N/A	N/A		
	25(C)→**27**(Si)	-0.62	2.37	1.76	1.19	1.19	N/A	N/A	N/A	N/A	-0.15	0.49
	difference			-0.61	-0.57	0.00	N/A	N/A	N/A	N/A		
	25(C)→**c4**(C)	-1.61	-1.15	-0.86	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.29
	difference			0.29	N/A	N/A	N/A	N/A	N/A	N/A		
AchE	**31**(C)→**32**(Si)	-0.86	0.10	-0.09	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0.20
	difference			-0.20	N/A	N/A	N/A	N/A	N/A	N/A		
	33(C)→**34**(Si)	-1.28	0.16	-0.44	-0.39	-0.46	N/A	N/A	N/A	N/A	-0.06	0.25
	difference			-0.60	0.05	-0.07	N/A	N/A	N/A	N/A		
								con2				
p38MAPK	**21**(C)→**22**(Si)	-0.15	0.01	0.01	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.01
	difference			0.00	N/A	N/A	N/A	N/A	N/A	N/A		
RORγ	**23**(C)→**24**(Si)	<-0.60	1.33	0.42	0.27	0.05	N/A	N/A	N/A	N/A	-0.20	-0.16
	difference			-0.91	-0.15	-0.22	N/A	N/A	N/A	N/A		
COX-1	**25**(C)→**26**(Si)	2.41	-3.38	-2.79	-2.62	-1.83	-1.53	-1.48	N/A	N/A	0.16	0.71
	difference			0.59	0.16	0.79	0.30	0.04	N/A	N/A		
	26(Si)→**27**(Si)	>0.78	-0.09	-0.44	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0.35

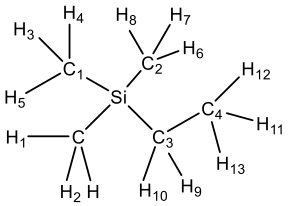
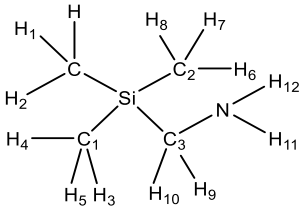
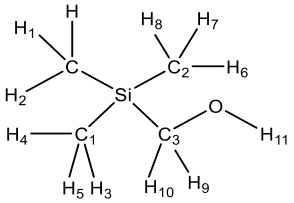
	difference			-0.35	N/A	N/A	N/A	N/A	N/A	N/A		
	25(C)→**27**(Si)	>3.19	1.04	1.86	2.50	0.20	1.59	2.06	N/A	N/A	0.10	0.75
	difference			0.82	0.64	-2.30	1.39	0.47	N/A	N/A		
COX-2	**25**(C)→**26**(Si)	-0.25	-3.42	-2.77	-2.39	-2.44	N/A	N/A	N/A	N/A	0.10	0.41
	difference			0.65	0.37	-0.05	N/A	N/A	N/A	N/A		
	26(Si)→**27**(Si)	-0.37	-1.94	-2.40	-1.69	-3.02	-2.11	-2.14	N/A	N/A	0.01	0.42
	difference			-0.47	0.72	-1.33	0.91	-0.04	N/A	N/A		
	25(C)→**27**(Si)	-0.62	-1.44	0.54	2.06	1.61	N/A	N/A	N/A	N/A	0.31	1.35
	difference			1.98	1.53	-0.46	N/A	N/A	N/A	N/A		
AChE	**31**(C)→**32**(Si)	-0.86	-0.50	-0.88	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0.39
	difference			-0.39	N/A	N/A	N/A	N/A	N/A	N/A		
	33(C)→**34**(Si)	-1.28	1.08	1.36	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.28
	difference			0.28	N/A	N/A	N/A	N/A	N/A	N/A		

