Table I. Total breakdown of energetic components of the binding process for HIV-1 protease inhibitors. Energetic components in kcal/mol. Experimental inhibition constants, K_i, in nM. $\Delta G^{nonpolar}_{desolvation}$ and $\Delta G^{polar}_{desolvation}$ denote, respectively, nonpolar and polar contribution of ligand and protein combined. $\Delta G^{n-n}_{interaction}$ stands for the interactions between nonpolar groups of ligands and nonpolar groups of the protein. $\Delta G^{n-p,p-p,p-n}_{interaction}$ depicts the sum of interactions between nonpolar(ligand)-polar(protein), polar(ligand)-polar(protein) and polar(ligand)-nonpolar(protein) groups. The notations are discussed in more detail in the text.

Energy component	**acetylpepstatin**	**U75875**	**SKF107457**
$\Delta G^{n-n}_{interaction}$	-17.0	-22.8	-16.8
$\Delta G^{n-p,p-p,p-n}_{interaction}$	-71.0	-72.2	-63.0
$\Delta G^{ligand-water}_{interaction}$	-3.0	-6.3	-1.7
$\Delta G^{water-protein}_{interaction}$	-12.4	-11.9	-2.0
$\Delta G^{nonpolar}_{desolvation}$	-12.3	-14.5	-11.7
$\Delta G^{polar}_{desolvation}$	62.6	52.3	50.2
$\Delta G^{protein}_{conform.change}$	-16.5	-14.2	-11.3
$T\Delta S^{ligand}_{conform}$	3.6	6.0	2.4
$T\Delta S^{protein}_{conform}$	32.0	31.4	28.0
$\Delta G^{ligand-protein}_{rot,transl}$	11.0	11.0	11.0
$\Delta G^{water}_{rot,transl}$	14.4	21.6	2.4
ΔG_{total}	-9.4	-19.6	-12.5
K_i (nM)	20.0	1.0	4.0

Table II. Effect of hydrophobic Ile-Val mutation on binding free energy for HIV-1 protease inhibitors. Energy components in kcal/mol.

Energy component	**JG–365**	**MVT–101**	**U75875**
$\Delta G_{desolvation}$	0.15	0.22	0.11
$\Delta G_{interaction}$	1.17	1.54	0.82
$\Delta\Delta G_{cavity}$	0.41	0.31	0.48
$\Delta(T\Delta S)$	0.38	0.38	0.38
$\Delta\Delta G_{total}$	1.35	1.69	1.03
Number of contacts within 6 Å of deleted group	14	17	13