Supplementary data for article:

Stabilizing non-covalent interactions of ligand aromatic moieties and proline in ligand – protein systems
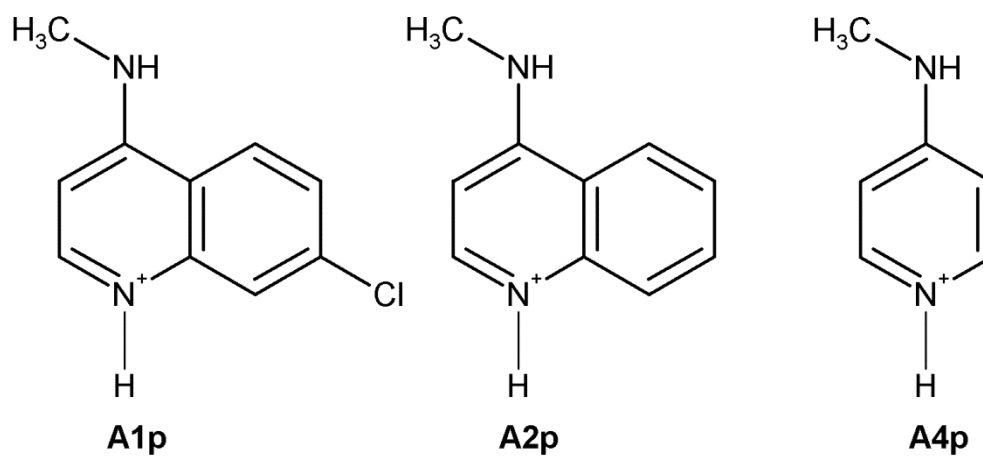
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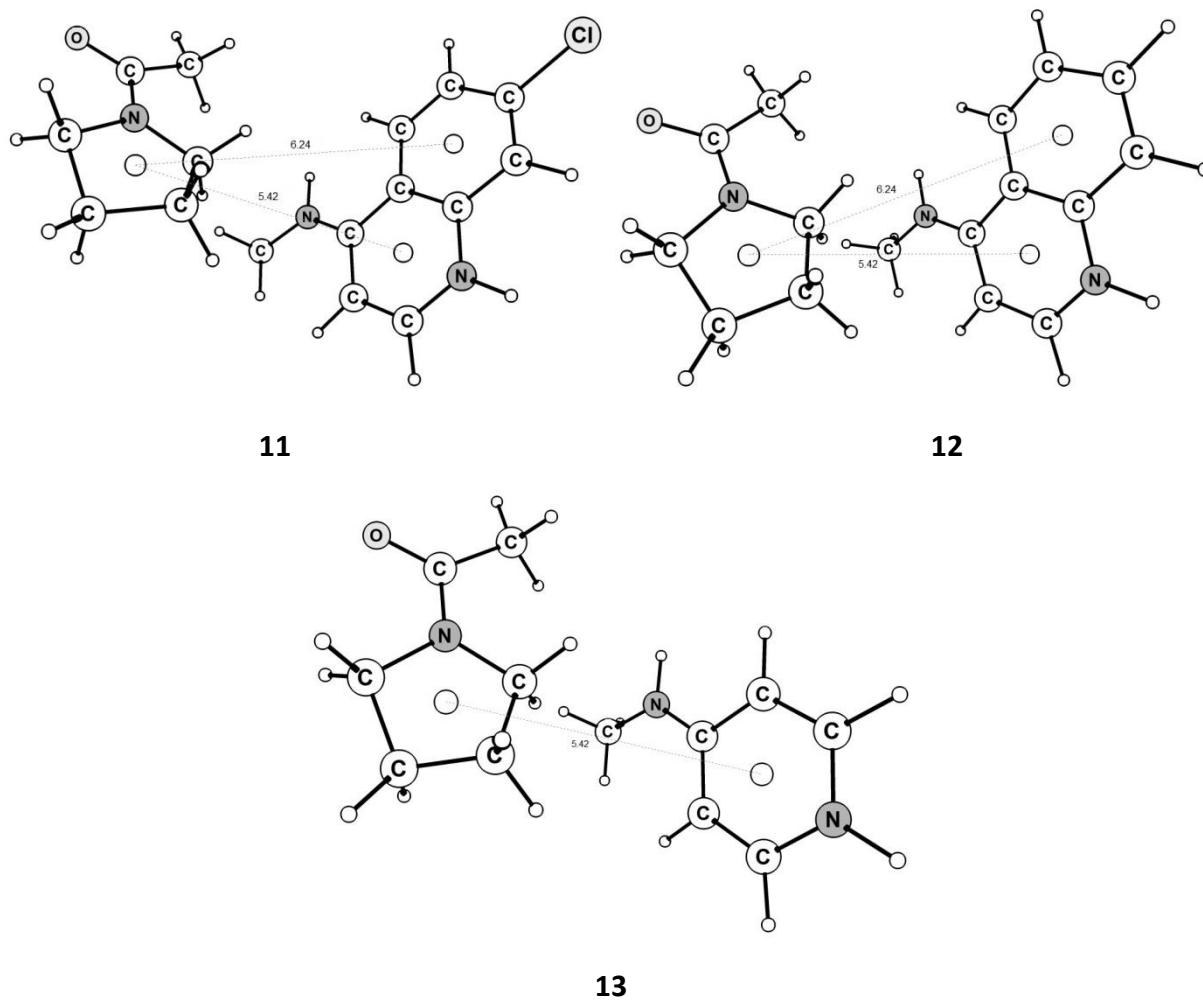
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Supplementary material