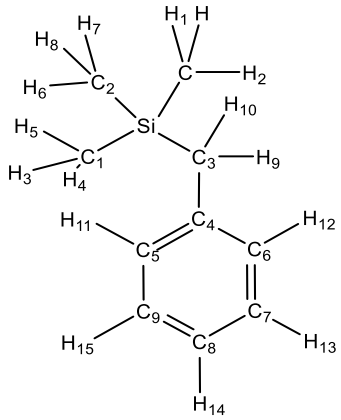
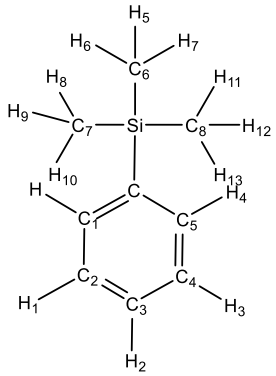
[a]All the differences were calculated as the difference between the n^{th} and $(n-1)^{th}$ nanosecond results.

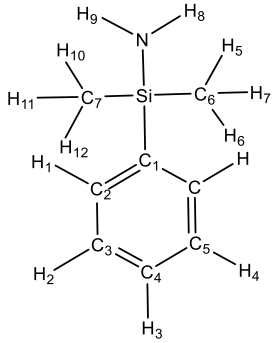
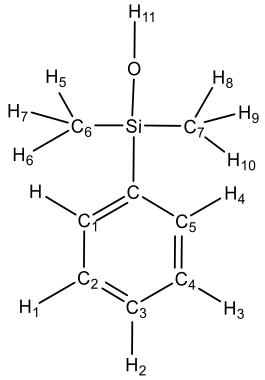
Table S10. Atom types and atomic AM1-BCC charges for the model compounds (**1**-**20**).

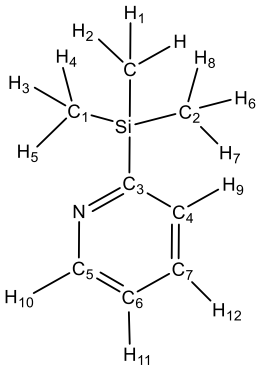
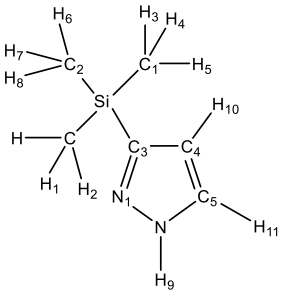
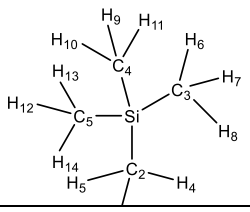
Compound	Atom	Type	AM1-BCC charge
1 	Si	si	0.5288
	H	hi	-0.1322
	H1	hi	-0.1322
	H2	hi	-0.1322
	H3	hi	-0.1322
2 	Si	si	0.5806
	H	hi	-0.1602
	H1	hi	-0.1602
	H2	hi	-0.1602
	C	ci	-0.2566
	H3	hc	0.0517
	H4	hc	0.0517
	H5	hc	0.0517
3 	Si	si	0.8609
	H	hi	-0.2050
	H1	hi	-0.2050
	H2	hi	-0.2050
	N	ng	-1.0309
	H3	hn	0.3926
	H4	hn	0.3926
4 	Si	si	0.9693
	H	hi	-0.1982
	H1	hi	-0.1982
	H2	hi	-0.1982
	O	oi	-0.7942
	H3	ho	0.4190
5 	Si	si	0.6124
	H	hi	-0.1852
	H1	hi	-0.1852
	C1	ci	-0.2721
	H5	hc	0.0504
	H6	hc	0.0504
	H7	hc	0.0504
	C	ci	-0.2721
	H2	hc	0.0504
	H3	hc	0.0504
	H4	hc	0.0504
6 	Si	si	0.6252
	H	hi	-0.2092
	C1	ci	-0.2851
	H4	hc	0.0490
	H5	hc	0.0490
	H6	hc	0.0490
	C2	ci	-0.2851
	H7	hc	0.0490

