Supporting Information part I for:

Improved Polarizable Dipole–Dipole Interaction Model for Hydrogen Bonding, Stacking, T-Shaped and X–H···π Interactions

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Table S1. Information on the 19 training dimers.

dimers	ref	name in original reference	geometry optimization level	reference energy level
U···U (BP)	1	uracil···uracil (BP)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
water···water	1	water···water	MP2/cc-pVTZ-CP	CCSD(T)/CBS
MeOH···$MeNH_2$	1	MeOH···$MeNH_2$	MP2/cc-pVTZ-CP	CCSD(T)/CBS
$MeNH_2$···MeOH	1	$MeNH_2$···MeOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
$MeNH_2$···$MeNH_2$	1	$MeNH_2$···$MeNH_2$	MP2/cc-pVTZ-CP	CCSD(T)/CBS
water···pyridine	1	water···pyridine	MP2/cc-pVTZ-CP	CCSD(T)/CBS
AcOH···AcOH	1	AcOH···AcOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
$AcNH_2$···$AcNH_2$	1	$AcNH_2$···$AcNH_2$	MP2/cc-pVTZ-CP	CCSD(T)/CBS
PHE PHE st	1	benzene···benzene (π-π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
PHE pyridine st	1	benzene···pyridine (π-π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
U U st	1	uracil···uracil (π-π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
PHE PHE TS	1	benzene···benzene (TS)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
PHE pyridine TS	1	benzene···pyridine (TS)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
pyridine pyridine TS	1	pyridine···pyridine (TS)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
PHE···water (OH···π)	1	benzene···water (OH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
PHE···$MeNH_2$ (NH···π)	1	benzene···$MeNH_2$ (NH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
U···ethyne	1	uracil···ethyne	MP2/cc-pVTZ-CP	CCSD(T)/CBS
pyridine···ethene	1	pyridine···ethene	MP2/cc-pVTZ-CP	CCSD(T)/CBS
neopentane···pentane	1	neopentane···pentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS

Reference

1. Řezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7*, 2427-2438.

Table S2. Parameters used in this work.

parameters for bond dipole moments μ_0 (Debye)			value
μ_0 (C=O)			2.65[a]
μ_0 (C–O)			0.70[a]
μ_0 (N–H)	sp^2 nitrogen		1.31[a]
	sp^3 nitrogen		1.51[b]
μ_0 (C–H)	carbon in aromatic, peptide and alkane		0.30[a]
	α-carbon in peptide		0.70[c]
	carbon in ethyne and ethene		0.70[b]
μ_0 (O–H)	oxygen in water and alcohol		1.51[a]
	oxygen in carboxylic acid		1.71[b]
parameters for lone pair dipole moments μ_0 (Debye)			value
μ_0 (N-lp)	sp^2 nitrogen with a lone pair in a 5-membered ring of adenine		1.43[b]
	sp^2 nitrogen with a lone pair in a 5-membered ring of histidine and guanine		1.80[b]
	sp^2 nitrogen with a lone pair in a 6-membered ring of adenine, guanine and pyridine		1.30[b]
	sp^2 nitrogen with a lone pair in a 6-membered ring of cytosine		1.95[b]
parameters for van der Waals interactions		R^* (Å)	ε (kcal/mol)
carbon	sp carbon in ethyne	1.8080[b]	0.2060[b]
	sp^2 carbon in ethene	1.8580[b]	0.1200[b]
	sp^2 carbon in benzene, pyridine	1.9080[d]	0.0860[d]
	sp^2 carbon in histidine	1.9080[b]	0.1260[b]
	sp^2 carbon in a 5-membered ring of indole including that at a junction of two rings	1.9080[d]	0.0860[d]
	sp^2 carbon in a 6-membered ring of indole except that at a junction of two rings	1.9080[b]	0.1260[b]
	sp^2 carbon at a junction of two 6-membered rings	1.9080[b]	0.1260[b]
	sp^2 carbon at a junction of three 6-membered rings	1.9080[b]	0.1060[b]
	sp^2 carbon in carbonyl group	1.8080[b]	0.1660[b]
	C4, C5 and C8 of adenine and guanine	1.7080[b]	0.0860[b]
	sp^2 carbon in a base except that at the junction of two rings and in a carbonyl group	1.9080[b]	0.1660[b]
	sp^3 carbon	1.9080[d]	0.1094[d]
	sp^3 carbon in cyclohexane	1.9080[d]	0.0860[d]
nitrogen	sp^2 nitrogen with a lone pair	1.8740[b]	0.1800[b]
	sp^2 nitrogen with no lone pair	1.8240[d]	0.1700[d]
	sp^3 nitrogen	1.7740[b]	0.1700[b]
oxygen	sp^2 oxygen in carboxylic acid	1.5612[b]	0.2100[b]
	sp^2 oxygen in carbonyl group	1.6612[d]	0.2100[d]
	sp^3 oxygen in water	1.7210[b]	0.1804[b]
	sp^3 oxygen in alcohol	1.6500[c]	0.1700[c]
	sp^3 oxygen in carboxylic acid	1.6737[b]	0.2104[b]
hydrogen	H in water	0.6500[b]	0.0157[b]
	H attached to an oxygen in alcohol	0.5800[c]	0.0157[c]
	H attached to an oxygen in carboxylic acid	0.4000[b]	0.0157[b]
	H attached to a nitrogen in a base, histidine, indole	0.5650[b]	0.0157[b]
	H attached to sp^2 nitrogen in amide	0.6000[d]	0.0157[d]
	H attached to sp^3 nitrogen	1.0000[b]	0.0157[b]
	H attached to guanine N1	0.4500[b]	0.0157[b]
	H in alkane	1.4370[b]	0.0157[b]

H in cyclohexane	1.3000[b]	0.0157[b]
H attached to an α-carbon in peptide	1.0000[c]	0.0157[d]
H attached to an aliphatic carbon except for a carbon in alkane and an α-carbon in peptide	1.1000[b]	0.0157[b]
H attached to an aromatic carbon with an electronegative neighbor	1.1000[b]	0.0157[b]
H attached to an aromatic carbon with no electronegative neighbor	1.3000[b]	0.0250[b]
H attached to a carbon in a 5-membered ring of indole	1.1000[d]	0.0150[d]
H attached to a carbon in a 6-membered ring of indole	1.4590[d]	0.0150[d]

parameters for the orbital overlap term[b]	D_m	α_m	p_m	q_m	a_m
N–H···O(sp^2) (HB)	4.60	0.093	0.06	0.171	1.5
N–H···O(sp^3) (HB)	0.47	0.008	0.05	0.35	1.5
N–H···N(sp^2) (HB)	1.95	0.085	0.02	0.16	1.5
N–H···N(sp^3) (HB)	1.55	0.03	0.01	0.25	1.5
O–H···O(sp^2) (HB)	3.27	0.008	0.01	0.15	1.5
O–H···O(sp^3) (HB)	1.47	0.01	0.13	0.30	1.5
O–H···N(sp^2) (HB)	0.55	0.01	0.02	0.16	1.5
O–H···N(sp^3) (HB)	3.15	0.008	0.05	0.30	1.5
C–H···O (HB)	0.65	0.005	0.04	0.14	1.5
C–H···N (HB)	1.05	0.01	0.005	0.07	1.5
O–H···C (X–H···π)	0.19	0.006	0.04	0.20	1.5
N–H···N (X–H···π)	1.52	0.11	0.011	0.21	1.5
N–H···C (X–H···π)	0.31	0.13	0.031	0.23	1.0
C–H···N (X–H···π)	0.75	0.09	0.061	0.14	1.5
C–H···C (X–H···π)	0.13	0.15	0.026	0.14	1.0

[a]Taken from the ref 1.
[b]Determined in this work.
[c]Taken from the ref 2.
[d]Taken from the ref 3.

References

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3. Wang, J.; Cieplak, P.; Kollman, P. A. How Well Does a Restrained Electrostatic Potential (RESP) Model Perform in Calculating Conformational Energies of Organic and Biological Molecules? *J. Comput. Chem.* **2000**, *21*, 1049-1074.

Table S3. Information on the 35 small hydrogen-bonded testing dimers.

dimers		ref	name in original references	geometry optimization level	reference energy level
1	U···U (C_{2h})	1	Uracil dimer (C_{2h})	MP2/cc-pVTZ-CP	CCSD(T)/CBS
2	U···U pl	2	U···U pl	MP2/cc-pVTZ	CCSD(T)/CBS
3	U···U Calcutta pl	2	U···U Calcutta pl	MP2/cc-pVTZ	CCSD(T)/CBS
4	A···A 1 pl	2	A···A 1 pl	MP2/cc-pVTZ	MP2/CBS
5	A···A 2 pl	2	A···A 2 pl	MP2/cc-pVTZ	MP2/CBS
6	A···A 3 pl	2	A···A 3 pl	MP2/cc-pVTZ	MP2/CBS
7	G···G pl	2	G···G pl	MP2/cc-pVTZ	MP2/CBS
8	A···C pl	2	A···C pl	MP2/cc-pVTZ	MP2/CBS
9	A···T WC	3	A···T WC	MP2/TZVPP	CCSD(T)/CBS
10	A···T WC (C_1)	1	Adenine thymine WC (C_1)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
11	mA···mT H	3	mA···mT H	MP2/TZVPP	CCSD(T)/CBS
12	G···A 1	2	G···A 1	MP2/cc-pVTZ	MP2/CBS
13	G···A 1 pl	2	G···A 1 pl	MP2/cc-pVTZ	MP2/CBS
14	G···A 2	2	G···A 2	MP2/cc-pVTZ	MP2/CBS
15	G···A 2 pl	2	G···A 2 pl	MP2/cc-pVTZ	MP2/CBS
16	G···A 3	2	G···A 3	MP2/cc-pVTZ	MP2/CBS
17	G···A 4	2	G···A 4	MP2/cc-pVTZ	MP2/CBS
18	G···C WC	3	G···C WC	MP2/TZVPP	CCSD(T)/CBS
19	mG···mC WC	3	mG···mC WC	MP2/TZVPP	CCSD(T)/CBS
20	G···U wobble	2	G···U wobble	MP2/cc-pVTZ	CCSD(T)/CBS
21	water···MeOH	4	water···MeOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
22	water···$MeNH_2$	4	water···$MeNH_2$	MP2/cc-pVTZ-CP	CCSD(T)/CBS
23	water···peptide	4	water···peptide	MP2/cc-pVTZ-CP	CCSD(T)/CBS
24	MeOH···MeOH	4	MeOH···MeOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
25	MeOH···peptide	4	MeOH···peptide	MP2/cc-pVTZ-CP	CCSD(T)/CBS
26	MeOH···water	4	MeOH···water	MP2/cc-pVTZ-CP	CCSD(T)/CBS
27	$MeNH_2$···peptide	4	$MeNH_2$···peptide	MP2/cc-pVTZ-CP	CCSD(T)/CBS
28	$MeNH_2$···water	4	$MeNH_2$···water	MP2/cc-pVTZ-CP	CCSD(T)/CBS
29	peptide···MeOH	4	peptide···MeOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
30	peptide···$MeNH_2$	4	peptide···$MeNH_2$	MP2/cc-pVTZ-CP	CCSD(T)/CBS
31	peptide···peptide	4	peptide···peptide	MP2/cc-pVTZ-CP	CCSD(T)/CBS
32	peptide···water	4	peptide···water	MP2/cc-pVTZ-CP	CCSD(T)/CBS
33	MeOH···pyridine	4	MeOH···pyridine	MP2/cc-pVTZ-CP	CCSD(T)/CBS
34	AcOH···U	4	AcOH···uracil	MP2/cc-pVTZ-CP	CCSD(T)/CBS
35	$AcNH_2$···U	4	$AcNH_2$···uracil	MP2/cc-pVTZ-CP	CCSD(T)/CBS

References

1. Jurečka, P.; Šponer, J.; Černý, J.; Hobza, P. Benchmark Database of Accurate (MP2 and CCSD(T) Complete Basis Set Limit) Interaction Energies of Small Model Complexes, DNA Base Pairs, and Amino Acid Pairs. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1985-1993.

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Table S4. Information on the 27 small stacked testing dimers.

dimers		ref	name in original references	geometry optimization level	reference energy level
36	A A st	1	AAst	MP2/6-31G*(0.25)	CCSD(T)/CBS
37	G G st	1	GGst	MP2/6-31G*(0.25)	CCSD(T)/CBS
38	C C st	1	CCst	MP2/6-31G*(0.25)	CCSD(T)/CBS
39	A C st	1	ACst	MP2/6-31G*(0.25)	CCSD(T)/CBS
40	A U st	1	AUst	MP2/6-31G*(0.25)	CCSD(T)/CBS
41	G A st	1	GAst	MP2/6-31G*(0.25)	CCSD(T)/CBS
42	G C st	1	GCst	MP2/6-31G*(0.25)	CCSD(T)/CBS
43	G U st	1	GUst	MP2/6-31G*(0.25)	CCSD(T)/CBS
44	C U st	1	CUst	MP2/6-31G*(0.25)	CCSD(T)/CBS
45	U PHE st	2	benzene···uracil (π-π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
46	T PHE st	3	T PHE stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
47	A PHE st	3	A PHE stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
48	G PHE st	3	G PHE stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
49	C PHE st	3	C PHE stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
50	TRP PHE st	1	Indole ·benzene	MP2/cc-pVTZ-CP	CCSD(T)/CBS
51	pyridine···pyridine st	2	pyridine···pyridine (π-π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
52	U pyridine st	2	pyridine···uracil (π-π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
53	U HIS st	3	U HIS stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
54	T HIS st	3	T HIS stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
55	A HIS st	3	A HIS stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
56	G HIS st	3	G HIS stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
57	C HIS st	3	C HIS stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
58	U TRP st	3	U TRP stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
59	T TRP st	3	T TRP stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
60	A TRP st	3	A TRP stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
61	G TRP st	3	G TRP stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS
62	C TRP st	3	C TRP stacked	MP2/6-31G*(0.25)	CCSD(T)/CBS

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1. Jurečka, P.; Šponer, J.; Černý, J.; Hobza, P. Benchmark Database of Accurate (MP2 and CCSD(T) Complete Basis Set Limit) Interaction Energies of Small Model Complexes, DNA Base Pairs, and Amino Acid Pairs. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1985-1993.

2. Řezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7*, 2427-2438.

3. Rutledge, L. R.; Durst, H. F.; Wetmore, S.D. Evidence for Stabilization of DNA/RNA-Protein Complexes Arising from Nucleobase-Amino Acid Stacking and T-Shaped Interactions. *J. Chem. Theory Comput.* **2009**, *5*, 1400-1410.

Table S5. Information on the 32 small T-shaped testing dimers.

dimers		ref	name in original references	geometry optimization level	reference energy level
63	benzene dimer (C_{2V})	1	Benzene dimer (C_{2V})	MP2/cc-pVTZ-CP	CCSD(T)/CBS
64	U PHE edge	2	U PHE edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
65	U PHE face	2	U PHE face 1	MP2/6-31G*(0.25)	CCSD(T)/CBS
66	T PHE edge	2	T PHE edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
67	T PHE face	2	T PHE face 1	MP2/6-31G*(0.25)	CCSD(T)/CBS
68	A PHE edge	2	A PHE edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
69	A PHE face	2	A PHE face 4	MP2/6-31G*(0.25)	CCSD(T)/CBS
70	G PHE edge	2	G PHE edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
71	G PHE face	2	G PHE face 5	MP2/6-31G*(0.25)	CCSD(T)/CBS
72	C PHE edge	2	C PHE edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
73	C PHE face	2	C PHE face 1	MP2/6-31G*(0.25)	CCSD(T)/CBS
74	TRP PHE TS	1	Indole benzene T-shaped (C_1)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
75	U HIS edge	2	U HIS edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
76	U HIS face	2	U HIS face 1	MP2/6-31G*(0.25)	CCSD(T)/CBS
77	T HIS edge	2	T HIS edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
78	T HIS face	2	T HIS face 1	MP2/6-31G*(0.25)	CCSD(T)/CBS
79	A HIS edge	2	A HIS edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
80	A HIS face	2	A HIS face 4	MP2/6-31G*(0.25)	CCSD(T)/CBS
81	G HIS edge	2	G HIS edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
82	G HIS face	2	G HIS face 5	MP2/6-31G*(0.25)	CCSD(T)/CBS
83	C HIS edge	2	C HIS edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
84	C HIS face	2	C HIS face 1	MP2/6-31G*(0.25)	CCSD(T)/CBS
85	U TRP edge	2	U TRP edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
86	U TRP face	2	U TRP face F	MP2/6-31G*(0.25)	CCSD(T)/CBS
87	T TRP edge	2	T TRP edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
88	T TRP face	2	T TRP face F	MP2/6-31G*(0.25)	CCSD(T)/CBS
89	A TRP edge	2	A TRP edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
90	A TRP face	2	A TRP face 4	MP2/6-31G*(0.25)	CCSD(T)/CBS
91	G TRP edge	2	G TRP edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
92	G TRP face	2	G TRP face E	MP2/6-31G*(0.25)	CCSD(T)/CBS
93	C TRP edge	2	C TRP edge	MP2/6-31G*(0.25)	CCSD(T)/CBS
94	C TRP face	2	C TRP face 4	MP2/6-31G*(0.25)	CCSD(T)/CBS

References

1. Jurečka, P.; Šponer, J.; Černý, J.; Hobza, P. Benchmark Database of Accurate (MP2 and CCSD(T) Complete Basis Set Limit) Interaction Energies of Small Model Complexes, DNA Base Pairs, and Amino Acid Pairs. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1985-1993.

2. Rutledge, L. R.; Durst, H. F.; Wetmore, S.D. Evidence for Stabilization of DNA/RNA-Protein Complexes Arising from Nucleobase-Amino Acid Stacking and T-Shaped Interactions. *J. Chem. Theory Comput.* **2009**, *5*, 1400-1410.