Figure S1. Protonated forms of **A1**, **A2** and **A4**

Figure S2. Structures of non-covalent complexes based on geometries from molecular docking experiments formed using protonated forms of **A1, A2** and **A4** (distances are in Å)

11

12

13
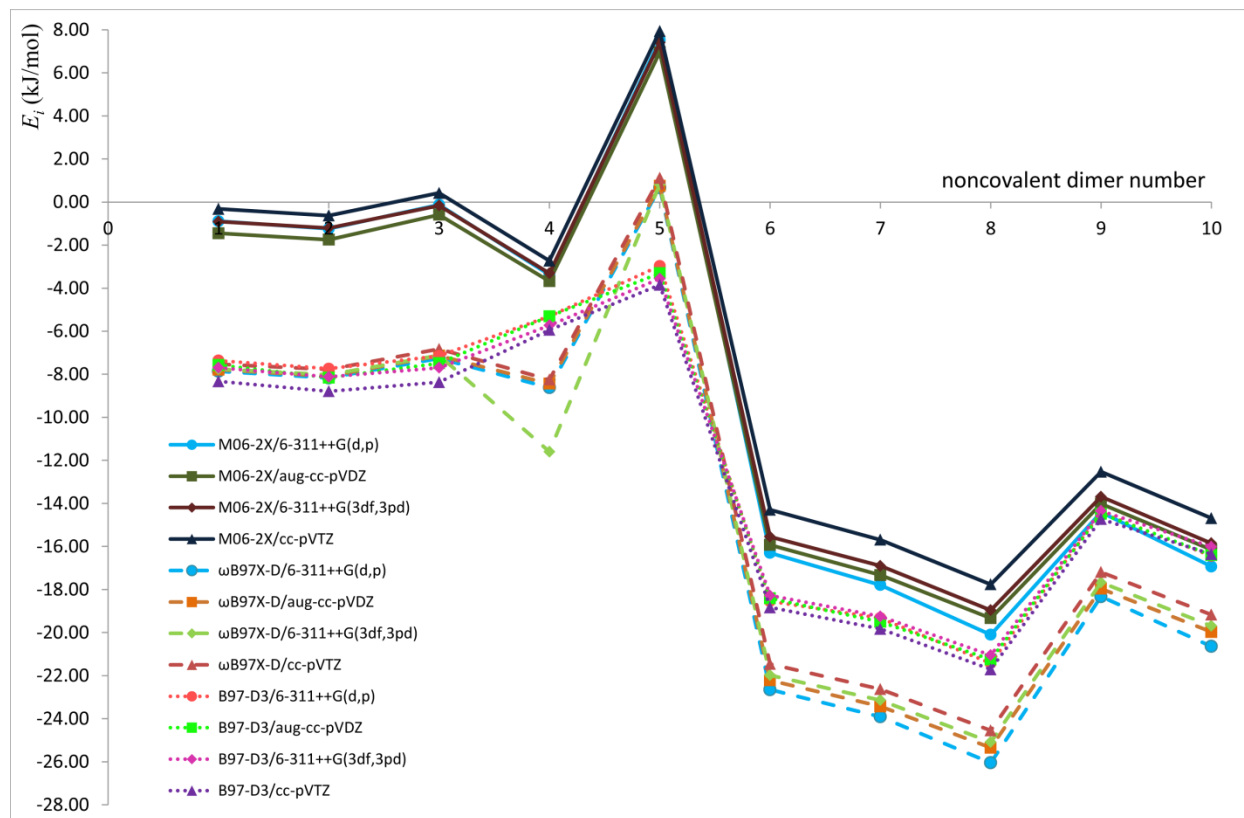
Figure S3. Structures of non-covalent complexes based on geometries from 2XPU formed using protonated forms of **A1, A2** and **A4** (distances are in Å)