		H8	hc	0.0490
		H9	hc	0.0490
		C	ci	-0.2851
		H1	hc	0.0490
		H2	hc	0.0490
		H3	hc	0.0490
7		Si	si	0.6220
		C1	ci	-0.2961
		H3	hc	0.0467
		H4	hc	0.0467
		H5	hc	0.0467
		C2	ci	-0.2961
		H6	hc	0.0467
		H7	hc	0.0467
		H8	hc	0.0467
		C3	ci	-0.2961
		H9	hc	0.0467
		H10	hc	0.0467
		H11	hc	0.0467
		C	ci	-0.2961
		H	hc	0.0467
		H1	hc	0.0467
		H2	hc	0.0467
8		C	ci	-0.3181
		H2	hc	0.0477
		H3	hc	0.0477
		H4	hc	0.0477
		Si	si	0.8697
		H	hi	-0.2192
		H1	hi	-0.2192
		N	ng	-1.0369
		H5	hn	0.3898
		H6	hn	0.3898
9		Si	si	0.9531
		H	hi	-0.2312
		H1	hi	-0.2312
		O	oi	-0.7877
		H5	ho	0.4170
		C	ci	-0.3021
		H2	hc	0.0604
		H3	hc	0.0604
		H4	hc	0.0604
10		Si	si	0.2726
		H3	hi	-0.0912
		H4	hi	-0.0912
		H5	hi	-0.0912
		Si1	si	0.2726
		H	hi	-0.0912
		H1	hi	-0.0912
		H2	hi	-0.0912

11		C	ci	-0.2944
		H	hc	0.0469
		H1	hc	0.0469
		H2	hc	0.0469
		Si	si	0.6170
		C1	ci	-0.2944
		H3	hc	0.0469
		H4	hc	0.0469
		H5	hc	0.0469
		C2	ci	-0.2944
		H6	hc	0.0469
		H7	hc	0.0469
		H8	hc	0.0469
		C3	ci	-0.2724
		H9	hc	0.0517
		H10	hc	0.0517
		C4	c3	-0.0761
		H11	hc	0.0294
		H12	hc	0.0294
		H13	hc	0.0294
12		C	ci	-0.3001
		H	hc	0.0487
		H1	hc	0.0487
		H2	hc	0.0487
		Si	si	0.6470
		C1	ci	-0.3001
		H3	hc	0.0487
		H4	hc	0.0487
		H5	hc	0.0487
		C2	ci	-0.3001
		H6	hc	0.0487
		H7	hc	0.0487
		H8	hc	0.0487
		C3	ci	-0.0342
		H9	h1	0.0317
		H10	h1	0.0317
		N	n3	-0.8938
		H11	hn	0.3388
		H12	hn	0.3388
13		C	ci	-0.3021
		H	hc	0.0509
		H1	hc	0.0509
		H2	hc	0.0509
		Si	si	0.6630
		C1	ci	-0.3021
		H3	hc	0.0509
		H4	hc	0.0509
		H5	hc	0.0509
		C2	ci	-0.3021
		H6	hc	0.0509
		H7	hc	0.0509

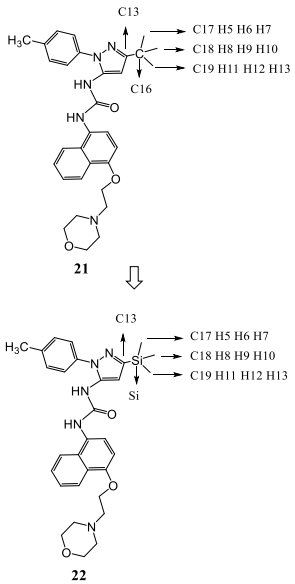
	H8	hc	0.0509
	C3	ci	-0.0556
	H9	h1	0.0227
	H10	h1	0.0227
	O	oh	-0.5898
	H11	ho	0.3870
14 	C	ci	-0.2978
	H	hc	0.0495
	H1	hc	0.0495
	H2	hc	0.0495
	Si	si	0.6200
	C1	ci	-0.2978
	H3	hc	0.0495
	H4	hc	0.0495
	H5	hc	0.0495
	C2	ci	-0.2978
	H6	hc	0.0495
	H7	hc	0.0495
	H8	hc	0.0495
	C3	ci	-0.2241
	H9	hc	0.0617
	H10	hc	0.0617
	C4	ca	-0.0493
	C6	ca	-0.1400
	C7	ca	-0.1240
	C8	ca	-0.1400
	H14	ha	0.1290
	H13	ha	0.1290
	H12	ha	0.1290
	C5	ca	-0.1400
	H11	ha	0.1290
	C9	ca	-0.1240
	H15	ha	0.1290
15 	C	ca	-0.2422
	Si	si	0.6422
	C6	ci	-0.2968
	H5	hc	0.0478
	H6	hc	0.0478
	H7	hc	0.0478
	C7	ci	-0.2968
	H8	hc	0.0478
	H9	hc	0.0478
	H10	hc	0.0478
	C8	ci	-0.2968
	H11	hc	0.0478
	H12	hc	0.0478
	H13	hc	0.0478
	C1	ca	-0.0900
	H	ha	0.1265
	C2	ca	-0.1425
	H1	ha	0.1290