Table S6. Information on the 30 small X–H···π and other testing dimers.

dimers		ref	name in original references	geometry optimization level	reference energy level
95	ethyne···ethyne (CH···π)	1	ethyne···ethyne (TS)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
96	PHE···ethyne (CH···π)	1	benzene···ethyne (CH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
97	PHE···AcOH (OH···π)	1	benzene···AcOH (OH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
98	PHE···$AcNH_2$ (NH···π)	1	benzene···$AcNH_2$ (NH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
99	PHE···MeOH (OH···π)	1	benzene···MeOH (OH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
100	PHE···peptide (NH···π)	1	benzene···peptide (NH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
101	ethyne···AcOH (OH···π)	1	ethyne···AcOH (OH···π)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
102	PHE···AcOH	1	benzene···AcOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
103	$MeNH_2$···pyridine	1	$MeNH_2$···pyridine	MP2/cc-pVTZ-CP	CCSD(T)/CBS
104	peptide···ethene	1	peptide···ethene	MP2/cc-pVTZ-CP	CCSD(T)/CBS
105	PHE···cyclopentane	1	benzene···cyclopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
106	PHE···neopentane	1	benzene···neopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
107	U···pentane	1	uracil···pentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
108	U···cyclopentane	1	uracil···cyclopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
109	U···neopentane	1	uracil···neopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
110	PHE···ethene	1	benzene···ethene	MP2/cc-pVTZ-CP	CCSD(T)/CBS
111	U···ethene	1	uracil···ethene	MP2/cc-pVTZ-CP	CCSD(T)/CBS
112	neopentane···neopentane	1	neopentane···neopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
113	cyclopentane···neopentane	1	cyclopentane···neopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
114	cyclopentane···cyclopentane	1	cyclopentane···cyclopentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
115	pentane···pentane	1	pentane···pentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
116	peptide···pentane	1	peptide···pentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
117	pentane···AcOH	1	pentane···AcOH	MP2/cc-pVTZ-CP	CCSD(T)/CBS
118	pentane···$AcNH_2$	1	pentane···$AcNH_2$	MP2/cc-pVTZ-CP	CCSD(T)/CBS
119	ethene···pentane	1	ethene···pentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
120	ethyne···pentane	1	ethyne···pentane	MP2/cc-pVTZ-CP	CCSD(T)/CBS
121	pyrene···methane	2	Pyrene-Methane (3a)	MP2/6-31G*(0.25)	CCSD(T)/CBS
122	pyridine···pyridine	1	pyridine···pyridine (CH···N)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
123	ethyne···water	1	ethyne···water (CH···O)	MP2/cc-pVTZ-CP	CCSD(T)/CBS
124	pyridine···ethyne	1	pyridine···ethyne	MP2/cc-pVTZ-CP	CCSD(T)/CBS

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Table S7. Equilibrium hydrogen bond distances (Å) of the 35 small hydrogen-bonded testing dimers.[a]

dimers		type	R_{ref}	R	$R-R_{ref}$
1	U···U (C_{2h})	N–H···O, N–H···O	1.77, 1.77	1.76, 1.76	-0.01, -0.01
2	U···U pl	N–H···O, N–H···O	1.81, 1.81	1.86, 1.86	0.05, 0.05
3	U···U Calcutta pl	N–H···O	1.85	1.85	0.00
4	A···A 1 pl	N–H···N, N–H···N	1.92, 1.92	1.94, 1.94	0.02, 0.02
5	A···A 2 pl	N–H···N, N–H···N	1.94, 1.95	1.95, 1.96	0.01, 0.01
6	A···A 3 pl	N–H···N, N–H···N	1.98, 1.99	1.98, 1.99	0.00, 0.00
7	G···G pl	N–H···N, N–H···O	1.85, 2.17	1.76, 2.08	-0.09, -0.09
8	A···C pl	N–H···N, N–H···N	1.89, 1.90	1.89, 1.90	0.00, 0.00
9	A···T WC	N–H···N, N–H···O	1.82, 1.93	1.84, 1.95	0.02, 0.02
10	A···T WC (C_1)	N–H···N, N–H···O	1.82, 1.93	1.84, 1.95	0.02, 0.02
11	mA···mT H	N–H···N, N–H···O	1.75, 1.93	1.82, 2.00	0.07, 0.07
12	G···A 1	N–H···O, N–H···N	1.81, 1.83	1.84, 1.86	0.03, 0.03
13	G···A 1 pl	N–H···O, N–H···N	1.77, 1.94	1.79, 1.96	0.02, 0.02
14	G···A 2	N–H···N, N–H···N	1.96, 2.01	1.95, 2.00	-0.01, -0.01
15	G···A 2 pl	N–H···N, N–H···N	1.93, 2.01	1.94, 2.02	0.01, 0.01
16	G···A 3	N–H···N, N–H···O	1.82, 1.85	1.84, 1.87	0.02, 0.02
17	G···A 4	N–H···N, N–H···N	1.92, 1.95	1.96, 1.99	0.04, 0.04
18	G···C WC	N–H···O, N–H···N, N–H···O	1.76, 1.91, 1.92	1.75, 1.90, 1.91	-0.01, -0.01, -0.01
19	mG···mC WC	N–H···O, N–H···N, N–H···O	1.73, 1.87, 1.88	1.75, 1.89, 1.90	0.02, 0.02, 0.02
20	G···U wobble	N–H···O, N–H···O	1.74, 1.75	1.83, 1.84	0.09, 0.09
21	water···MeOH	O–H···O	1.96	1.96	0.00
22	water···$MeNH_2$	O–H···N	2.01	1.99	-0.02
23	water···peptide	O–H···O	1.90	1.94	0.04
24	MeOH···MeOH	O–H···O	1.94	1.86	-0.08
25	MeOH···peptide	O–H···O	1.88	1.90	0.02
26	MeOH···water	O–H···O	1.99	1.89	-0.10
27	$MeNH_2$···peptide	N–H···O	2.24	2.24	0.00
28	$MeNH_2$···water	O–H···N	1.98	2.04	0.06
29	peptide···MeOH	N–H···O	2.01	1.91	-0.10
30	peptide···$MeNH_2$	N–H···N	2.07	1.99	-0.08
31	peptide···peptide	N–H···O	1.97	1.89	-0.08
32	peptide···water	N–H···O	2.08	2.08	0.00
33	MeOH···pyridine	O–H···N	1.95	1.85	-0.10
34	AcOH···U	O–H···O, N–H···O	1.70, 1.77	1.72, 1.79	0.02, 0.02
35	$AcNH_2$···U	N–H···O, N–H···O	1.73, 1.88	1.74, 1.89	0.01, 0.01
RMSD					0.04
MAD					0.10
MRD					1.68%

[a] R_{ref} are the benchmark equilibrium intermolecular distances taken from references. R are the equilibrium intermolecular distances produced by our model.

Table S8. Equilibrium intermolecular distances (Å) of the 27 small stacked testing dimers.[a]

dimers		R_{ref}	R	$R-R_{ref}$
36	A A st	3.65	3.61	-0.04
37	G G st	3.40	3.37	-0.03
38	C C st	3.53	3.63	0.10
39	A C st	3.51	3.54	0.03
40	A U st	3.33	3.36	0.03
41	G A st	3.55	3.51	-0.04
42	G C st	3.57	3.59	0.02
43	G U st	3.39	3.41	0.02
44	C U st	3.49	3.53	0.04
45	U PHE st	3.51	3.58	0.07
46	T PHE st	3.57	3.48	-0.09
47	A PHE st	3.40	3.41	0.01
48	G PHE st	3.49	3.44	-0.05
49	C PHE st	3.67	3.59	-0.08
50	TRP PHE st	3.50	3.64	0.14
51	pyridine···pyridine st	3.50	3.61	0.11
52	U pyridine st	3.52	3.67	0.15
53	U HIS st	3.63	3.56	-0.07
54	T HIS st	3.52	3.45	-0.07
55	A HIS st	3.42	3.46	0.04
56	G HIS st	3.51	3.41	-0.10
57	C HIS st	3.87	3.69	-0.18
58	U TRP st	3.43	3.41	-0.02
59	T TRP st	3.34	3.44	0.10
60	A TRP st	3.67	3.55	-0.08
61	G TRP st	3.50	3.48	-0.02
62	C TRP st	3.47	3.49	0.02
RMSD				0.08
MAD				0.18
MRD				1.87%

[a] R_{ref} are the benchmark equilibrium intermolecular distances taken from references. R are the equilibrium intermolecular distances produced by our model.

Table S9. Equilibrium intermolecular distances (Å) of the 32 small T-shaped testing dimers.[a]

dimers		R_{ref}	R	$R-R_{ref}$
63	benzene dimer (C_{2V})	2.43	2.55	0.12
64	U PHE edge	3.33	3.31	-0.02
65	U PHE face	2.36	2.16	-0.20
66	T PHE edge	2.78	2.78	0.00
67	T PHE face	2.41	2.27	-0.14
68	A PHE edge	2.78	2.82	0.04
69	A PHE face	2.20	2.12	-0.08
70	G PHE edge	2.83	2.73	-0.10
71	G PHE face	2.30	2.10	-0.20
72	C PHE edge	2.78	2.82	0.04
73	C PHE face	2.35	2.17	-0.18
74	TRP PHE TS	2.23	2.15	-0.08
75	U HIS edge	3.36	3.32	-0.04
76	U HIS face	2.55	2.59	0.04
77	T HIS edge	3.36	3.34	-0.02
78	T HIS face	2.40	2.42	0.02
79	A HIS edge	2.75	2.75	0.00
80	A HIS face	2.54	2.58	0.04
81	G HIS edge	2.69	2.67	-0.02
82	G HIS face	2.55	2.57	0.02
83	C HIS edge	2.65	2.57	-0.08
84	C HIS face	2.35	2.31	-0.04
85	U TRP edge	2.69	2.51	-0.18
86	U TRP face	2.51	2.41	-0.10
87	T TRP edge	2.56	2.46	-0.10
88	T TRP face	2.51	2.39	-0.12
89	A TRP edge	2.61	2.61	0.00
90	A TRP face	2.24	2.14	-0.10
91	G TRP edge	2.67	2.65	-0.02
92	G TRP face	2.61	2.43	-0.18
93	C TRP edge	2.94	2.92	-0.02
94	C TRP face	2.43	2.27	-0.16
RMSD				0.10
MAD				0.20
MRD				3.14%

[a] R_{ref} are the benchmark equilibrium intermolecular distances taken from references. R are the equilibrium intermolecular distances produced by our model.

Table S10. Equilibrium intermolecular distances (Å) of the 30 small X–H···π and other testing dimers.[a]

dimers		R_{ref}	R	$R-R_{ref}$
95	ethyne···ethyne (CH···π)	2.72	2.56	-0.16
96	PHE···ethyne (CH···π)	2.43	2.37	-0.06
97	PHE···AcOH (OH···π)	3.87	3.83	-0.04
98	PHE···$AcNH_2$ (NH···π)	2.98	2.86	-0.12
99	PHE···MeOH (OH···π)	2.40	2.44	0.04
100	PHE···peptide (NH···π)	2.37	2.31	-0.06
101	ethyne···AcOH (OH···π)	2.34	2.16	-0.18
102	PHE···AcOH	3.48	3.44	-0.04
103	$MeNH_2$···pyridine	2.36	2.46	0.10
104	peptide···ethene	3.73	3.59	-0.14
105	PHE···cyclopentane	3.94	4.00	0.06
106	PHE···neopentane	2.66	2.66	0.00
107	U···pentane	3.60	3.67	0.07
108	U···cyclopentane	3.89	3.94	0.05
109	U···neopentane	4.49	4.48	-0.01
110	PHE···ethene	3.43	3.48	0.05
111	U···ethene	3.35	3.33	-0.02
112	neopentane···neopentane	5.30	5.12	-0.18
113	cyclopentane···neopentane	4.66	4.65	-0.01
114	cyclopentane···cyclopentane	4.24	4.27	0.03
115	pentane···pentane	3.85	3.86	0.01
116	peptide···pentane	3.75	3.75	0.00
117	pentane···AcOH	3.77	3.69	-0.08
118	pentane···$AcNH_2$	3.75	3.73	-0.02
119	ethene···pentane	3.82	3.64	-0.18
120	ethyne···pentane	3.64	3.58	-0.06
121	pyrene···methane	3.47	3.44	-0.03
122	pyridine···pyridine	2.48	2.54	0.06
123	ethyne···water	2.23	2.37	0.14
124	pyridine···ethyne	2.25	2.39	0.14
RMSD				0.09
MAD				0.18
MRD				2.36%

[a] R_{ref} are the benchmark equilibrium intermolecular distances taken from references. R are the equilibrium intermolecular distances produced by our model.

Table S11. Interaction energies (kcal/mol) of the 35 small hydrogen-bonded testing dimers.[a]

			our model		M06-2X				M06-2X-D3				AMBER99		AMOEBA	
					without CP		with CP		without CP		with CP					
dimers		IE_{ref}	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$
1	U···U (C_{2h})	-20.65	-20.94	-0.29	-20.25	0.40	-19.23	1.42	-20.64	0.01	-19.62	1.03	-16.43	4.22	-17.99	2.66
2	U···U pl	-13.70	-13.71	-0.01	-13.44	0.26	-12.47	1.23	-13.83	-0.13	-12.86	0.84	-11.42	2.28	-12.53	1.17
3	U···U Calcutta pl	-10.30	-10.01	0.29	-10.08	0.22	-9.27	1.03	-10.43	-0.13	-9.62	0.68	-7.39	2.91	-9.76	0.54
4	A···A 1 pl	-14.50	-15.73	-1.23	-13.77	0.73	-12.65	1.85	-14.23	0.27	-13.11	1.39	-9.80	4.70	-14.08	0.42
5	A···A 2 pl	-13.70	-14.96	-1.26	-12.80	0.90	-11.65	2.05	-13.31	0.39	-12.16	1.54	-7.79	5.91	-13.48	0.22
6	A···A 3 pl	-12.20	-12.66	-0.46	-11.19	1.01	-10.05	2.15	-11.74	0.46	-10.61	1.59	-5.54	6.66	-11.99	0.21
7	G···G pl	-21.30	-22.04	-0.74	-21.22	0.08	-20.10	1.20	-21.76	-0.46	-20.65	0.65	-20.46	0.84	-21.38	-0.08
8	A···C pl	-17.60	-19.25	-1.65	-17.03	0.57	-15.87	1.73	-17.50	0.10	-16.34	1.26	-11.18	6.42	-16.56	1.04
9	A···T WC	-16.86	-17.70	-0.84	-16.07	0.79	-14.96	1.90	-16.58	0.28	-15.47	1.39	-13.09	3.77	-16.52	0.34
10	A···T WC (C_1)	-16.37	-17.70	-1.33	-16.07	0.30	-14.96	1.41	-16.57	-0.20	-15.47	0.90	-13.09	3.28	-16.52	-0.15
11	mA···mT H	-18.16	-16.89	1.27	-17.40	0.76	-16.07	2.09	-18.02	0.14	-16.69	1.47	-7.00	11.16	-17.21	0.95
12	G···A 1	-19.40	-19.08	0.32	-19.05	0.35	-17.90	1.50	-19.61	-0.21	-18.46	0.94	-14.34	5.06	-18.85	0.55
13	G···A 1 pl	-18.90	-18.73	0.17	-18.56	0.34	-17.26	1.64	-19.10	-0.20	-17.81	1.09	-13.70	5.20	-18.16	0.74
14	G···A 2	-14.40	-16.08	-1.68	-12.57	1.83	-11.66	2.74	-13.16	1.24	-12.25	2.15	-5.33	9.07	-12.90	1.50
15	G···A 2 pl	-12.80	-13.74	-0.94	-11.91	0.89	-10.75	2.05	-12.48	0.32	-11.32	1.48	-4.05	8.75	-12.32	0.48
16	G···A 3	-18.80	-17.94	0.86	-18.15	0.65	-17.01	1.79	-18.76	0.04	-17.61	1.19	-11.58	7.22	-19.31	-0.51
17	G···A 4	-13.50	-15.36	-1.86	-12.69	0.81	-11.73	1.77	-13.22	0.28	-12.26	1.24	-7.12	6.38	-12.21	1.29
18	G···C WC	-32.06	-30.02	2.04	-30.74	1.32	-29.41	2.65	-31.30	0.76	-29.96	2.10	-23.86	8.20	-27.97	4.09
19	mG···mC WC	-31.59	-30.26	1.33	-30.95	0.64	-29.53	2.06	-31.57	0.02	-30.15	1.44	-20.39	11.20	-27.74	3.85
20	G···U wobble	-19.10	-18.34	0.76	-18.65	0.45	-17.54	1.56	-19.13	-0.03	-18.02	1.08	-13.22	5.88	-18.92	0.18
21	water···MeOH	-5.59	-4.73	0.86	-5.87	-0.28	-5.54	0.05	-5.93	-0.34	-5.59	0.00	-5.19	0.40	-5.82	-0.23
22	water···$MeNH_2$	-6.91	-7.06	-0.15	-7.27	-0.36	-6.83	0.08	-7.34	-0.43	-6.90	0.01	-	-	-8.63	-1.72
23	water···peptide	-8.10	-8.48	-0.38	-8.78	-0.68	-8.25	-0.15	-8.89	-0.79	-8.35	-0.25	-7.42	0.68	-7.36	0.74
24	MeOH···MeOH	-5.76	-5.62	0.14	-5.82	-0.06	-5.47	0.29	-5.94	-0.18	-5.59	0.17	-6.06	-0.30	-5.86	-0.10
25	MeOH···peptide	-8.23	-9.17	-0.94	-8.60	-0.37	-8.11	0.12	-8.81	-0.58	-8.32	-0.09	-9.32	-1.09	-7.80	0.43
26	MeOH···water	-5.01	-5.81	-0.80	-5.13	-0.12	-4.91	0.10	-5.20	-0.19	-4.98	0.03	-7.34	-2.33	-5.19	-0.18
27	$MeNH_2$···peptide	-5.42	-5.42	0.00	-6.15	-0.73	-5.46	-0.04	-6.44	-1.02	-5.75	-0.33	-	-	-4.77	0.65

28	$MeNH_2$···water	-7.27	-6.62	0.65	-7.91	-0.64	-7.35	-0.08	-7.97	-0.70	-7.41	-0.14	-	-	-7.66	-0.39
29	peptide···MeOH	-6.19	-6.28	-0.09	-6.57	-0.38	-5.89	0.30	-6.82	-0.63	-6.15	0.04	-4.91	1.28	-5.13	1.06
30	peptide···$MeNH_2$	-7.45	-7.83	-0.38	-8.05	-0.60	-7.14	0.31	-8.34	-0.89	-7.42	0.03	-	-	-6.86	0.59
31	peptide···peptide	-8.63	-8.17	0.46	-9.16	-0.53	-8.30	0.33	-9.58	-0.95	-8.72	-0.09	-6.58	2.05	-7.74	0.89
32	peptide···water	-5.12	-5.71	-0.59	-5.37	-0.25	-4.90	0.22	-5.52	-0.40	-5.05	0.07	-4.88	0.24	-4.42	0.70
33	MeOH···pyridine	-7.41	-8.59	-1.18	-7.29	0.12	-6.83	0.58	-7.50	-0.09	-7.04	0.37	-	-	-7.25	0.16
34	AcOH···U	-19.49	-18.67	0.82	-19.78	-0.29	-18.95	0.54	-20.05	-0.56	-19.21	0.28	-30.64	-11.15	-16.53	2.96
35	$AcNH_2$···U	-19.19	-19.24	-0.05	-19.35	-0.16	-18.45	0.74	-19.64	-0.45	-18.75	0.44	-21.92	-2.73	-17.85	1.34
RMSD				0.94		0.65		1.41		0.50		1.02		5.78		1.37
MAD				2.04		1.83		2.74		1.24		2.15		11.20		4.09
MRD				6.23%		4.55%		7.45%		4.20%		5.17%		30.11%		7.02%

[a] IE_{ref} are the benchmark interaction energies taken from references, IE are the interaction energies produced by different methods, the DFT calculations employed aug-cc-pVDZ basis set.