14

15

16
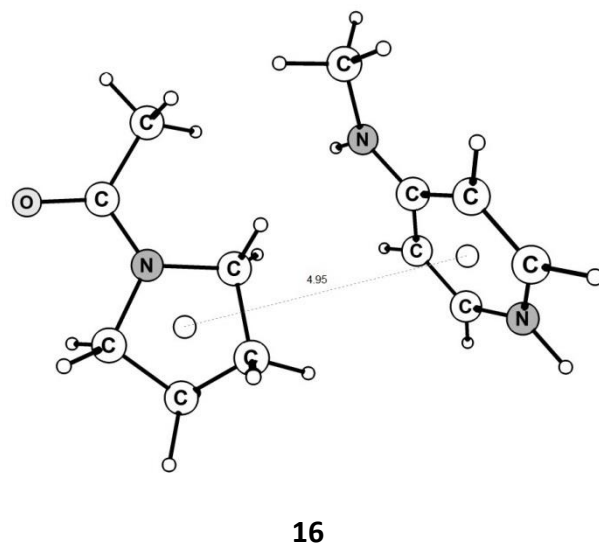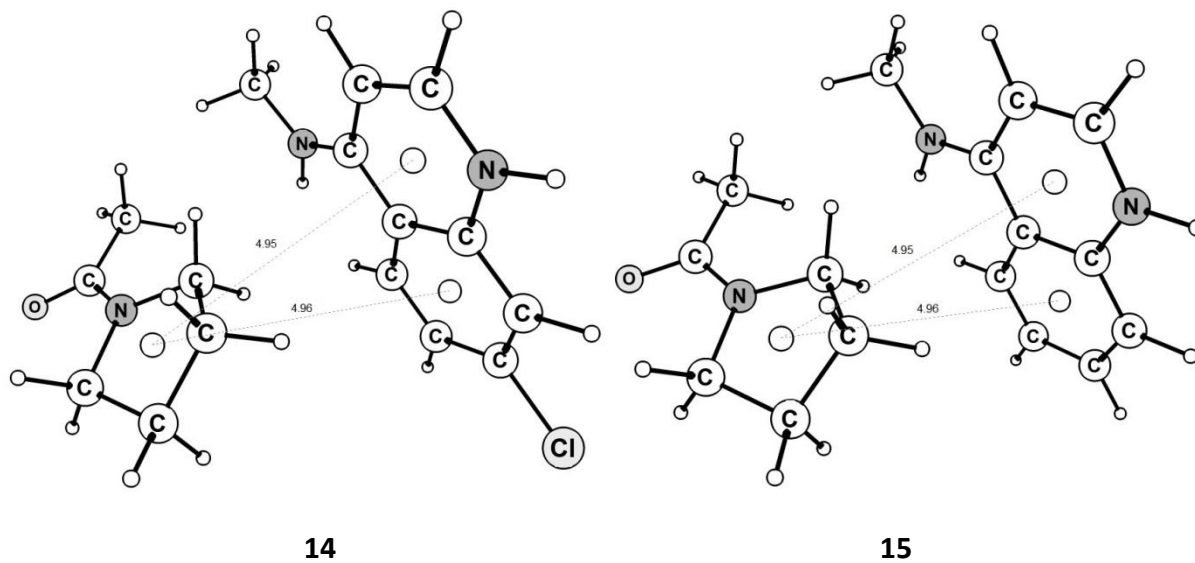
Figure S4. Interaction energies between proline and aromatic systems **1 - 10** calculated on different level of theory using different basis sets

Table S1. Interaction energies (in kJ/mol) for non-covalent dimers **11 - 16** calculated with different methods.

Method	Basis set	Non-covalent dimer					
		11	**12**	**13**	**14**	**15**	**16**
M06-2X	6-311++G(3df,3pd)	12.36	11.95	16.68	5.87	6.93	7.14
ωB97X-D	6-311++G(3df,3pd)	5.00	4.67	10.43	-2.01	-0.75	12.80
B97-D3	6-311++G(3df,3pd)	6.69	6.57	12.05	0.33	1.80	8.74
OPLS-2005	N/A	18.06	16.75	28.70	11.10	13.04	23.61
OPLS-2005, ε=4[*]	N/A	15.58	15.22	26.38	7.50	10.56	19.77
M06-2X, ε=4[*]	6-311++G(3df,3pd)	14.07	12.72	15.91	6.63	6.96	11.24
B97-D3, ε=4[*]	6-311++G(3df,3pd)	8.88	7.61	12.78	1.75	2.40	8.97

[*] Implicit solvent calculation with dielectric constant ε = 4

Table S2. Interaction energies of dimers **6 – 10** calculated using B97-D3/aug-cc-pVDZ with fixed position of heavy atoms and fixed positions of all atoms.

Non-covalent dimer	Interaction energies for different methods (kJ/mol)	
	heavy atoms fixed	all atoms fixed
6	-18.62	-18.41
7	-19.54	-19.50
8	-21.46	-21.24
9	-15.06	-14.84
10	-16.23	-16.40