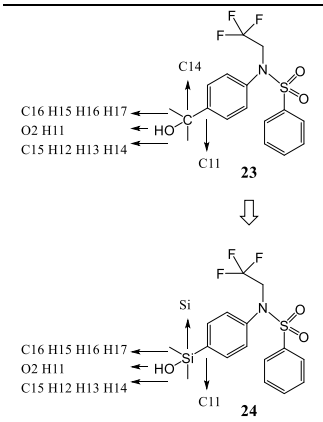
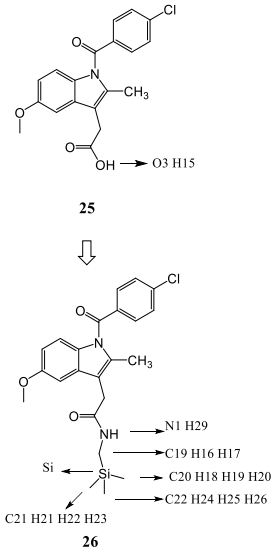
	C3	ca	-0.1130
	H2	ha	0.1290
	C4	ca	-0.1425
	H3	ha	0.1290
	C5	ca	-0.0900
	H4	ha	0.1265
16 	C	ca	-0.0875
	H	ha	0.1255
	C1	ca	-0.2742
	Si	si	0.8595
	C6	ci	-0.3226
	H5	hc	0.0477
	H6	hc	0.0477
	H7	hc	0.0477
	N	ng	-1.0509
	H8	hn	0.3868
	H9	hn	0.3868
	C7	ci	-0.3226
	H10	hc	0.0477
	H11	hc	0.0477
	H12	hc	0.0477
	C2	ca	-0.0875
	H1	ha	0.1255
	C3	ca	-0.1450
	H2	ha	0.1270
	C4	ca	-0.1140
	H3	ha	0.1270
	C5	ca	-0.1450
	H4	ha	0.1270
17 	C	ca	-0.2752
	Si	si	0.9519
	C6	ci	-0.3501
	H5	hc	0.0544
	H6	hc	0.0544
	H7	hc	0.0544
	C7	ci	-0.3501
	H8	hc	0.0544
	H9	hc	0.0544
	H10	hc	0.0544
	O	oi	-0.8177
	H11	ho	0.4140
	C1	ca	-0.0800
	H	ha	0.1375
	C2	ca	-0.1465
	H1	ha	0.1300
	C3	ca	-0.1070
	H2	ha	0.1290
	C4	ca	-0.1465
	H3	ha	0.1300
	C5	ca	-0.0800
	H4	ha	0.1375