Table S12. Decomposed interaction energies (kcal/mol) of the 35 small hyerogen-bonded testing dimers calculated at the geometries optimized with our model.

dimers		IE	E_{es}	E_{pol}	E_{vdw}	E_{orb}
1	U···U (C_{2h})	-20.94	-9.87	-2.82	-0.10	-8.15
2	U···U pl	-13.71	-7.46	-1.68	-1.16	-3.41
3	U···U Calcutta pl	-10.01	-5.04	-1.25	-1.55	-2.17
4	A···A 1 pl	-15.73	-9.93	-2.00	0.51	-4.32
5	A···A 2 pl	-14.96	-9.79	-1.85	0.47	-3.79
6	A···A 3 pl	-12.66	-9.02	-1.60	0.47	-2.51
7	G···G pl	-22.04	-17.27	-3.53	1.33	-2.57
8	A···C pl	-19.25	-12.91	-2.99	1.30	-4.65
9	A···T WC	-17.70	-11.74	-2.01	-0.15	-3.80
10	A···T WC (C_1)	-17.70	-11.74	-2.01	-0.15	-3.80
11	mA···mT H	-16.89	-12.79	-2.04	0.32	-2.38
12	G···A 1	-19.08	-12.37	-2.30	-0.34	-4.07
13	G···A 1 pl	-18.73	-10.26	-2.16	-0.75	-5.56
14	G···A 2	-16.08	-9.18	-1.67	-0.14	-5.09
15	G···A 2 pl	-13.74	-8.36	-1.52	0.06	-3.93
16	G···A 3	-17.94	-12.57	-2.26	0.18	-3.28
17	G···A 4	-15.36	-8.91	-1.67	-0.14	-4.65
18	G···C WC	-30.02	-18.35	-4.46	0.44	-7.65
19	mG···mC WC	-30.26	-18.43	-4.50	0.35	-7.67
20	G···U wobble	-18.34	-8.31	-2.58	-1.36	-6.09
21	water···MeOH	-4.73	-2.95	-0.31	-0.06	-1.41
22	water···$MeNH_2$	-7.06	-3.59	-0.53	0.26	-3.20
23	water···peptide	-8.48	-4.36	-0.72	-0.11	-3.30
24	MeOH···MeOH	-5.62	-3.44	-0.45	-0.26	-1.47
25	MeOH···peptide	-9.17	-4.22	-0.84	-0.87	-3.26
26	MeOH···water	-5.81	-4.12	-0.54	0.33	-1.47
27	$MeNH_2$···peptide	-5.42	-2.27	-0.57	-1.46	-1.11
28	$MeNH_2$···water	-6.62	-3.01	-0.51	0.05	-3.15
29	peptide···MeOH	-6.28	-4.01	-0.60	-0.79	-0.88
30	peptide···$MeNH_2$	-7.83	-4.34	-0.81	-0.83	-1.85
31	peptide···peptide	-8.17	-5.01	-1.08	-1.43	-0.64
32	peptide···water	-5.71	-4.22	-0.58	-0.01	-0.90
33	MeOH···pyridine	-8.59	-8.12	-1.14	1.24	-0.57
34	AcOH···U	-18.67	-10.03	-1.71	-0.13	-6.80
35	$AcNH_2$···U	-19.24	-10.23	-2.68	0.06	-6.39

Table S13. Interaction energies (kcal/mol) of the 27 small stacked testing dimers.[a]

			our model		M06-2X				M06-2X-D3				AMBER99		AMOEBA	
					without CP		with CP		without CP		with CP					
dimers		IE_{ref}	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$
36	A A st	-8.58	-9.24	-0.66	-8.69	-0.11	-7.46	1.12	-9.58	-1.00	-8.35	0.23	-6.77	1.81	-9.18	-0.60
37	G G st	-12.67	-12.72	-0.05	-12.76	-0.09	-11.36	1.31	-13.81	-1.14	-12.41	0.26	-12.86	-0.19	-12.38	0.29
38	C C st	-10.02	-9.87	0.15	-10.58	-0.56	-9.36	0.66	-11.30	-1.28	-10.07	-0.05	-3.22	6.80	-10.66	-0.64
39	A C st	-10.22	-9.79	0.43	-10.79	-0.57	-9.52	0.70	-11.57	-1.35	-10.30	-0.08	-7.71	2.51	-11.39	-1.17
40	A U st	-9.79	-10.05	-0.26	-10.54	-0.75	-9.21	0.58	-11.29	-1.50	-9.96	-0.17	-10.80	-1.01	-9.69	0.10
41	G A st	-11.38	-10.60	0.78	-11.77	-0.39	-10.40	0.98	-12.72	-1.34	-11.35	0.03	-13.54	-2.16	-12.13	-0.75
42	G C st	-10.60	-10.73	-0.13	-11.10	-0.50	-9.81	0.79	-11.95	-1.35	-10.66	-0.06	-3.41	7.19	-9.96	0.64
43	G U st	-12.09	-11.67	0.42	-12.60	-0.51	-11.27	0.82	-13.42	-1.33	-12.09	0.00	-14.21	-2.12	-11.34	0.75
44	C U st	-10.42	-9.80	0.62	-11.17	-0.75	-9.98	0.44	-11.84	-1.42	-10.66	-0.24	-10.94	-0.52	-9.44	0.98
45	U PHE st	-5.71	-5.81	-0.10	-7.06	-1.35	-5.82	-0.11	-7.63	-1.92	-6.39	-0.68	-5.93	-0.22	-5.62	0.09
46	T PHE st	-5.85	-6.06	-0.21	-6.71	-0.86	-5.42	0.43	-7.45	-1.60	-6.17	-0.32	-7.11	-1.26	-5.86	-0.01
47	A PHE st	-5.57	-6.07	-0.50	-6.41	-0.84	-5.06	0.51	-7.12	-1.55	-5.77	-0.20	-5.81	-0.24	-5.16	0.41
48	G PHE st	-6.04	-6.76	-0.72	-6.77	-0.73	-5.41	0.63	-7.53	-1.49	-6.17	-0.13	-6.17	-0.13	-5.73	0.31
49	C PHE st	-4.92	-5.15	-0.23	-5.58	-0.66	-4.53	0.39	-6.24	-1.32	-5.19	-0.27	-6.01	-1.09	-5.07	-0.15
50	TRP PHE st	-5.22	-4.48	0.74	-6.27	-1.05	-4.79	0.43	-6.95	-1.73	-5.47	-0.25	-2.92	2.30	-4.30	0.92
51	pyridine···pyridine st	-3.90	-3.46	0.44	-4.90	-1.00	-3.88	0.02	-5.39	-1.49	-4.36	-0.46	-	-	-4.24	-0.34
52	U pyridine st	-6.82	-5.89	0.93	-8.03	-1.21	-6.88	-0.06	-8.56	-1.74	-7.40	-0.58	-	-	-6.34	0.48
53	U HIS st	-6.95	-7.27	-0.32	-7.39	-0.44	-6.56	0.39	-7.86	-0.91	-7.02	-0.07	-9.23	-2.28	-6.71	0.24
54	T HIS st	-6.47	-6.12	0.35	-7.09	-0.62	-6.09	0.38	-7.68	-1.21	-6.68	-0.21	-6.91	-0.44	-7.18	-0.71
55	A HIS st	-7.12	-6.77	0.35	-7.71	-0.59	-6.66	0.46	-8.23	-1.11	-7.18	-0.06	-9.84	-2.72	-7.96	-0.84
56	G HIS st	-7.81	-8.52	-0.71	-8.31	-0.50	-7.34	0.47	-8.89	-1.08	-7.92	-0.11	-8.90	-1.09	-7.98	-0.17
57	C HIS st	-7.05	-7.11	-0.06	-7.35	-0.30	-6.58	0.47	-7.85	-0.80	-7.08	-0.03	-8.05	-1.00	-7.30	-0.25
58	U TRP st	-8.79	-8.98	-0.19	-9.61	-0.82	-8.22	0.57	-10.40	-1.61	-9.01	-0.22	-9.30	-0.51	-8.64	0.15
59	T TRP st	-9.20	-9.67	-0.47	-10.78	-1.58	-8.95	0.25	-11.70	-2.50	-9.87	-0.67	-9.59	-0.39	-8.56	0.64
60	A TRP st	-7.31	-8.45	-1.14	-7.51	-0.20	-6.13	1.18	-8.47	-1.16	-7.08	0.23	-3.33	3.98	-7.68	-0.37
61	G TRP st	-10.30	-10.21	0.09	-11.29	-0.99	-9.69	0.61	-12.27	-1.97	-10.68	-0.38	-6.53	3.77	-9.26	1.04
62	C TRP st	-8.46	-8.31	0.15	-9.39	-0.93	-7.99	0.47	-10.23	-1.77	-8.83	-0.37	-6.80	1.66	-7.94	0.52

RMSD	0.50	0.78	0.64	1.48	0.30	2.64	0.59
MAD	1.14	1.58	1.31	2.50	0.68	7.19	1.17
MRD	5.72%	9.91%	6.80%	19.34%	3.43%	22.38%	6.26%

[a]IE_{ref} are the benchmark interaction energies taken from references, IE are the interaction energies produced by different methods, the DFT calculations employed aug-cc-pVDZ basis set.

Table S14. Decomposed interaction energies (kcal/mol) of the 27 small stacked testing dimers calculated at the geometries optimized with our model.

dimers		IE	E_{es}	E_{pol}	E_{vdw}	E_{orb}
36	A A st	-9.24	-0.38	-0.02	-8.84	0.00
37	G G st	-12.72	-1.98	-0.16	-10.58	0.00
38	C C st	-9.87	-1.63	-0.21	-8.03	0.00
39	A C st	-9.79	-1.12	-0.10	-8.57	0.00
40	A U st	-10.05	-1.00	-0.07	-8.97	0.00
41	G A st	-10.60	-0.82	-0.09	-9.69	0.00
42	G C st	-10.73	-1.81	-0.16	-8.76	0.00
43	G U st	-11.67	-1.60	-0.11	-9.96	0.00
44	C U st	-9.80	-1.15	-0.11	-8.53	0.00
45	U PHE st	-5.81	-0.72	-0.09	-5.00	0.00
46	T PHE st	-6.06	-0.42	-0.07	-5.45	-0.12
47	A PHE st	-6.07	-0.20	-0.02	-5.85	0.00
48	G PHE st	-6.76	-0.59	-0.08	-6.09	0.00
49	C PHE st	-5.15	-0.20	0.00	-4.95	0.00
50	TRP PHE st	-4.48	0.42	-0.03	-4.88	0.00
51	pyridine···pyridine st	-3.46	-0.08	-0.02	-3.36	0.00
52	U pyridine st	-5.89	-0.86	-0.08	-4.95	0.00
53	U HIS st	-7.27	-1.58	-0.57	-5.12	0.00
54	T HIS st	-6.12	-0.70	0.00	-5.34	-0.08
55	A HIS st	-6.77	-0.82	-0.39	-5.55	0.00
56	G HIS st	-8.52	-1.60	-0.89	-6.03	0.00
57	C HIS st	-7.11	-1.58	-0.82	-4.70	0.00
58	U TRP st	-8.98	-1.50	-0.18	-7.29	0.00
59	T TRP st	-9.67	-1.28	-0.16	-8.10	-0.13
60	A TRP st	-8.45	-0.49	-0.03	-7.94	0.00
61	G TRP st	-10.21	-1.49	-0.15	-8.58	0.00
62	C TRP st	-8.31	-0.96	-0.14	-7.21	0.00

Table S15. Interaction energies (kcal/mol) of the 32 small T-shaped testing dimers.[a]

			our model		M06-2X				M06-2X-D3				AMBER99		AMOEBA	
					without CP		with CP		without CP		with CP					
dimers		IE_{ref}	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$
63	benzene dimer (C_{2V})	-2.74	-2.63	0.11	-3.29	-0.55	-2.35	0.39	-3.74	-1.00	-2.80	-0.06	-2.02	0.72	-1.67	1.07
64	U PHE edge	-2.80	-2.38	0.42	-2.64	0.16	-1.97	0.83	-3.12	-0.32	-2.44	0.36	-2.50	0.30	-2.26	0.54
65	U PHE face	-6.59	-7.02	-0.43	-7.14	-0.55	-6.17	0.42	-7.62	-1.03	-6.65	-0.06	-9.72	-3.13	-5.25	1.34
66	T PHE edge	-2.94	-2.87	0.07	-3.03	-0.09	-2.17	0.77	-3.61	-0.67	-2.74	0.20	-2.06	0.88	-2.66	0.28
67	T PHE face	-5.30	-6.27	-0.97	-6.27	-0.97	-5.28	0.02	-6.79	-1.49	-5.80	-0.50	-8.82	-3.52	-6.30	-1.00
68	A PHE edge	-3.63	-3.29	0.34	-3.66	-0.03	-2.81	0.82	-4.25	-0.62	-3.40	0.23	-2.98	0.65	-2.80	0.83
69	A PHE face	-6.31	-6.31	0.00	-6.80	-0.49	-5.69	0.62	-7.34	-1.03	-6.23	0.08	-11.91	-5.60	-6.46	-0.15
70	G PHE edge	-3.82	-3.60	0.22	-3.68	0.14	-2.88	0.94	-4.29	-0.47	-3.49	0.33	-3.36	0.46	-3.08	0.74
71	G PHE face	-5.81	-6.42	-0.61	-6.11	-0.30	-5.11	0.70	-6.70	-0.89	-5.71	0.10	-9.79	-3.98	-6.20	-0.39
72	C PHE edge	-3.34	-2.98	0.36	-3.29	0.05	-2.56	0.78	-3.80	-0.46	-3.07	0.27	-2.60	0.74	-2.95	0.39
73	C PHE face	-6.07	-7.05	-0.98	-6.56	-0.49	-5.57	0.50	-7.05	-0.98	-6.06	0.01	-12.04	-5.97	-7.12	-1.05
74	TRP PHE TS	-5.73	-6.14	-0.41	-6.30	-0.57	-5.06	0.67	-6.86	-1.13	-5.63	0.10	-6.93	-1.20	-4.01	1.72
75	U HIS edge	-5.45	-5.72	-0.27	-5.40	0.05	-4.85	0.60	-5.82	-0.37	-5.27	0.18	-7.00	-1.55	-4.92	0.53
76	U HIS face	-8.82	-8.06	0.76	-9.01	-0.19	-8.33	0.49	-9.38	-0.56	-8.70	0.12	-11.06	-2.24	-7.12	1.70
77	T HIS edge	-5.57	-5.93	-0.36	-5.51	0.06	-4.87	0.70	-6.01	-0.44	-5.37	0.20	-7.66	-2.09	-5.17	0.40
78	T HIS face	-8.17	-8.67	-0.50	-8.76	-0.59	-8.00	0.17	-9.15	-0.98	-8.39	-0.22	-10.69	-2.52	-8.79	-0.62
79	A HIS edge	-5.35	-5.16	0.19	-5.46	-0.11	-4.75	0.60	-5.98	-0.63	-5.27	0.08	-3.13	2.22	-4.88	0.47
80	A HIS face	-7.96	-7.22	0.74	-7.81	0.15	-7.12	0.84	-8.24	-0.28	-7.56	0.40	-11.60	-3.64	-8.89	-0.93
81	G HIS edge	-6.50	-6.81	-0.31	-6.59	-0.09	-5.89	0.61	-7.14	-0.64	-6.44	0.06	-4.04	2.46	-5.50	1.00
82	G HIS face	-6.38	-7.08	-0.70	-6.16	0.22	-5.46	0.92	-6.65	-0.27	-5.95	0.43	-8.88	-2.50	-7.28	-0.90
83	C HIS edge	-6.57	-6.37	0.20	-6.58	-0.01	-6.03	0.54	-7.01	-0.44	-6.47	0.10	-3.18	3.39	-6.07	0.50
84	C HIS face	-8.62	-9.98	-1.36	-9.09	-0.47	-8.34	0.28	-9.46	-0.84	-8.72	-0.10	-12.24	-3.62	-9.19	-0.57
85	U TRP edge	-4.59	-4.82	-0.23	-4.34	0.25	-3.55	1.04	-4.97	-0.38	-4.17	0.42	-3.92	0.67	-4.07	0.52
86	U TRP face	-9.01	-8.85	0.16	-9.64	-0.63	-8.51	0.50	-10.29	-1.28	-9.16	-0.15	-4.38	4.63	-6.74	2.27
87	T TRP edge	-5.28	-5.59	-0.31	-5.09	0.19	-4.11	1.17	-5.85	-0.57	-4.87	0.41	-3.84	1.44	-5.36	-0.08
88	T TRP face	-9.05	-9.27	-0.22	-9.61	-0.56	-8.40	0.65	-10.38	-1.33	-9.17	-0.12	-4.86	4.19	-8.62	0.43
89	A TRP edge	-5.47	-4.62	0.85	-5.03	0.44	-4.01	1.46	-5.81	-0.34	-4.79	0.68	-2.63	2.84	-4.53	0.94

90	A TRP face	-8.31	-8.01	0.30	-8.29	0.02	-7.19	1.12	-9.01	-0.70	-7.91	0.40	-9.18	-0.87	-8.52	-0.21
91	G TRP edge	-6.90	-6.57	0.33	-6.48	0.42	-5.50	1.40	-7.29	-0.39	-6.32	0.58	-4.59	2.31	-6.13	0.77
92	G TRP face	-7.74	-7.48	0.26	-8.08	-0.34	-7.12	0.62	-8.72	-0.98	-7.76	-0.02	-7.10	0.64	-8.01	-0.27
93	C TRP edge	-6.88	-5.81	1.07	-6.55	0.33	-5.76	1.12	-7.19	-0.31	-6.40	0.48	-2.99	3.89	-6.45	0.43
94	C TRP face	-8.10	-6.96	1.14	-8.69	-0.59	-7.80	0.30	-9.36	-1.26	-8.47	-0.37	-5.96	2.14	-6.62	1.48
RMSD				0.58		0.39		0.78		0.80		0.30		2.84		0.91
MAD				1.36		0.97		1.46		1.49		0.68		5.97		2.27
MRD				7.86%		5.35%		13.23%		12.65%		4.54%		38.01%		13.34%

[a] IE_{ref} are the benchmark interaction energies taken from references, IE are the interaction energies produced by different methods, the DFT calculations employed aug-cc-pVDZ basis set.

Table S16. Decomposed interaction energies (kcal/mol) of the 32 small T-shaped testing dimers calculated at the geometries optimized with our model.

dimers		IE	E_{es}	E_{pol}	E_{vdw}	E_{orb}
63	benzene dimer (C_{2V})	-2.63	-0.14	-0.05	-1.72	-0.73
64	U PHE edge	-2.38	-0.10	0.00	-2.28	0.00
65	U PHE face	-7.02	-1.75	-0.43	-2.91	-1.92
66	T PHE edge	-2.87	0.00	-0.05	-2.68	-0.14
67	T PHE face	-6.27	-1.40	-0.29	-2.95	-1.63
68	A PHE edge	-3.29	0.09	0.00	-2.83	-0.56
69	A PHE face	-6.31	-1.53	-0.32	-2.51	-1.95
70	G PHE edge	-3.60	-0.05	-0.05	-2.97	-0.54
71	G PHE face	-6.42	-1.52	-0.28	-2.62	-1.99
72	C PHE edge	-2.98	-0.03	-0.07	-2.63	-0.26
73	C PHE face	-7.05	-1.74	-0.42	-3.00	-1.89
74	TRP PHE TS	-6.14	-1.27	-0.23	-2.72	-1.92
75	U HIS edge	-5.72	-2.19	-0.36	-3.17	0.00
76	U HIS face	-8.06	-1.26	-0.15	-2.97	-3.69
77	T HIS edge	-5.93	-2.28	-0.38	-3.26	0.00
78	T HIS face	-8.67	-1.14	-0.18	-3.13	-4.22
79	A HIS edge	-5.16	0.37	-0.03	-3.65	-1.85
80	A HIS face	-7.22	-0.91	-0.09	-2.50	-3.72
81	G HIS edge	-6.81	0.03	-0.04	-3.66	-3.13
82	G HIS face	-7.08	-0.58	-0.07	-2.68	-3.74
83	C HIS edge	-6.37	-1.46	-0.18	-3.24	-1.50
84	C HIS face	-9.98	-1.67	-0.27	-3.11	-4.93
85	U TRP edge	-4.82	-1.22	-0.18	-2.89	-0.53
86	U TRP face	-8.85	-1.87	-0.31	-3.91	-2.77
87	T TRP edge	-5.59	-1.14	-0.18	-3.42	-0.86
88	T TRP face	-9.27	-1.88	-0.31	-4.20	-2.88
89	A TRP edge	-4.62	0.25	-0.01	-3.02	-1.84
90	A TRP face	-8.01	-2.12	-0.28	-3.55	-2.06
91	G TRP edge	-6.57	-0.12	-0.04	-3.68	-2.74
92	G TRP face	-7.48	-1.49	-0.22	-3.45	-2.32
93	C TRP edge	-5.81	-1.19	-0.18	-2.82	-1.62
94	C TRP face	-6.96	-1.09	-0.23	-4.11	-1.52

Table S17. Interaction energies (kcal/mol) of the 30 small X–H···π and other testing dimers.[a]

			our model		M06-2X				M06-2X-D3				AMBER99		AMOEBA	
					without CP		with CP		without CP		with CP					
dimers		IE_{ref}	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$	IE	$IE-IE_{ref}$
95	ethyne···ethyne (CH···π)	-1.52	-1.49	0.03	-1.66	-0.14	-1.33	0.19	-1.71	-0.19	-1.38	0.14	-	-	-	-
96	PHE···ethyne (CH···π)	-2.87	-3.29	-0.42	-3.54	-0.67	-2.77	0.10	-3.70	-0.83	-2.93	-0.06	-	-	-	-
97	PHE···AcOH (OH···π)	-4.71	-5.17	-0.46	-5.35	-0.64	-4.64	0.07	-5.66	-0.95	-4.95	-0.24	-4.44	0.27	-3.45	1.26
98	PHE···$AcNH_2$ (NH···π)	-4.36	-4.27	0.09	-4.89	-0.53	-4.28	0.08	-5.20	-0.84	-4.59	-0.23	-4.80	-0.44	-4.47	-0.11
99	PHE···MeOH (OH···π)	-4.19	-4.17	0.02	-4.98	-0.79	-4.28	-0.09	-5.24	-1.05	-4.54	-0.35	-5.67	-1.48	-3.28	0.91
100	PHE···peptide (NH···π)	-5.28	-5.83	-0.55	-6.42	-1.14	-5.25	0.03	-6.94	-1.66	-5.76	-0.48	-5.12	0.16	-4.57	0.71
101	ethyne···AcOH (OH···π)	-4.87	-5.11	-0.24	-5.42	-0.55	-5.07	-0.20	-5.51	-0.64	-5.16	-0.29	-	-	-	-
102	PHE···AcOH	-3.80	-3.99	-0.19	-4.82	-1.02	-3.90	-0.10	-5.21	-1.41	-4.29	-0.49	-2.19	1.61	-3.34	0.46
103	$MeNH_2$···pyridine	-3.97	-3.99	-0.02	-4.55	-0.58	-3.91	0.06	-4.82	-0.85	-4.19	-0.22	-	-	-2.87	1.10
104	peptide···ethene	-3.00	-3.41	-0.41	-3.55	-0.55	-2.95	0.05	-3.81	-0.81	-3.21	-0.21	-	-	-2.63	0.37
105	PHE···cyclopentane	-3.58	-3.62	-0.04	-4.65	-1.07	-3.50	0.08	-5.26	-1.68	-4.11	-0.53	-	-	-3.18	0.40
106	PHE···neopentane	-2.90	-3.12	-0.22	-3.58	-0.68	-2.53	0.37	-4.22	-1.32	-3.18	-0.28	-	-	-2.77	0.13
107	U···pentane	-4.85	-4.96	-0.11	-6.16	-1.31	-4.79	0.06	-6.92	-2.07	-5.56	-0.71	-	-	-4.23	0.62
108	U···cyclopentane	-4.14	-4.89	-0.75	-4.99	-0.85	-3.79	0.35	-5.67	-1.53	-4.47	-0.33	-	-	-3.61	0.53
109	U···neopentane	-3.71	-3.96	-0.25	-4.51	-0.80	-3.42	0.29	-5.20	-1.49	-4.11	-0.40	-	-	-3.47	0.24
110	PHE···ethene	-1.43	-1.22	0.21	-2.18	-0.75	-1.68	-0.25	-2.47	-1.04	-1.97	-0.54	-	-	-1.20	0.23
111	U···ethene	-3.38	-3.16	0.22	-4.24	-0.86	-3.57	-0.19	-4.53	-1.15	-3.86	-0.48	-	-	-3.01	0.37
112	neopentane···neopentane	-1.78	-2.13	-0.35	-2.18	-0.40	-1.05	0.73	-2.82	-1.04	-1.70	0.08	-	-	-2.06	-0.28
113	cyclopentane···neopentane	-2.40	-2.58	-0.18	-3.12	-0.72	-1.89	0.51	-3.78	-1.38	-2.55	-0.15	-	-	-2.58	-0.18
114	cyclopentane···cyclopentane	-3.00	-2.98	0.02	-3.53	-0.53	-2.41	0.59	-4.17	-1.17	-3.06	-0.06	-	-	-2.82	0.18
115	pentane···pentane	-3.78	-3.70	0.08	-5.30	-1.52	-3.68	0.10	-6.11	-2.33	-4.48	-0.70	-	-	-3.62	0.16
116	peptide···pentane	-4.26	-4.22	0.04	-5.86	-1.60	-4.34	-0.08	-6.52	-2.26	-5.00	-0.74	-	-	-3.61	0.65
117	pentane···AcOH	-2.91	-3.30	-0.39	-3.82	-0.91	-2.77	0.14	-4.30	-1.39	-3.25	-0.34	-	-	-2.82	0.09
118	pentane···$AcNH_2$	-3.53	-3.51	0.02	-4.50	-0.97	-3.47	0.06	-5.02	-1.49	-3.99	-0.46	-	-	-3.30	0.23
119	ethene···pentane	-2.01	-1.84	0.17	-2.66	-0.65	-1.98	0.03	-2.98	-0.97	-2.31	-0.30	-	-	-1.57	0.44
120	ethyne···pentane	-1.75	-1.96	-0.21	-2.30	-0.55	-1.86	-0.11	-2.53	-0.78	-2.09	-0.34	-	-	-	-
121	pyrene···methane	-2.50	-2.47	0.03	-3.63	-1.13	-2.69	-0.19	-4.09	-1.59	-3.16	-0.66	-	-	-2.33	0.17

122	pyridine···pyridine	-4.15	-4.41	-0.26	-4.22	-0.07	-3.46	0.69	-4.53	-0.38	-3.77	0.38	-	-	-2.95	1.20
123	ethyne···water	-2.85	-2.71	0.14	-3.25	-0.40	-2.78	0.07	-3.28	-0.43	-2.82	0.03	-	-	-	-
124	pyridine···ethyne	-3.99	-3.53	0.46	-4.29	-0.30	-3.57	0.42	-4.42	-0.43	-3.70	0.29	-	-	-	-
RMSD				0.28		0.83		0.29		1.28		0.40		1.01		0.57
MAD				0.75		1.60		0.73		2.33		0.74		1.61		1.26
MRD				6.99%		23.63%		7.52%		36.87%		11.06%		19.31%		12.80%

[a]IE_{ref} are the benchmark interaction energies taken from references, IE are the interaction energies produced by different methods, the DFT calculations employed aug-cc-pVDZ basis set.

Table S18. Decomposed interaction energies (kcal/mol) of the 30 small X–H···π and other dimers testing dimers calculated at the geometries optimized with our model.

dimers		IE	E_{es}	E_{pol}	E_{vdw}	E_{orb}
95	ethyne···ethyne (CH···π)	-1.49	-0.33	-0.02	-0.62	-0.52
96	PHE···ethyne (CH···π)	-3.29	-0.48	-0.07	-1.39	-1.35
97	PHE···AcOH (OH···π)	-5.17	-1.57	-0.24	-2.23	-1.13
98	PHE···$AcNH_2$ (NH···π)	-4.27	-1.26	-0.38	-1.72	-0.92
99	PHE···MeOH (OH···π)	-4.17	-1.02	-0.12	-1.94	-1.10
100	PHE···peptide (NH···π)	-5.83	-1.32	-0.18	-2.85	-1.48
101	ethyne···AcOH (OH···π)	-5.11	-2.31	-0.34	-0.99	-1.47
102	PHE···AcOH	-3.99	-0.51	-0.11	-2.66	-0.71
103	$MeNH_2$···pyridine	-3.99	-0.39	-0.05	-1.52	-2.02
104	peptide···ethene	-3.41	-0.69	-0.28	-1.66	-0.78
105	PHE···cyclopentane	-3.62	0.08	-0.05	-3.11	-0.54
106	PHE···neopentane	-3.12	0.00	-0.05	-2.52	-0.56
107	U···pentane	-4.96	-0.28	-0.11	-4.48	-0.09
108	U···cyclopentane	-4.89	-0.22	-0.06	-4.13	-0.48
109	U···neopentane	-3.96	-0.08	-0.03	-3.73	-0.12
110	PHE···ethene	-1.22	0.46	-0.01	-1.67	0.00
111	U···ethene	-3.16	-0.66	-0.04	-2.46	0.00
112	neopentane···neopentane	-2.13	-0.01	0.00	-2.12	0.00
113	cyclopentane···neopentane	-2.58	-0.01	-0.01	-2.56	0.00
114	cyclopentane···cyclopentane	-2.98	0.04	0.00	-3.02	0.00
115	pentane···pentane	-3.70	0.03	-0.01	-3.72	0.00
116	peptide···pentane	-4.22	-0.08	-0.30	-3.68	-0.16
117	pentane···AcOH	-3.30	-0.17	-0.08	-2.88	-0.17
118	pentane···$AcNH_2$	-3.51	-0.10	-0.35	-2.96	-0.11
119	ethene···pentane	-1.84	-0.05	-0.02	-1.77	0.00
120	ethyne···pentane	-1.96	0.04	-0.01	-1.57	-0.42
121	pyrene···methane	-2.47	0.00	-0.02	-2.41	-0.04
122	pyridine···pyridine	-4.41	-1.27	-0.43	-0.96	-1.76
123	ethyne···water	-2.71	-1.09	-0.20	-0.15	-1.28
124	pyridine···ethyne	-3.53	-1.66	-0.32	-0.36	-1.19

Table S19. Interaction energies (kcal/mol) of the S66 data set obtained at the different theoretical levels.[a]

dimers (name in ref 1)	CCSD(T)/CBS	our model	AM1	PM3	PM6	PM6				PM7	OM1	OM2	OM2		OM3	OM3	
						DH2	DH+	D3H+	D3H4				D2	D3		D2	D3
water···water	-4.92	-5.16	-2.9	-2.6	-3.91	-4.89	-6.47	-6.69	-4.88	-4.9	-2.8	-4.0	-4.3	-4.3	-4.2	-4.6	-4.7
water···MeOH	-5.59	-4.73	-2.1	-2.5	-4.24	-6.82	-6.95	-7.25	-5.48	-5.0	-2.0	-3.9	-4.5	-4.5	-3.7	-4.4	-4.5
water···$MeNH_2$	-6.91	-7.06	-0.4	-2.2	-4.05	-6.29	-7.12	-6.90	-7.53	-6.8	-2.3	-4.4	-5.0	-5.1	-5.2	-5.9	-6.0
water···peptide	-8.10	-8.48	-2.8	-4.5	-6.28	-8.02	-9.12	-8.80	-7.85	-7.6	-3.6	-6.2	-7.1	-7.1	-5.8	-6.9	-7.0
MeOH···MeOH	-5.76	-5.62	-1.6	-2.4	-3.49	-6.27	-6.48	-6.71	-6.31	-4.6	-1.9	-3.3	-4.1	-4.1	-3.1	-4.0	-4.1
MeOH···$MeNH_2$	-7.55	-8.16	0.0	-2.4	-3.09	-5.72	-6.64	-6.42	-7.05	-6.0	-2.3	-3.8	-4.8	-4.9	-4.6	-5.9	-6.1
MeOH···peptide	-8.23	-9.17	-1.8	-4.0	-4.92	-6.95	-7.93	-7.72	-8.17	-6.8	-2.9	-5.0	-6.2	-6.2	-4.6	-6.0	-6.2
MeOH···water	-5.01	-5.81	-2.4	-2.5	-3.19	-4.27	-5.91	-6.08	-5.68	-4.3	-2.6	-3.4	-3.8	-3.8	-3.5	-4.0	-4.1
$MeNH_2$···MeOH	-3.06	-2.88	-1.8	0.0	-2.29	-3.99	-5.15	-4.89	-4.05	-4.6	-1.2	-1.4	-2.3	-2.4	-1.2	-2.2	-2.4
$MeNH_2$···$MeNH_2$	-4.16	-3.88	0.0	0.8	-1.84	-3.30	-4.27	-4.08	-4.58	-5.4	-0.8	-1.5	-2.7	-2.7	-1.2	-2.7	-2.8
$MeNH_2$···peptide	-5.42	-5.42	-1.9	0.7	-3.85	-5.35	-5.65	-6.54	-6.07	-6.2	-1.8	-2.8	-4.4	-4.6	-2.2	-4.2	-4.4
$MeNH_2$···water	-7.27	-6.62	-0.1	-2.0	-3.86	-5.99	-6.55	-6.63	-7.42	-6.5	-1.8	-4.3	-5.1	-5.1	-5.0	-5.9	-6.0
peptide···MeOH	-6.19	-6.28	-2.6	-1.0	-4.23	-6.39	-6.03	-6.33	-6.45	-6.5	-2.5	-3.9	-5.0	-5.2	-3.4	-4.8	-5.0
peptide···$MeNH_2$	-7.45	-7.83	-1.3	-1.6	-4.18	-6.88	-7.51	-7.51	-7.49	-9.4	-2.9	-4.1	-5.5	-5.8	-4.2	-5.9	-6.2
peptide···peptide	-8.63	-8.17	-3.1	-2.8	-5.91	-8.43	-9.31	-9.39	-8.74	-9.5	-3.5	-5.3	-7.0	-7.3	-4.5	-6.5	-6.9
peptide···water	-5.12	-5.71	-3.3	-1.4	-3.85	-4.82	-5.36	-5.59	-5.46	-6.1	-3.1	-3.8	-4.3	-4.5	-3.7	-4.4	-4.6
uracil···uracil (BP)	-17.18	-16.99	-3.9	-8.3	-11.34	-18.89	-17.39	-17.36	-16.42	-16.1	-8.1	-13.8	-15.4	-15.7	-12.7	-14.5	-15.1
water···pyridine	-6.86	-6.77	0.7	-1.8	-3.13	-4.53	-6.39	-6.17	-6.96	-6.1	-1.9	-3.7	-4.4	-4.5	-4.5	-5.3	-5.5
MeOH···pyridine	-7.41	-8.59	1.1	-1.8	-2.18	-3.88	-5.88	-5.57	-6.27	-5.5	-1.9	-3.2	-4.1	-4.3	-4.1	-5.2	-5.5
AcOH···AcOH	-19.09	-19.42	0.9	-10.5	-11.10	-19.29	-17.96	-17.41	-18.46	-18.8	-6.3	-13.8	-15.1	-15.1	-11.9	-13.4	-13.8
$AcNH_2$···$AcNH_2$	-16.26	-16.61	-5.9	-8.4	-12.38	-16.09	-17.85	-17.89	-16.94	-16.7	-7.7	-12.9	-14.3	-14.4	-11.8	-13.4	-13.8
AcOH···uracil	-19.49	-18.67	-2.4	-10.8	-12.03	-19.99	-18.29	-18.11	-18.41	-18.2	-8.7	-15.4	-16.8	-17.0	-13.8	-15.5	-16.0
$AcNH_2$···uracil	-19.19	-19.24	-6.3	-10.3	-14.05	-19.48	-19.83	-19.73	-18.94	-18.9	-10.1	-16.1	-17.6	-17.8	-14.9	-16.7	-17.1
benzene···benzene (π-π)	-2.82	-3.03	2.6	1.7	0.04	-3.47	-3.47	-2.38	-2.93	-4.4	0.7	1.2	-1.2	-2.1	1.0	-1.9	-2.9
pyridine···pyridine (π-π)	-3.90	-3.46	2.4	2.0	-1.03	-4.62	-4.62	-3.62	-4.10	-5.3	-0.2	-0.2	-2.8	-3.6	-0.2	-3.3	-4.2
uracil···uracil (π-π)	-9.83	-9.93	0.2	6.3	-4.37	-9.38	-9.35	-8.96	-9.15	-8.5	-2.7	-4.4	-8.8	-9.4	-3.9	-9.3	-10.2
benzene···pyridine (π-π)	-3.44	-3.33	2.5	1.8	-0.56	-4.12	-4.12	-3.09	-3.59	-4.9	0.1	0.5	-2.0	-2.9	0.3	-2.7	-3.6
benzene···uracil (π-π)	-5.71	-5.81	3.9	3.5	-1.63	-5.99	-5.99	-5.06	-5.44	-5.5	-0.5	-1.1	-4.6	-5.4	-0.9	-5.2	-6.1