18		C	ci	-0.3041
		H	hc	0.0507
		H1	hc	0.0507
		H2	hc	0.0507
		Si	si	0.8780
		C1	ci	-0.3041
		H3	hc	0.0507
		H4	hc	0.0507
		H5	hc	0.0507
		C2	ci	-0.3041
		H6	hc	0.0507
		H7	hc	0.0507
		H8	hc	0.0507
		C3	ca	-0.0367
		N	nb	-0.6450
		C5	ca	0.3802
		C6	ca	-0.2323
		H11	ha	0.1400
		H10	h4	0.0181
		C4	ca	-0.2163
		H9	ha	0.1410
		C7	ca	-0.1040
		H12	ha	0.1350
19		C	ci	-0.3024
		H	hc	0.0485
		H1	hc	0.0485
		H2	hc	0.0485
		Si	si	0.8980
		C1	ci	-0.3024
		H3	hc	0.0485
		H4	hc	0.0485
		H5	hc	0.0485
		C2	ci	-0.3024
		H6	hc	0.0485
		H7	hc	0.0485
		H8	hc	0.0485
		C3	cc	-0.1387
		N1	nd	-0.4908
		N	na	-0.0206
		H9	hn	0.3157
		C4	cc	-0.2653
		H10	ha	0.1630
		C5	cd	-0.1623
		H11	h4	0.1730
20		C	c3	-0.1761
		H	hc	0.0637
		H1	hc	0.0637
		H2	hc	0.0637
		C1	c	0.6411
		O	o	-0.6041

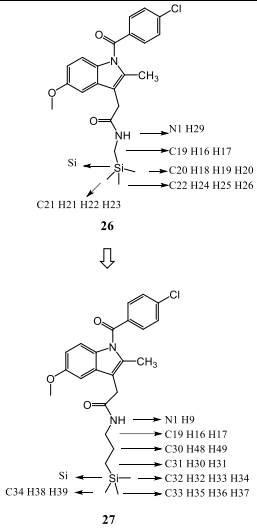
	N	n	-0.5439
	H3	hn	0.2965
	C2	ci	-0.1040
	H4	h1	0.0592
	H5	h1	0.0592
	Si	si	0.6270
	C4	ci	-0.3004
	H9	hc	0.0506
	H10	hc	0.0506
	H11	hc	0.0506
	C5	ci	-0.3004
	H12	hc	0.0506
	H13	hc	0.0506
	H14	hc	0.0506
	C3	ci	-0.3004
	H6	hc	0.0506
	H7	hc	0.0506
	H8	hc	0.0506

Table S11. AM1-BCC charges of the compounds in protein-ligand MD simulations.

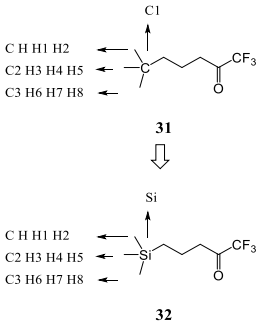
Comp.		Atom type	Charge		Atom type	Charge
	21(C)			**22**（Si）		
	C13	cd	0.334600	C13	cd	0.334600
	C14	cd	-0.271300	C14	cd	-0.271300
	H4	ha	0.190000	H4	ha	0.190000
	C16	c3	-0.076300	Si	si	0.795677
	C17	c3	-0.085100	C17	ci	-0.407091
	H5	hc	0.039256	H5	hc	0.049700
	H6	hc	0.039256	H6	hc	0.049700
	H7	hc	0.039256	H7	hc	0.049700
	C18	c3	-0.085100	C18	ci	-0.407091
	H8	hc	0.039256	H8	hc	0.049700
	H9	hc	0.039256	H9	hc	0.049700
	H10	hc	0.039256	H10	hc	0.049700