pyridine···uracil (π-π)	-6.82	-5.89	2.4	3.2	-3.25	-7.51	-7.51	-6.66	-7.02	-6.9	-1.8	-2.4	-5.9	-6.6	-2.2	-6.4	-7.3
benzene···ethene	-1.43	-1.22	1.6	1.0	0.12	-1.88	-1.88	-1.31	-1.63	-2.1	0.4	1.0	-0.4	-0.9	0.8	-0.9	-1.5
uracil···ethene	-3.38	-3.16	1.6	1.7	-1.04	-3.24	-3.24	-2.95	-3.09	-2.7	-0.2	-0.9	-2.8	-3.2	-0.7	-3.0	-3.5
uracil···ethyne	-3.74	-3.48	1.2	1.3	-1.08	-2.89	-2.89	-2.73	-2.73	-2.3	-1.0	-1.7	-3.3	-3.7	-1.5	-3.5	-4.0
pyridine···ethene	-1.87	-1.85	1.6	1.2	-0.24	-2.21	-2.21	-1.75	-2.03	-2.3	0.1	0.5	-1.0	-1.4	0.3	-1.4	-2.0
pentane···pentane	-3.78	-3.70	-0.3	-3.4	-0.64	-3.06	-3.06	-3.90	-3.18	-4.1	1.4	-0.2	-3.5	-4.0	1.1	-3.1	-3.5
neopentane···pentane	-2.61	-2.63	-0.7	-3.0	-0.69	-2.48	-2.48	-3.03	-2.36	-3.5	0.9	-0.4	-2.7	-3.2	0.5	-2.4	-2.7
neopentane···neopentane	-1.78	-2.13	-0.7	-2.6	-0.55	-1.99	-1.99	-2.24	-1.87	-2.8	0.5	-0.5	-2.1	-2.6	0.1	-1.9	-2.3
cyclopentane···neopentane	-2.40	-2.58	-0.7	-2.9	-0.69	-2.37	-2.37	-2.85	-2.29	-3.3	0.9	-0.6	-2.7	-3.2	0.3	-2.4	-2.7
cyclopentane···cyclopentane	-3.00	-2.98	-0.5	-3.0	-0.39	-2.33	-2.33	-2.86	-2.08	-3.4	1.3	-0.4	-3.0	-3.3	0.7	-2.6	-2.8
benzene···cyclopentane	-3.58	-3.62	1.2	-0.5	-0.54	-3.02	-3.02	-3.22	-3.37	-4.2	0.8	0.3	-2.3	-3.0	0.8	-2.5	-3.1
benzene···neopentane	-2.90	-3.12	0.6	-0.7	-0.71	-2.71	-2.71	-2.91	-3.11	-3.9	0.5	-0.1	-2.1	-2.8	0.3	-2.2	-2.8
uracil···pentane	-4.85	-4.96	1.5	2.1	-1.79	-4.96	-4.96	-5.45	-5.52	-5.1	0.7	-0.6	-4.2	-4.8	0.0	-4.6	-5.1
uracil···cyclopentane	-4.14	-4.89	1.5	1.6	-1.24	-4.09	-4.09	-4.40	-4.49	-4.5	0.8	-0.3	-3.4	-3.9	0.2	-3.8	-4.3
uracil···neopentane	-3.71	-3.96	1.2	1.5	-1.05	-3.41	-3.41	-3.71	-3.79	-3.6	0.6	-0.4	-2.9	-3.5	0.0	-3.2	-3.7
ethene···pentane	-2.01	-1.84	-0.1	-1.7	-0.46	-1.73	-1.73	-2.19	-1.78	-2.1	0.6	-0.2	-1.9	-2.2	0.5	-1.6	-1.9
ethyne···pentane	-1.75	-1.96	0.7	-0.3	-0.29	-1.48	-1.48	-1.58	-1.78	-1.7	0.3	0.1	-1.1	-1.5	0.3	-1.2	-1.6
peptide···pentane	-4.26	-4.22	0.4	-0.3	-1.26	-3.66	-3.66	-4.46	-4.00	-3.8	1.0	-0.4	-3.5	-3.9	0.6	-3.4	-3.8
benzene···benzene (TS)	-2.88	-2.73	0.6	-0.4	-0.81	-2.66	-2.66	-2.74	-2.59	-3.2	0.4	-0.6	-2.3	-2.8	0.0	-2.1	-2.6
pyridine···pyridine (TS)	-3.54	-3.52	0.8	0.7	-1.23	-3.01	-3.01	-3.23	-2.93	-3.3	0.1	-1.2	-2.9	-3.3	-0.5	-2.7	-3.2
benzene···pyridine (TS)	-3.33	-3.48	0.3	-0.6	-1.16	-3.01	-3.01	-3.13	-2.92	-3.5	0.2	-1.0	-2.8	-3.3	-0.3	-2.5	-3.0
benzene···ethyne (CH···π)	-2.87	-3.29	-0.1	-0.8	-1.01	-2.01	-2.01	-2.32	-1.92	-2.1	-0.1	-1.8	-3.0	-3.1	-0.8	-2.3	-2.5
ethyne···ethyne (TS)	-1.52	-1.49	-0.4	-0.9	-0.46	-0.79	-0.79	-0.95	-0.81	-0.8	-0.3	-1.2	-1.6	-1.7	-0.7	-1.2	-1.3
benzene···AcOH (OH···π)	-4.71	-5.17	-0.4	-1.4	-2.57	-4.10	-4.10	-4.30	-4.18	-3.9	-0.6	-2.7	-4.4	-4.6	-1.6	-3.7	-4.0
benzene···$AcNH_2$ (NH···π)	-4.36	-4.27	-1.2	-0.9	-2.38	-3.75	-3.75	-3.99	-3.89	-3.7	-1.2	-3.0	-4.5	-4.7	-2.1	-3.9	-4.3
benzene···water (OH···π)	-3.28	-3.30	-0.7	-1.5	-2.31	-3.23	-3.23	-3.45	-3.33	-2.8	-0.8	-2.4	-3.5	-3.6	-1.7	-3.1	-3.3
benzene···MeOH (OH···π)	-4.19	-4.17	0.0	-1.1	-1.91	-3.46	-3.46	-3.67	-3.64	-3.3	-0.3	-1.8	-3.6	-3.8	-1.1	-3.3	-3.6
benzene···$MeNH_2$ (NH···π)	-3.23	-3.41	0.2	-0.4	-1.42	-3.14	-3.14	-3.23	-3.23	-3.6	0.0	-0.8	-2.6	-2.9	-0.3	-2.5	-2.9
benzene···peptide (NH···π)	-5.28	-5.83	-0.1	-1.0	-2.28	-4.72	-4.72	-4.81	-4.82	-5.4	-0.4	-1.9	-4.4	-4.8	-0.9	-4.0	-4.5
pyridine···pyridine (CH···N)	-4.15	-4.41	-0.1	0.0	-2.51	-3.44	-3.44	-3.80	-3.22	-3.6	-1.1	-2.6	-3.7	-3.9	-1.8	-3.2	-3.4

ethyne···water (CH···O)	-2.85	-2.71	-1.8	-0.6	-1.76	-1.94	-1.94	-2.12	-1.98	-1.5	-1.8	-3.1	-3.4	-3.4	-2.7	-3.1	-3.2
ethyne···AcOH (OH···π)	-4.87	-5.11	-1.4	-1.8	-1.83	-2.40	-2.40	-2.85	-2.50	-2.3	-1.4	-4.0	-5.0	-5.0	-2.9	-4.0	-4.2
pentane···AcOH	-2.91	-3.30	0.2	-0.3	-1.32	-3.14	-3.14	-3.60	-3.42	-2.8	0.3	-0.6	-2.8	-3.2	0.0	-2.8	-3.2
pentane···$AcNH_2$	-3.53	-3.51	0.1	-0.3	-1.54	-3.54	-3.54	-4.06	-3.78	-3.5	0.4	-0.8	-3.2	-3.6	-0.1	-3.2	-3.5
benzene···AcOH	-3.80	-3.99	1.3	0.7	-1.60	-3.72	-3.72	-3.79	-3.71	-3.4	-0.2	-1.5	-3.6	-4.0	-0.7	-3.3	-3.8
peptide···ethene	-3.00	-3.41	0.1	0.3	-1.26	-2.53	-2.53	-2.89	-2.72	-2.4	-0.1	-1.2	-2.7	-2.9	-0.7	-2.5	-2.8
pyridine···ethyne	-3.99	-3.53	0.4	-0.5	-1.25	-1.75	-1.75	-1.90	-1.87	-1.8	-1.7	-3.4	-3.9	-4.1	-2.9	-3.6	-3.9
$MeNH_2$···pyridine	-3.97	-3.99	1.0	1.9	-1.28	-2.85	-2.97	-3.12	-4.47	-4.3	-0.2	-1.0	-2.6	-2.9	-0.6	-2.7	-3.0

[a]The benchmark CCSD(T)/CBS interaction energies are taken from ref 1. The AM1, PM3, PM7, OM1, OM2, OM2-D2, OM2-D3, OM3, OM3-D2, OM3-D3 interaction energies are taken from ref 2. The PM6, PM6-DH2, PM6-DH+, PM6-D3H+ interaction energies are taken from ref 3. The PM6-D3H4 interaction energies are taken from ref 4.

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1. Řezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7*, 2427-2438.
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Table S20. Information on the 14 large noncovalent complexes.

dimers		ref	name in original references	geometry optimization level	reference energy level
125	antiparallel Gly pentapeptide dimer	1	antiparallel Gly pentapeptide dimer	MP2/6-31G(d)	MP2/aug-cc-pVTZ-CP
126	parallel Gly pentapeptide dimer	1	parallel Gly pentapeptide dimer	MP2/6-31G(d)	MP2/aug-cc-pVTZ-CP
127	parallel Ala tripeptide dimer	1	parallel Ala tripeptide dimer	MP2/6-31G(d)	MP2/aug-cc-pVTZ-CP
128	anthracene dimer st	2	anthracene dimer (π-π stacked)	B97-D/TZV(2d,2p)	B2PLYP-D/QZV3P(1/2CP)
129	tetracene dimer st	2	tetracene dimer (π-π stacked)	B97-D/TZV(2d,2p)	B2PLYP-D/QZV3P(1/2CP)
130	coronene dimer st	3	coronene dimer	QCISD(T)/aug-cc-pVDZ*	QCISD(T)/CBS
131	adenine···circumcoronene st	3	circumcoronene···adenine	TPSS-D/TZVP	QCISD(T)/CBS
132	anthracene dimer TS	2	anthracene dimer (T-shaped)	B97-D/TZV(2d,2p)	B2PLYP-D/QZV3P(1/2CP)
133	tetracene dimer TS	2	tetracene dimer (T-shaped)	B97-D/TZV(2d,2p)	B2PLYP-D/QZV3P(1/2CP)
134	tetradecahydroanthracene dimer	2	tetradecahydroanthracene dimer	B97-D/TZV(2d,2p)	B2PLYP-D/QZV3P(1/2CP)
135	octadecahydrotetracene dimer	2	octadecahydrotetracene dimer	B97-D/TZV(2d,2p)	B2PLYP-D/QZV3P(1/2CP)
136	[4]-ladderane dimer (C_s)	4	[4]-ladderane parallel-displaced dimer (C_s)	MP2/aug-cc-pVDZ	CCSD(T)/CBS
137	[5]-ladderane dimer (C_i)	4	[5]-ladderane parallel-displaced dimer (C_i)	MP2/aug-cc-pVDZ	CCSD(T)/CBS
138	octadecane dimer	3	octadecane dimer	TPSS-D/TZVP	QCISD(T)/CBS

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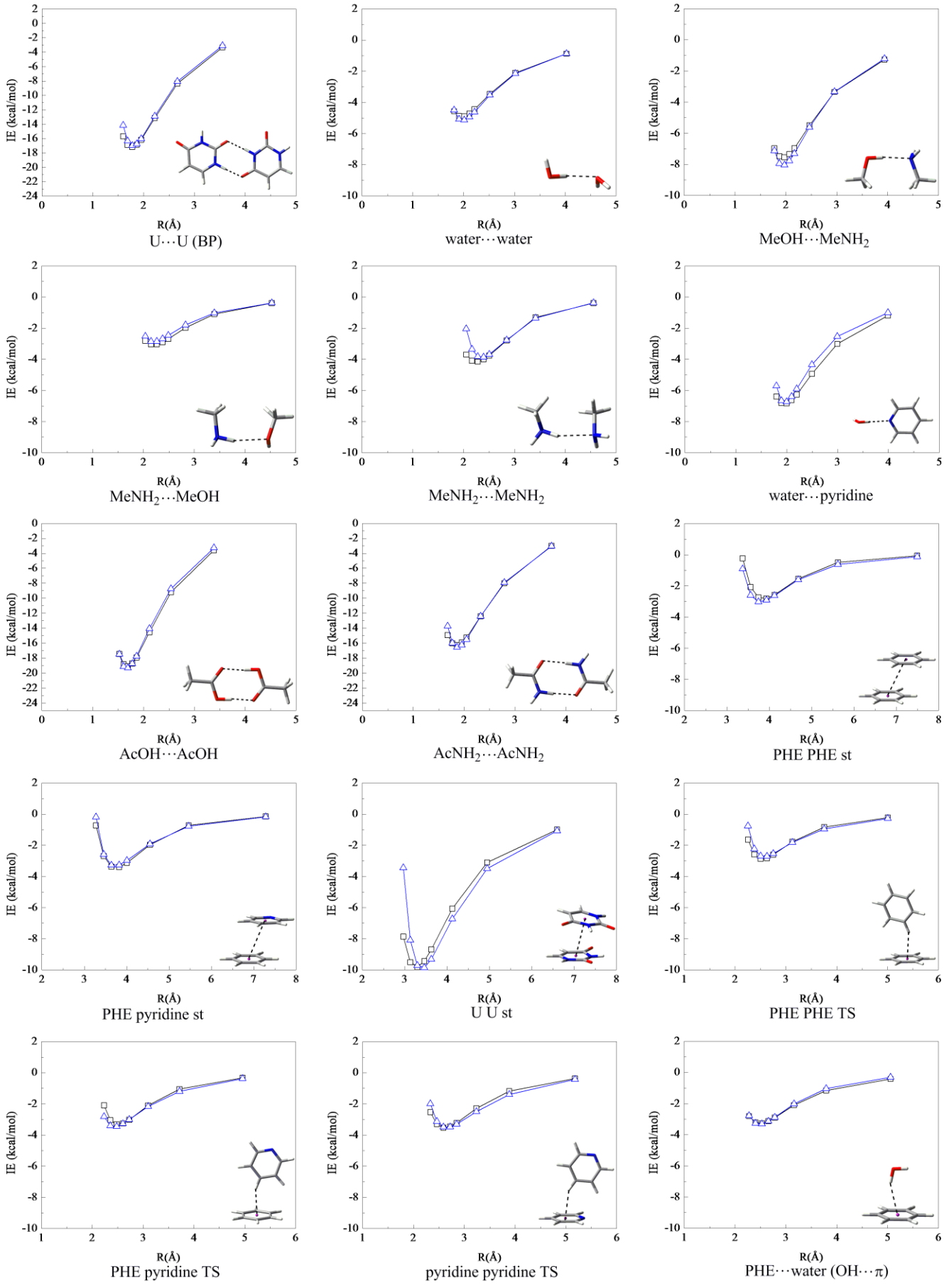
Table S21. Decomposed interaction energies (kcal/mol) of the 8 small and 14 large noncovalent complexes calculated at the reference geometries.

		our model						AMBER99								AMOEBA				
								with AMBER99's vdw values				with the vdw values of Table S2								
dimers	IE_{ref}	IE	$IE-IE_{ref}$	E_{es}	E_{pol}	E_{vdw}	E_{orb}	IE	$IE-IE_{ref}$	E_{es}	E_{vdw}	IE	$IE-IE_{ref}$	E_{es}	E_{vdw}	IE	$IE-IE_{ref}$	E_{es}	E_{pol}	E_{vdw}
9	-16.86	-17.79	-0.93	-12.14	-2.19	0.34	-3.80	-13.09	3.77	-13.49	0.40	-13.15	3.71	-13.49	0.34	-16.52	0.34	-12.63	-7.57	3.68
23	-8.10	-8.37	-0.27	-4.77	-0.85	0.50	-3.25	-7.42	0.68	-8.11	0.69	-7.61	0.49	-8.11	0.50	-7.36	0.74	-8.32	-2.03	2.99
43	-12.09	-11.66	0.43	-1.61	-0.12	-9.93	0.00	-14.21	-2.12	-7.00	-7.21	-16.93	-4.84	-7.00	-9.93	-11.34	0.75	-5.05	-0.11	-6.18
58	-8.79	-8.96	-0.17	-1.48	-0.12	-7.31	0.00	-9.30	-0.51	-3.30	-6.00	-10.61	-1.82	-3.30	-7.31	-8.64	0.15	-6.03	-0.38	-2.23
75	-5.45	-5.51	-0.06	-2.13	-0.34	-3.04	0.00	-7.00	-1.55	-4.74	-2.26	-7.78	-2.33	-4.74	-3.04	-4.92	0.53	-2.31	-0.93	-1.68
76	-8.82	-8.05	0.77	-1.25	-0.16	-2.96	-3.68	-11.06	-2.24	-8.55	-2.51	-11.51	-2.69	-8.55	-2.96	-7.12	1.70	-5.45	-1.11	-0.56
99	-4.19	-4.17	0.02	-1.06	-0.13	-1.88	-1.10	-5.67	-1.48	-3.80	-1.87	-5.68	-1.49	-3.80	-1.88	-3.28	0.91	-1.75	-0.48	-1.05
100	-5.28	-5.79	-0.51	-1.25	-0.17	-2.90	-1.47	-5.12	0.16	-2.16	-2.97	-5.06	0.22	-2.16	-2.90	-4.57	0.71	-1.92	-0.51	-2.14
125	-33.69	-32.31	1.38	-19.93	-3.84	-8.07	-0.47	-36.08	-2.39	-29.51	-6.57	-37.58	-3.89	-29.51	-8.07	-36.10	-2.41	-24.01	-13.64	1.55
126	-27.18	-27.12	0.06	-17.51	-3.02	-6.59	0.00	-25.34	1.84	-23.7	-1.63	-30.29	-3.11	-23.70	-6.59	-26.42	0.76	-16.77	-8.55	-1.10
127	-24.54	-24.50	0.04	-14.43	-3.28	-5.66	-1.13	-22.92	1.62	-19.49	-3.44	-25.15	-0.61	-19.49	-5.66	-21.17	3.37	-14.52	-9.27	2.62
128	-11.46	-10.76	0.70	0.54	-0.04	-11.26	0.00	-7.62	3.84	2.34	-9.96	-8.92	2.54	2.34	-11.26	-9.20	2.26	2.04	-0.53	-10.71
129	-16.33	-14.83	1.50	0.70	-0.05	-15.48	0.00	-10.57	5.76	2.87	-13.44	-12.61	3.72	2.87	-15.48	-12.43	3.90	2.69	-0.75	-14.37
130	-24.36	-24.47	-0.11	0.87	-0.08	-25.26	0.00	-17.96	6.40	3.58	-21.54	-21.68	2.68	3.58	-25.26	-19.00	5.36	3.40	-0.59	-21.81
131	-18.19	-19.59	-1.40	-0.26	-0.01	-19.28	-0.04	-13.97	4.22	2.71	-16.68	-16.57	1.62	2.71	-19.28	-15.48	2.71	0.45	-0.92	-15.01
132	-8.25	-8.60	-0.35	-0.41	-0.13	-5.97	-2.09	-6.37	1.88	-2.38	-3.99	-8.35	-0.1	-2.38	-5.97	-4.99	3.26	-1.04	-0.52	-3.42
133	-11.12	-11.76	-0.64	-0.55	-0.17	-8.24	-2.80	-8.09	3.03	-2.65	-5.44	-10.89	0.23	-2.65	-8.24	-6.64	4.48	-1.36	-0.69	-4.59
134	-8.88	-9.07	-0.19	-0.03	-0.03	-9.01	0.00	-	-	-	-	-	-	-	-	-7.59	1.29	-0.13	-0.20	-7.27
135	-11.83	-12.19	-0.36	-0.05	-0.03	-12.11	0.00	-	-	-	-	-	-	-	-	-10.18	1.65	-0.05	-0.25	-9.88
136	-5.5	-5.37	0.13	-0.13	-0.05	-5.19	0.00	-	-	-	-	-	-	-	-	-	-	-	-	-
137	-6.6	-6.79	-0.19	-0.16	-0.07	-6.56	0.00	-	-	-	-	-	-	-	-	-	-	-	-	-
138	-11.06	-12.60	-1.54	0.14	0.00	-12.74	0.00	-	-	-	-	-	-	-	-	-11.54	-0.48	1.14	0.09	-12.76

Table S22. Computational times (Intel Core i7-3770K 3.50 GHz, 4 cores, 32 GB memory).[a]

complex		number of atoms	CPU Time [second]				
			our model	M06-2X without CP	M06-2X-D3 with CP	AMBER99	AMOEBA
99	PHE···MeOH (OH···π)	18	0.65	437	1,025	0.21	0.23
45	U PHE st	24	0.68	1,796	4,427	0.20	0.24
91	G TRP edge	32	0.78	6,450	13,966	0.21	0.24
128	anthracene dimer st	48	0.92	23,610	60,926	0.22	0.26
126	parallel Gly pentapeptide dimer	80	1.05	38,839	99,325	0.20	0.23
138	octadecane dimer	112	2.55	100,231	370,322	0.21	0.24

[a]Aug-cc-pVDZ basis set was employed for these DFT calculations.


IE (kcal/mol)
R(Å)
U···U (BP)
water···water
MeOH···MeNH2
MeNH2···MeOH
MeNH2···MeNH2
water···pyridine
AcOH···AcOH
AcNH2···AcNH2
PHE PHE st
PHE pyridine st
U U st
PHE PHE TS
PHE pyridine TS
pyridine pyridine TS
PHE···water (OH···π)

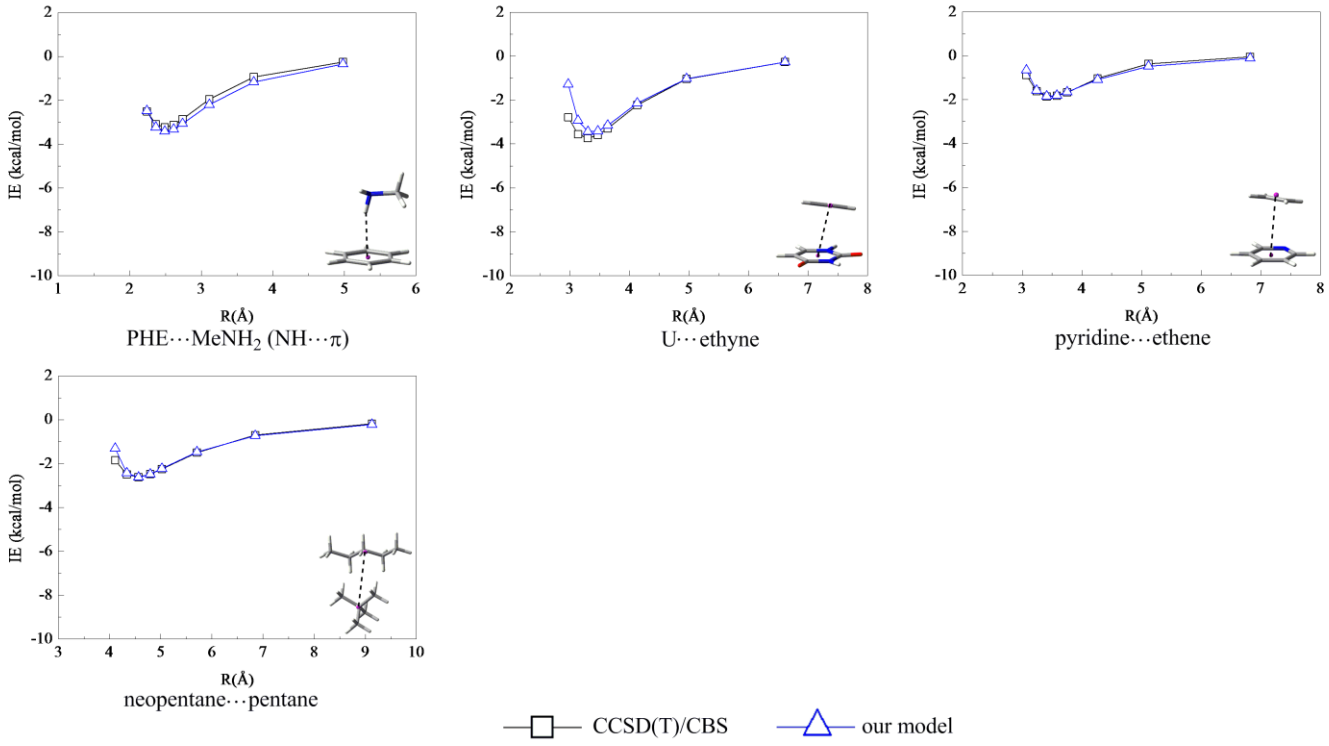


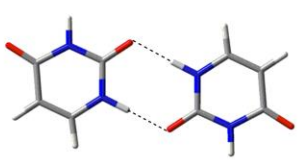
Figure S1. Potential energy curves for 19 training dimers.

CCSD(T)/CBS potential energy curves shown in this figure are taken from ref 1.

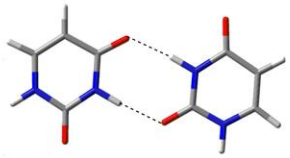
Reference

1. Řezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7*, 2427-2438.

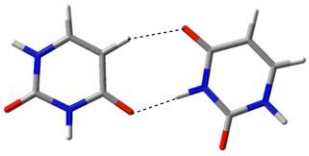
Hydrogen-bonded dimers (35)



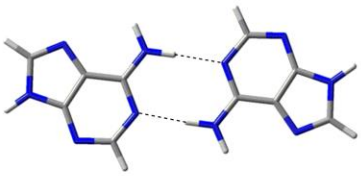
1 U···U (C_{2h})



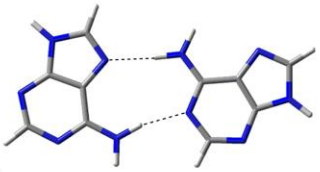
2 U···U pl



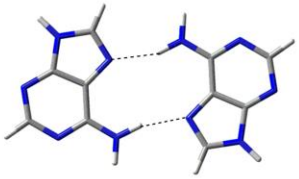
3 U···U Calcutta pl



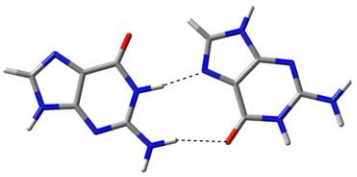
4 A···A 1 pl



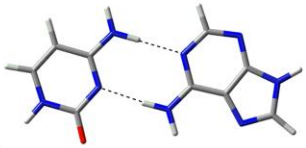
5 A···A 2 pl



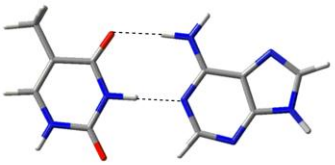
6 A···A 3 pl



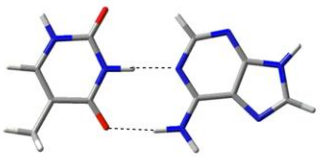
7 G···G pl



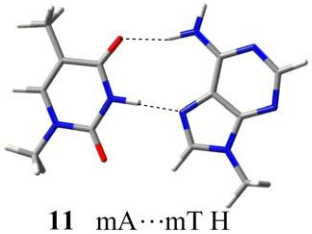
8 A···C pl



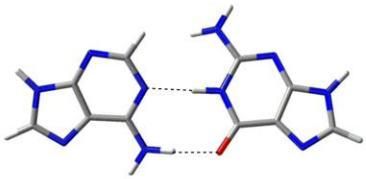
9 A···T WC



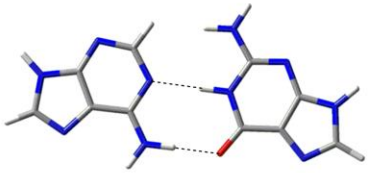
10 A···T WC (C_1)



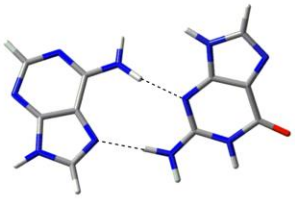
11 mA···mT H



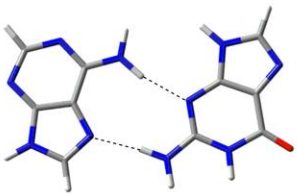
12 G···A 1



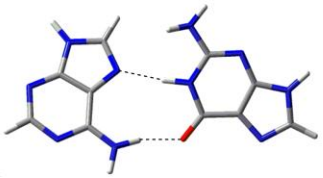
13 G···A 1 pl



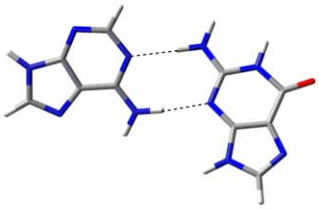
14 G···A 2



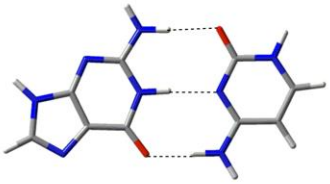
15 G···A 2 pl



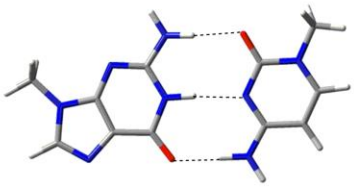
16 G···A 3



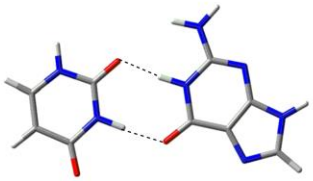
17 G···A 4



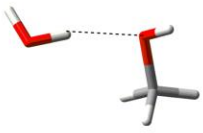
18 G···C WC



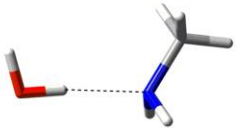
19 mG···mC WC



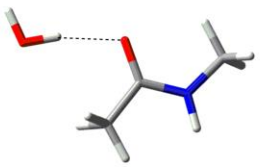
20 G···U wobble



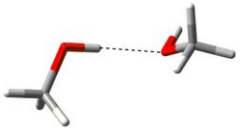
21 water···MeOH



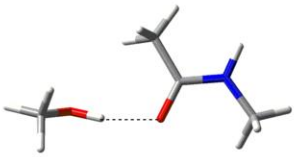
22 water···$MeNH_2$



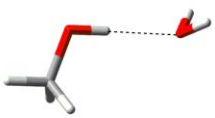
23 water···peptide



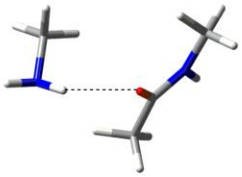
24 MeOH···MeOH



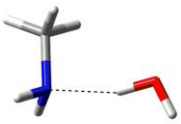
25 MeOH···peptide



26 MeOH···water



27 $MeNH_2$···peptide



28 $MeNH_2$···water

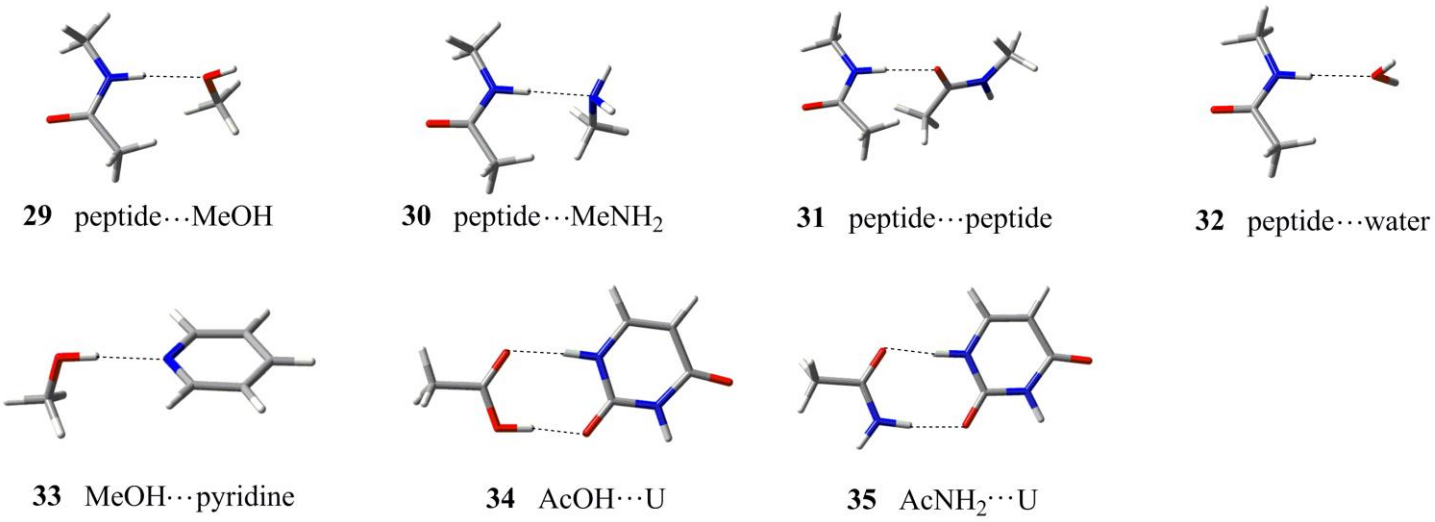


Figure S2. Structures of the 35 small hydrogen-bonded testing dimers.

Stacked dimers (27)

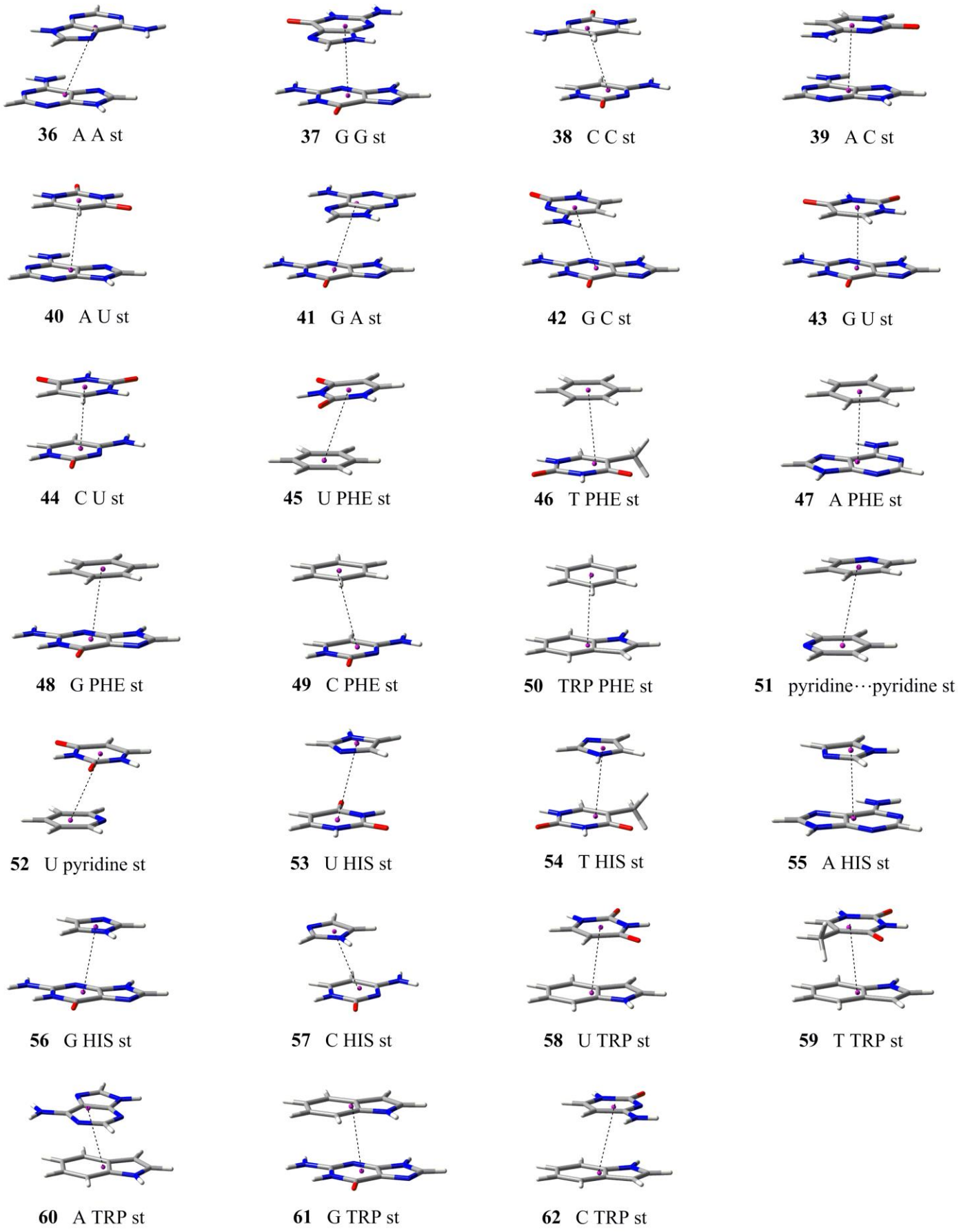
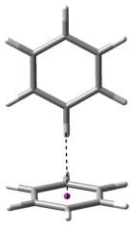
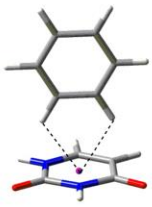


Figure S3. Structures of the 27 small stacked testing dimers.

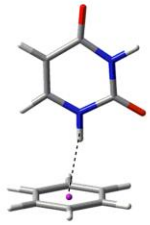
T-shaped dimers (32)



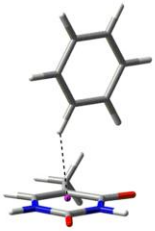
63 benzene dimer (C_{2V})



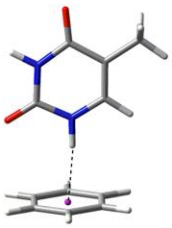
64 U PHE edge



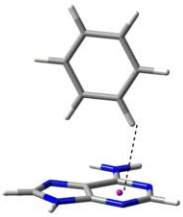
65 U PHE face



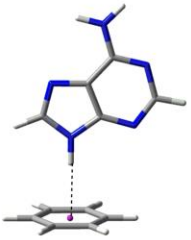
66 T PHE edge



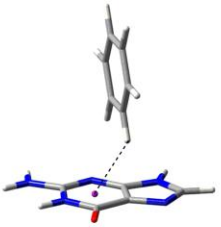
67 T PHE face



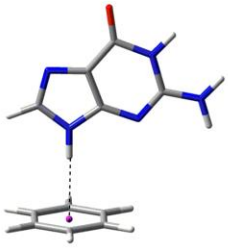
68 A PHE edge



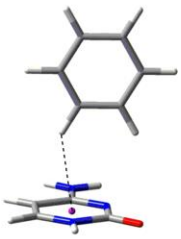
69 A PHE face



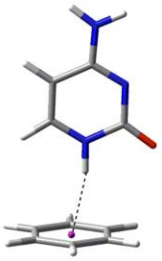
70 G PHE edge



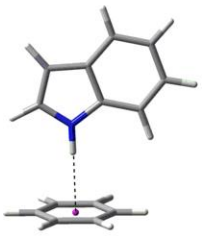
71 G PHE face



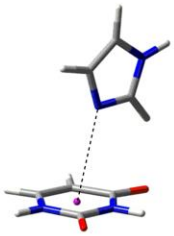
72 C PHE edge



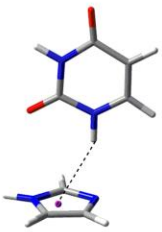
73 C PHE face



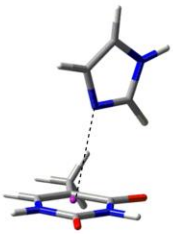
74 TRP PHE TS



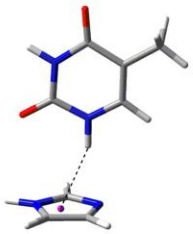
75 U HIS edge



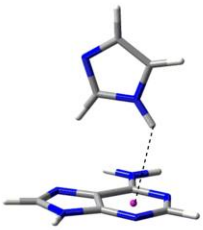
76 U HIS face



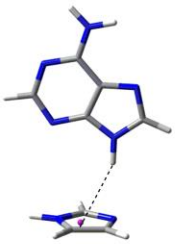
77 T HIS edge



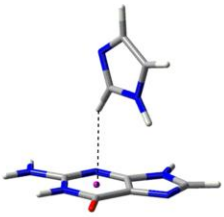
78 T HIS face



79 A HIS edge



80 A HIS face



81 G HIS edge

82 G HIS face

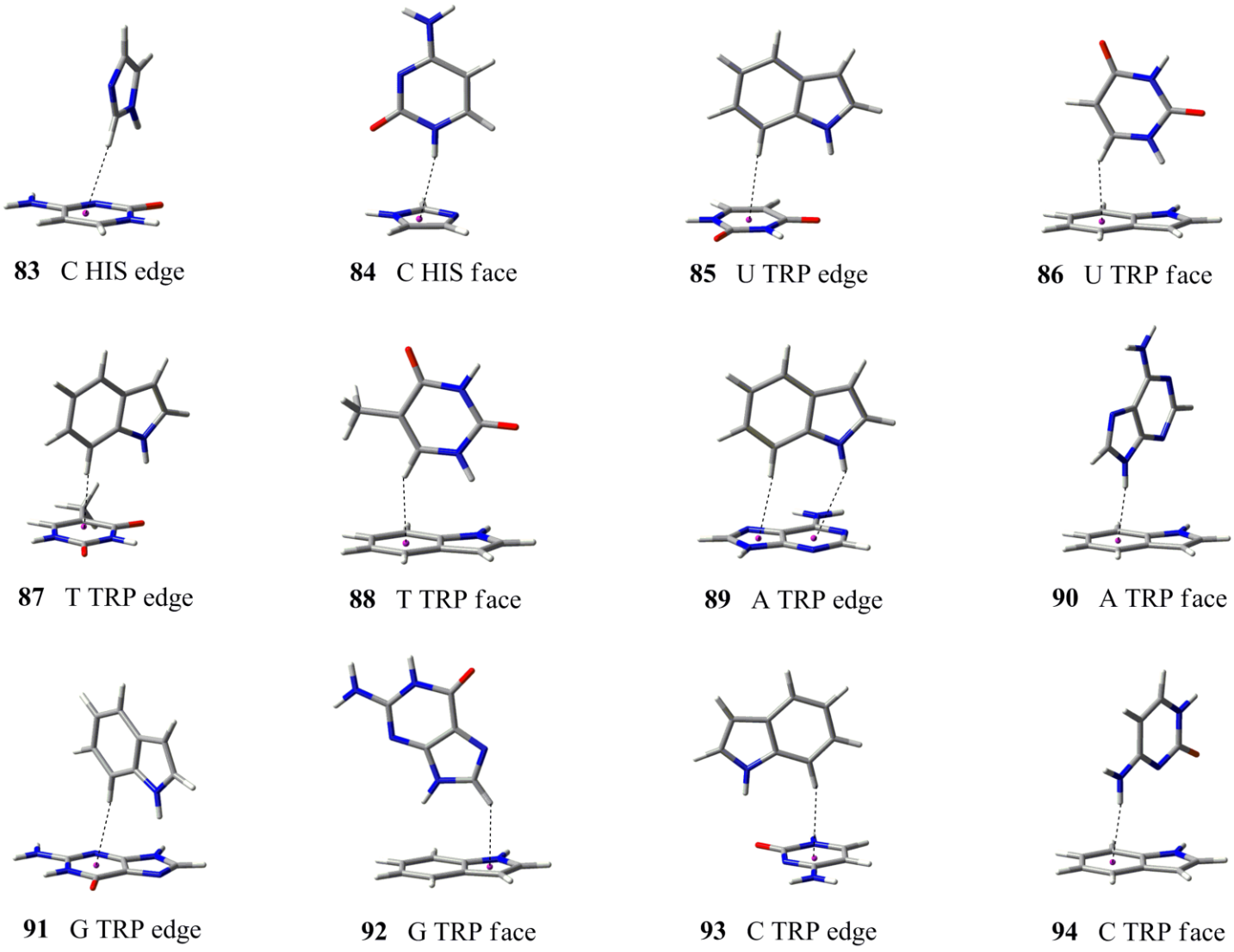


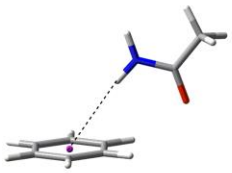
Figure S4. Structures of the 32 small T-shaped testing dimers.