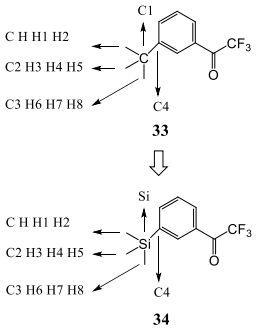
	C19	c3	-0.085100	C19	ci	-0.407091
	H11	hc	0.039256	H11	hc	0.049700
	H12	hc	0.039256	H12	hc	0.049700
	H13	hc	0.039256	H13	hc	0.049700
	23(C)			**24**(Si)		
	C11	ca	-0.068300	C11	ca	-0.068300
	C14	c3	0.197100	Si	si	0.903925
	O2	oh	-0.601800	O2	oi	-0.859675
	H11	ho	0.405000	H11	ho	0.415000
	C15	c3	-0.120600	C15	ci	-0.383075
	H12	hc	0.046867	H12	hc	0.057867
	H13	hc	0.046867	H13	hc	0.057867
	H14	hc	0.046867	H14	hc	0.057867
	C16	c3	-0.120600	C16	ci	-0.383075
	H15	hc	0.046867	H15	hc	0.057867
	H16	hc	0.046867	H16	hc	0.057867
	H17	hc	0.046867	H17	hc	0.057867
	25(C)			**26**(Si)		
	O3	oh	-0.605100	N1	n	-0.595951
	H15	ho	0.444000	H79	hn	0.307500
				C19	ci	-0.170051
				Si	si	0.626000
				C20	ci	-0.299767
				H18	hc	0.050367
				H19	hc	0.050367
				H20	hc	0.050367
				C21	ci	-0.299767
				H21	hc	0.050367

				H22	hc	0.050367
				H23	hc	0.050367
				C22	ci	-0.299767
				H24	hc	0.050367
				H25	hc	0.050367
				H26	hc	0.050367
				H16	h1	0.058700
				H17	h1	0.058700

	26(Si)			**27**(Si)		
	C19	ci	-0.106000	N1	n	-0.531900
	H16	h1	0.058700	C19	c3	0.091000
	H17	h1	0.058700	H16	h1	0.058700
	Si	si	0.626000	H17	h1	0.058700
	C20	ci	-0.299767	C30	c3	-0.080400
	H18	hc	0.050367	C31	ci	-0.296393
	H19	hc	0.050367	Si	si	0.620000
	H20	hc	0.050367	C32	ci	-0.295767
	C21	ci	-0.299767	H32	hc	0.048144
	H21	hc	0.050367	H33	hc	0.048144
	H22	hc	0.050367	H34	hc	0.048144
	H23	hc	0.050367	C33	ci	-0.295767
	C22	ci	-0.299767	H35	hc	0.048144
	H24	hc	0.050367	H36	hc	0.048144
	H25	hc	0.050367	H37	hc	0.048144
	H26	hc	0.050367	C34	ci	-0.295767
				H38	hc	0.048144
				H39	hc	0.048144
				H40	hc	0.048144

				H30	hc	0.056200
				H31	hc	0.056200
				H48	hc	0.040700
				H49	hc	0.040700

	31(C)			**32**(Si)		
	C	c3	-0.088433	C	ci	-0.297767
	H	hc	0.036033	H	hc	0.049811
	H1	hc	0.036033	H1	hc	0.049811
	H2	hc	0.036033	H2	hc	0.049811
	C1	c3	-0.056000	Si	si	0.626000
	C2	c3	-0.088433	C2	ci	-0.297767
	H3	hc	0.036033	H3	hc	0.049811
	H4	hc	0.036033	H4	hc	0.049811
	H5	hc	0.036033	H5	hc	0.049811
	C3	c3	-0.088433	C3	ci	-0.297767
	H6	hc	0.036033	H6	hc	0.049811
	H7	hc	0.036033	H7	hc	0.049811
	H8	hc	0.036033	H8	hc	0.049811

	33(C)			**33**(Si)		
	C	c3	-0.088767	C	ci	-0.330492
	H	hc	0.040144	H	hc	0.051033
	H1	hc	0.040144	H1	hc	0.051033
	H2	hc	0.040144	H2	hc	0.051033
	C1	c3	-0.010700	Si	si	0.616474
	C2	c3	-0.088767	C2	ci	-0.330492
	H3	hc	0.040144	H3	hc	0.051033
	H4	hc	0.040144	H4	hc	0.051033
	H5	hc	0.040144	H5	hc	0.051033

C3	c3	-0.088767	C3	ci	-0.330492
H6	hc	0.040144	H6	hc	0.051033
H7	hc	0.040144	H7	hc	0.051033
H8	hc	0.040144	H8	hc	0.051033

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