X–H···π and other dimers (30)

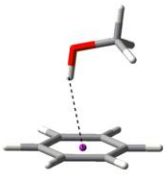
95 ethyne···ethyne (CH···π)

96 PHE···ethyne (CH···π)

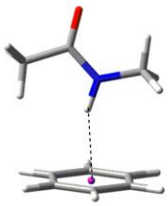
97 PHE···AcOH (OH···π)



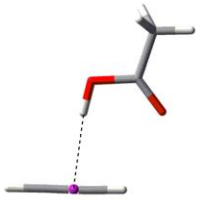
98 PHE···$AcNH_2$ (NH···π)



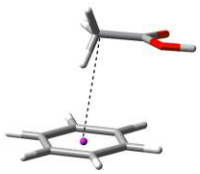
99 PHE···MeOH (OH···π)



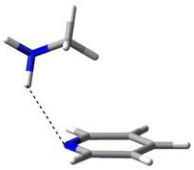
100 PHE···peptide (NH···π)



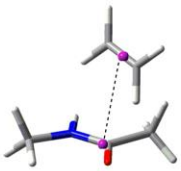
101 ethyne···AcOH (OH···π)



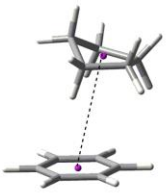
102 PHE···AcOH



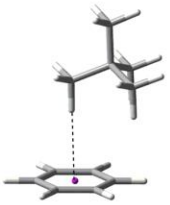
103 $MeNH_2$···pyridine



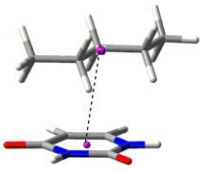
104 peptide···ethene



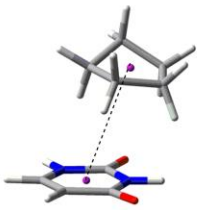
105 PHE···cyclopentane



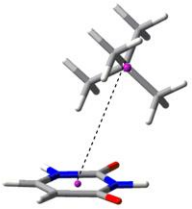
106 PHE···neopentane



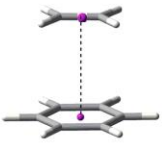
107 U···pentane



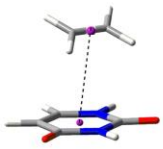
108 U···cyclopentane



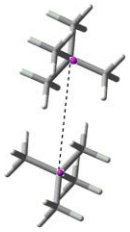
109 U···neopentane



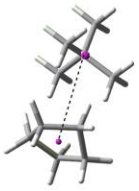
110 PHE···ethene



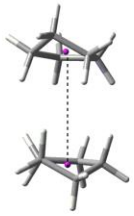
111 U···ethene



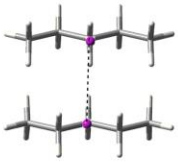
112 neopentane···neopentane



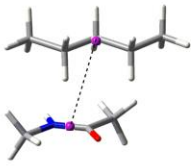
113 cyclopentane···neopentane



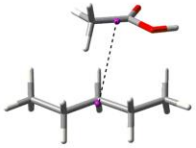
114 cyclopentane···cyclopentane



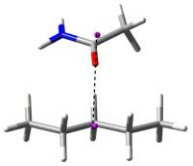
115 pentane···pentane



116 peptide···pentane



117 pentane···AcOH



118 pentane···$AcNH_2$

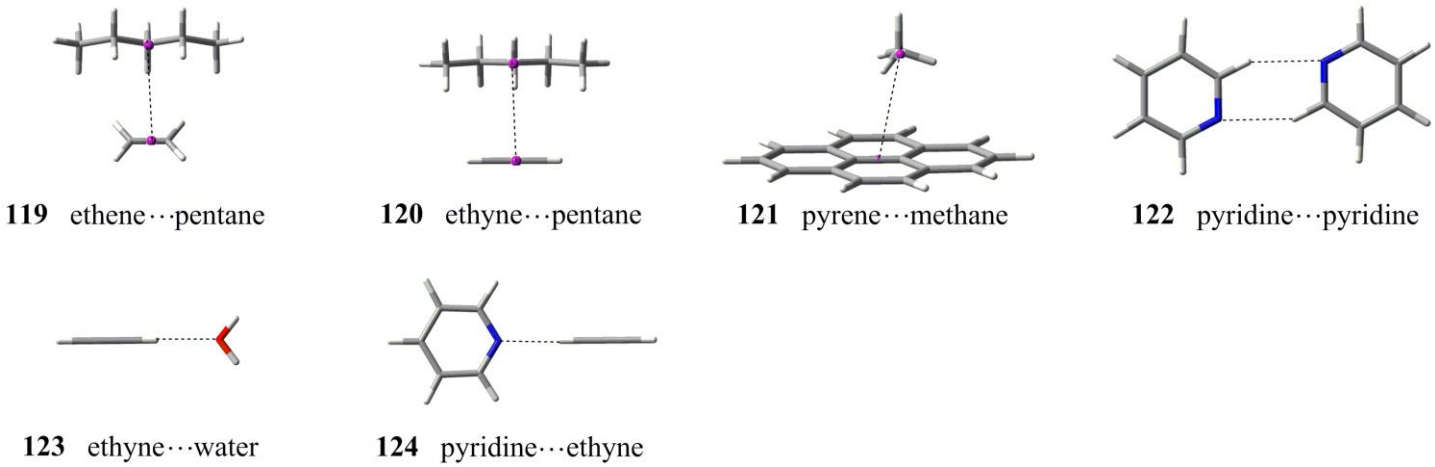
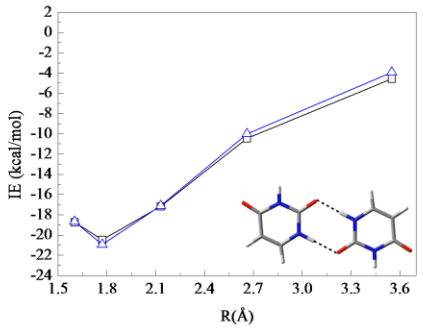
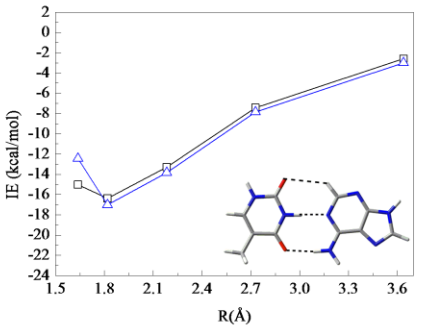


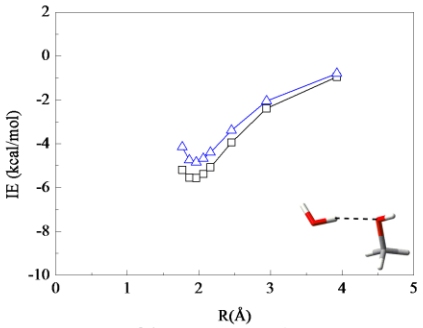
Figure S5. Structures of the 30 small X–H···π and other testing dimers.



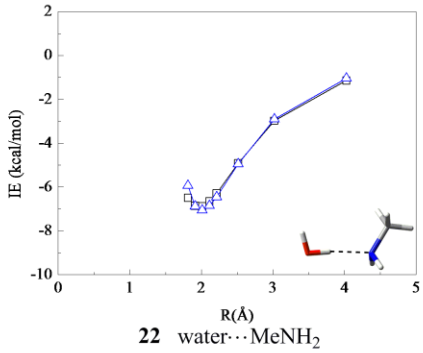
1 U···U (C_{2h})



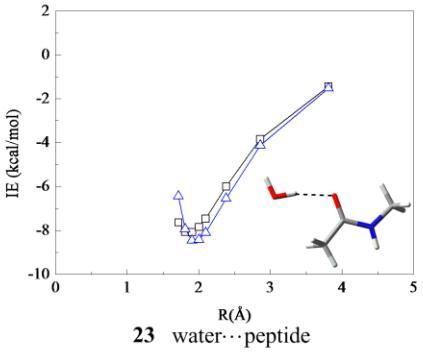
9 A···T WC



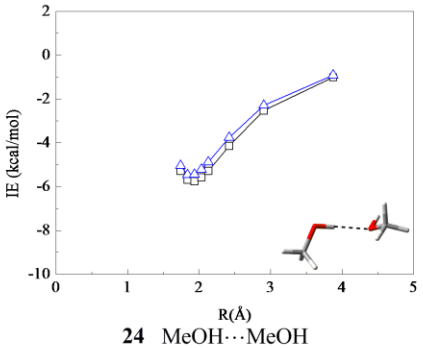
21 water···MeOH



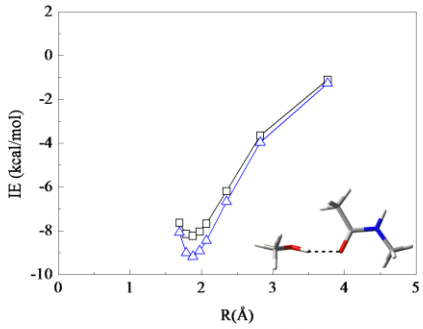
22 water···$MeNH_2$



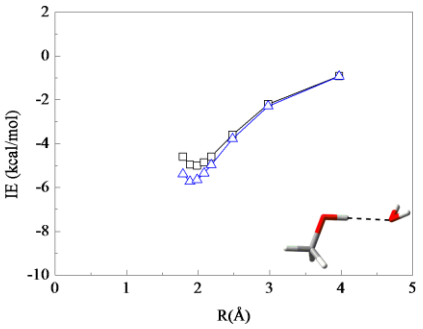
23 water···peptide



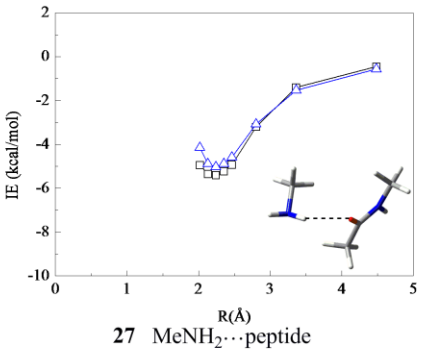
24 MeOH···MeOH



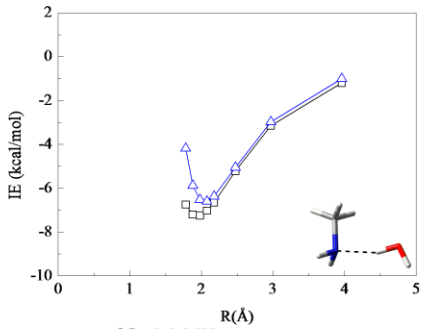
25 MeOH···peptide



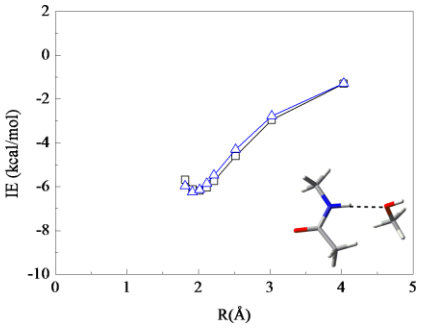
26 MeOH···water



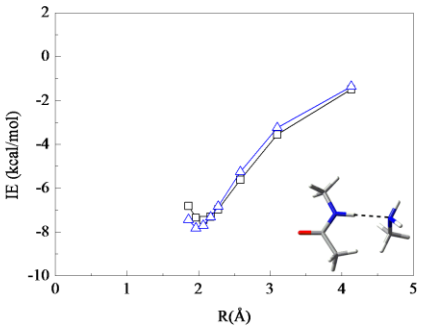
27 $MeNH_2$···peptide



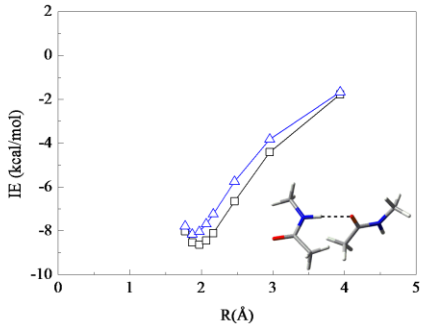
28 $MeNH_2$···water



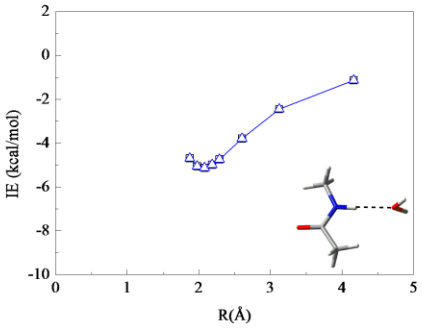
29 peptide···MeOH



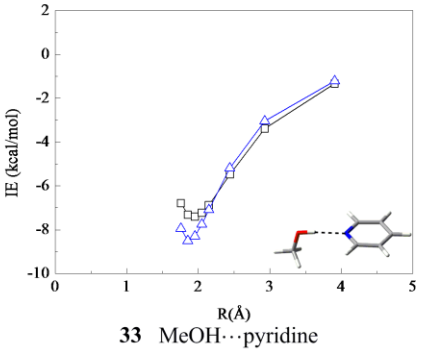
30 peptide···$MeNH_2$



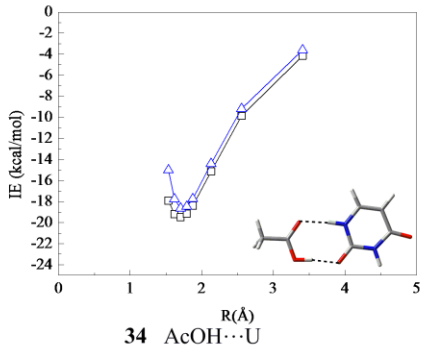
31 peptide···peptide



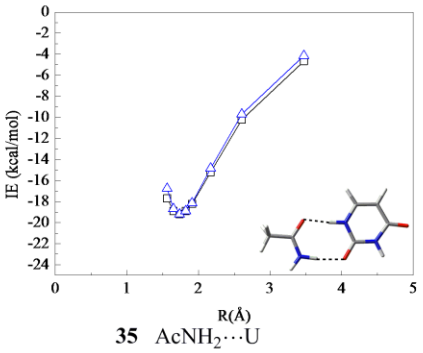
32 peptide···water



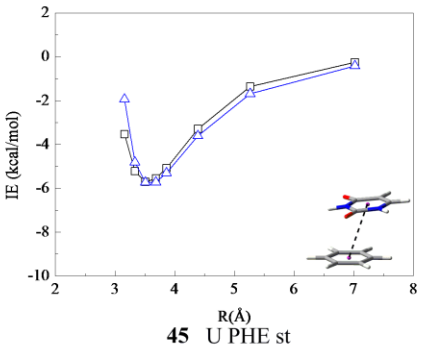
33 MeOH···pyridine



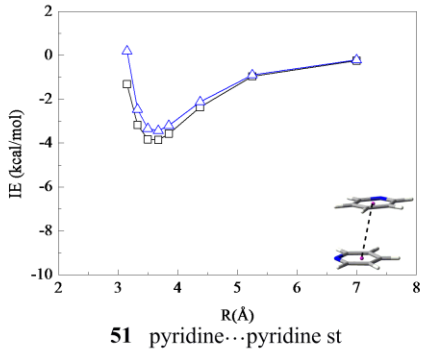
34 AcOH···U



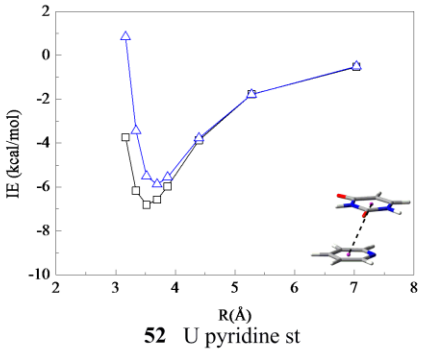
35 $AcNH_2$···U



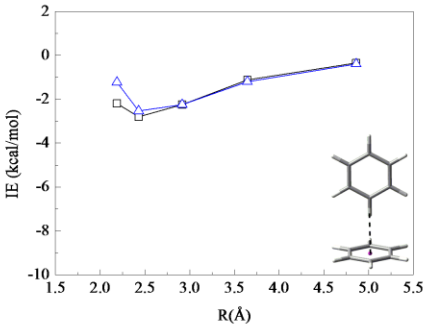
45 U PHE st



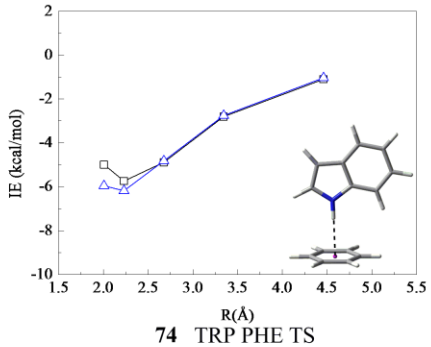
51 pyridine···pyridine st



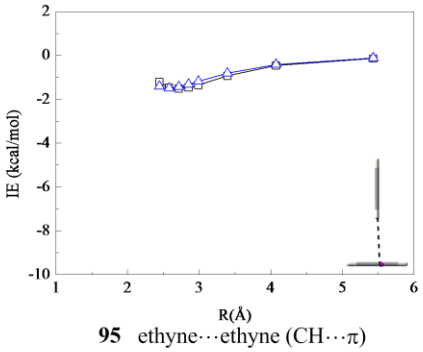
52 U pyridine st



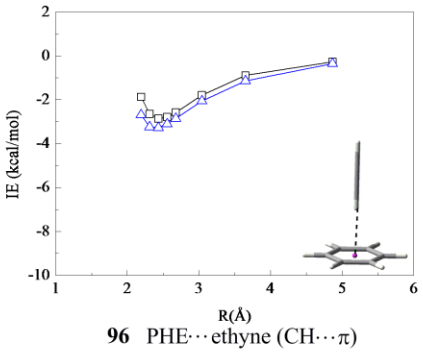
63 benzene dimer (C_{2V})



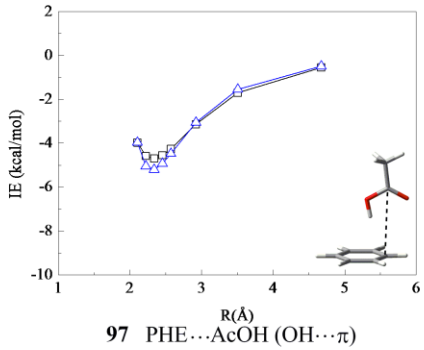
74 TRP PHE TS



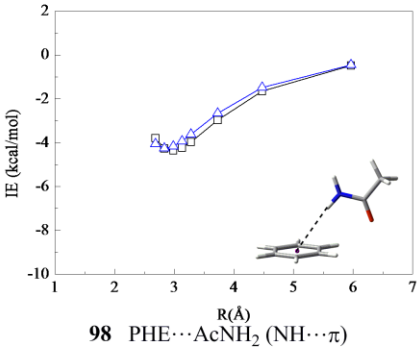
95 ethyne···ethyne (CH···π)



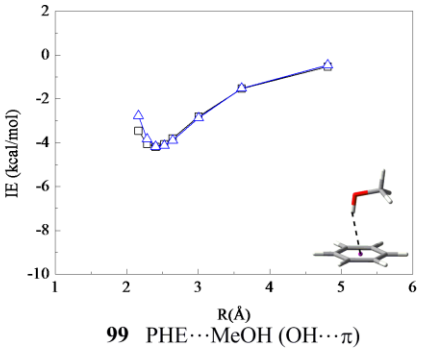
96 PHE···ethyne (CH···π)



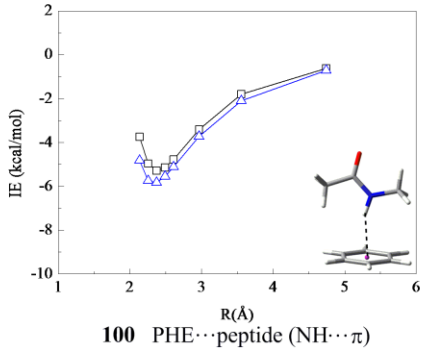
97 PHE···AcOH (OH···π)



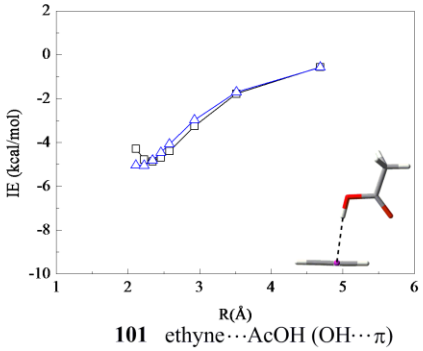
98 PHE···$AcNH_2$ (NH···π)



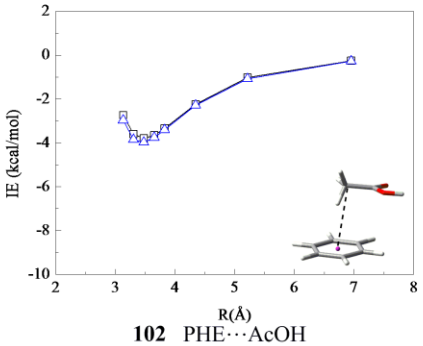
99 PHE···MeOH (OH···π)



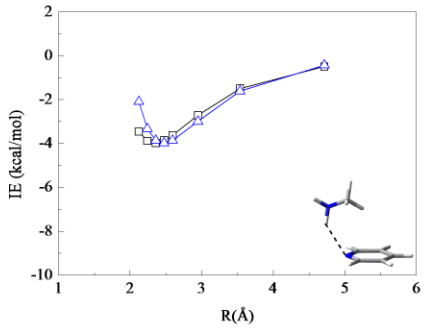
100 PHE···peptide (NH···π)



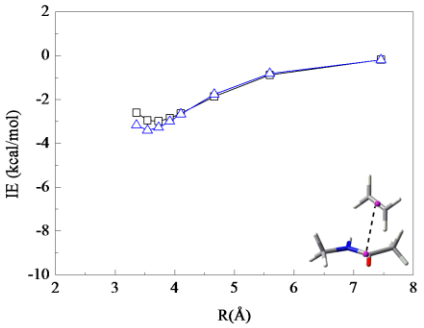
101 ethyne···AcOH (OH···π)



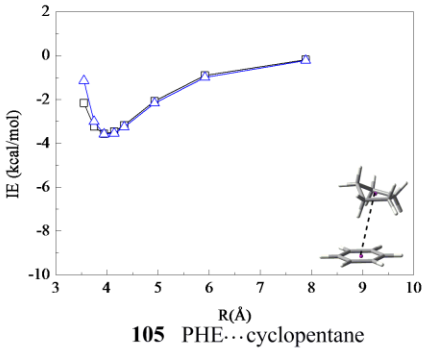
102 PHE···AcOH



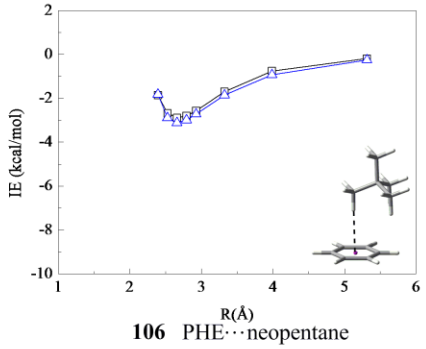
103 $MeNH_2$···pyridine



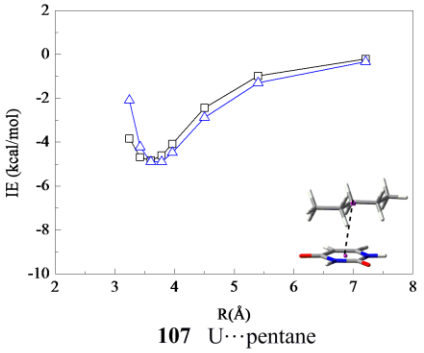
104 peptide···ethene



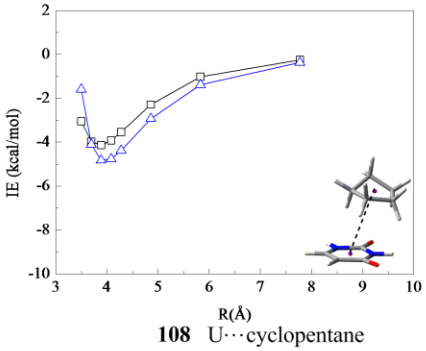
105 PHE···cyclopentane



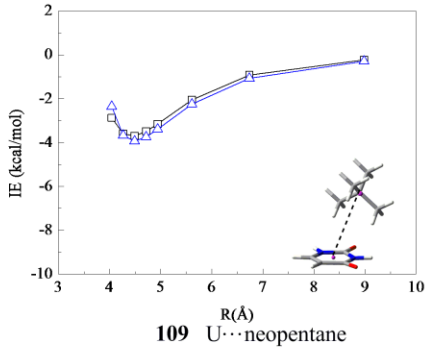
106 PHE···neopentane



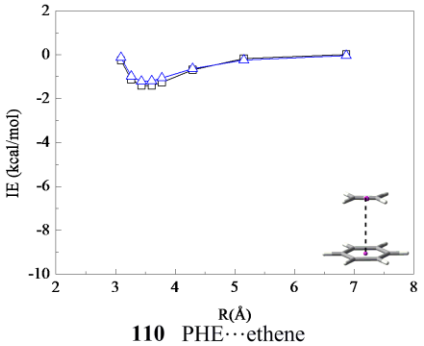
107 U···pentane



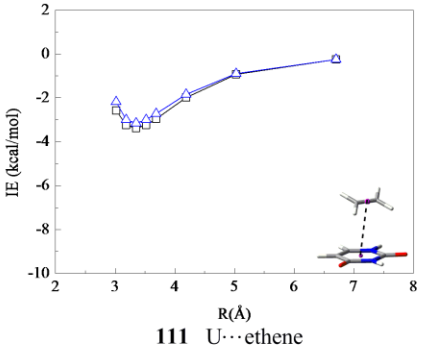
108 U···cyclopentane



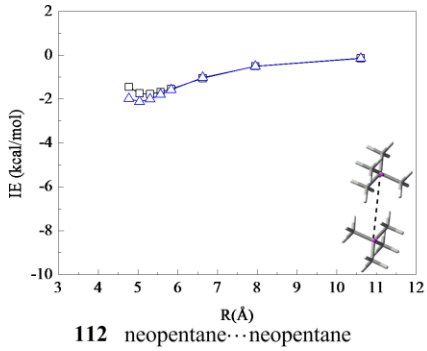
109 U···neopentane



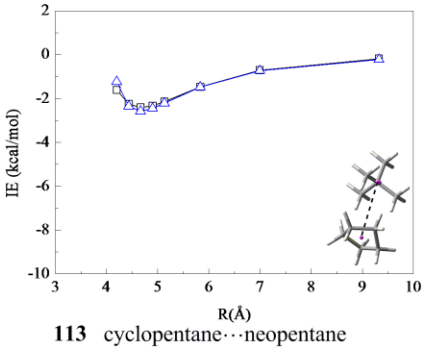
110 PHE···ethene



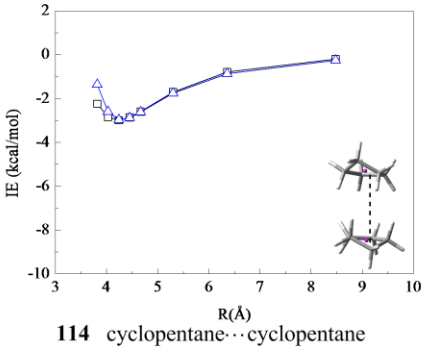
111 U···ethene



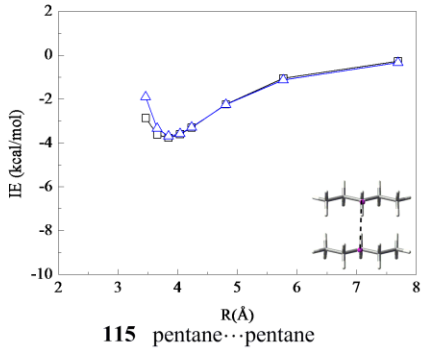
112 neopentane···neopentane



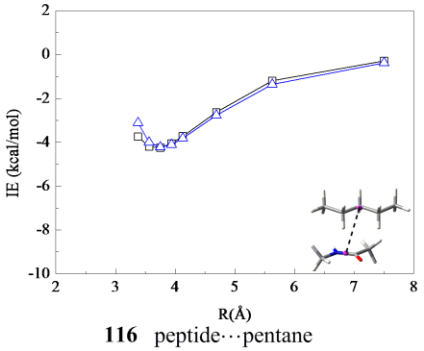
113 cyclopentane···neopentane



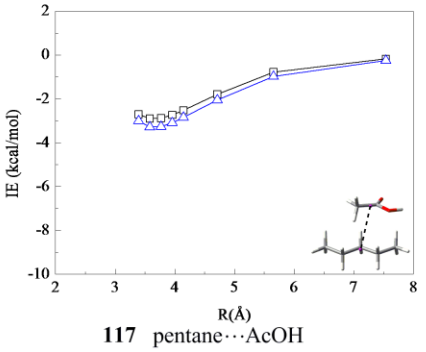
114 cyclopentane···cyclopentane



115 pentane···pentane



116 peptide···pentane



117 pentane···AcOH

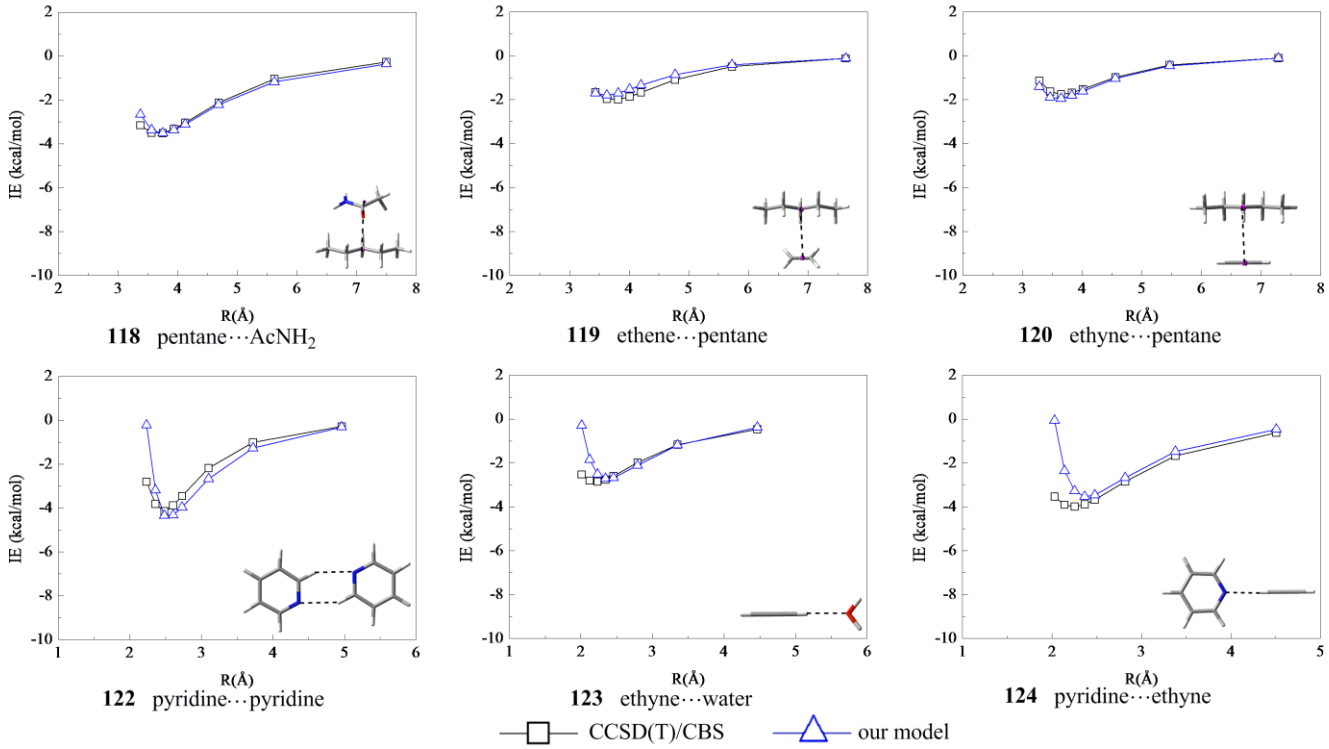


Figure S6. Comparison of the potential energy curves for 51 testing dimers, of which CCSD(T)/CBS level results are currently available from literatures 1 and 2.

References

1. Řezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7*, 2427-2438.

2. Jurečka, P.; Šponer, J.; Černý, J.; Hobza, P. Benchmark Database of Accurate (MP2 and CCSD(T) Complete Basis Set Limit) Interaction Energies of Small Model Complexes, DNA Base Pairs, and Amino Acid Pairs. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1985-1993.

Dipole–Dipole Interactions

Electrostatic interaction term (E_{es}): As described in our previous papers,[1-4] The electrostatic interaction E_{es} is estimated by summing up all the permanent bond dipole–dipole interaction between the two molecules (**I** and **J**). When calculating the electrostatic interaction energies for noncovalent complexes, we employed the following equation

$$E_{es} = \sum_{\substack{i \in \mathbf{I} \\ j \in \mathbf{J}}} \frac{\mu_i \mu_j}{r_{ij}^3} \left(2\cos\theta \cos\theta' + \sin\theta \sin\theta' \cos\zeta \right)$$

where μ_i and μ_j are the permanent bond dipole moments, r, θ, θ', and ζ are the structural parameters determining the relative orientation of the two dipoles.

Polarization contribution term (E_{pol}): The polarized bond dipole–dipole interaction E_{pol} is estimated by all the interaction between permanent bond dipole and induced bond dipole moments or between two induced bond dipole moments. The following equation was employed for calculating the polarization contributions

$$E_{pol} = \sum_{\substack{i \in \mathbf{I} \\ j \in \mathbf{J}}} \frac{\left(\mu_i \delta\mu_j + \mu_j \delta\mu_i + \delta\mu_i \delta\mu_j \right)}{r_{ij}^3} \left(2\cos\theta \cos\theta' + \sin\theta \sin\theta' \cos\zeta \right)$$

where $\delta\mu_i$ and $\delta\mu_j$ are the induced bond dipole moment.

It is worth to be mentioned; we take all the permanent bond dipoles and induced bond dipoles (no matter if they are directly or indirectly interacted) into account when evaluating these interactions.

References

(1) Li, S. -S.; Huang, C. -Y.; Hao, J. -J.; Wang, C. -S. A Polarizable Dipole-Dipole Interaction Model for Evaluation of the Interaction Energies for N–H···O=C and C–H···O=C Hydrogen-Bonded Complexes. *J. Comput. Chem.* **2014**, *35*, 415-426.

(2) Gao, X. -C.; Huang, C. -Y.; Wang, C. -S. Rapid Evaluation of the Interaction Energies for Hydrogen-Bonded Uracil and Thymine Dimers,Trimers and Tetramers. *Comput. Theor. Chem.* **2014**, *1048*, 46-53.

(3) Hao, J. -J.; Li, S. -S.; Jiang, X. -N.; Li, X. -L.; Wang, C. -S. Rapid Evaluation of the Interaction Energies for O–H···O Hydrogen-Bonded Complexes. *Theor. Chem. Acc.* **2014**, *133*, 1516-1527.

(4) Hao, J. -J.; Wang, C. -S. Rapid Evaluation of the Interaction Energies for Carbohydrate-Containing Hydrogen-Bonded Complexes via the Polarizable Dipole-Dipole Interaction Model Combined with NBO or AM1 Charge. *RSC Adv.* **2015**, *5*, 6452-6461.

Parametrization for the E_{orb} term

Firstly, $R_{eq,m}$, which denotes the equilibrium intermolecular distance, is determined by using the following energy function: $E_{es}+E_{vdw}+E_{pol}$. Then, p_m and q_m, which denote the maximum and minimum overlap integral, is initialized according to the corresponding theoretical results. Lastly, D_m, p_m, q_m, α_m and a_m are determined by matching the QM [CCSD(T)/CBS level of theory] interaction energies curves through the iteration method.

After these parameters were preliminarily determined, another macro iteration which re-examined and re-optimized all the parameters involved in eqs 1-6 was performed.