Table 1. Predicted relative binding affinities of p-xylene to T4L/L99A compared with benzene using various methods

Starting conformation	Method	ΔG in complex	$\Delta\Delta G$
	FEP	−3.31 ± 0.10	0.95 ± 0.15
Trans	λ-hopping	−3.36 ± 0.10	0.90 ± 0.15
	FEP/REST	−3.78 ± 0.10	0.48 ± 0.15
	FEP	−3.96 ± 0.10	0.30 ± 0.15
Gauche	λ-hopping	−3.83 ± 0.10	0.43 ± 0.15
	FEP/REST	−3.77 ± 0.10	0.49 ± 0.15
Exp			0.52 ± 0.09

Free energies in kcal/mol; ΔG in solvent is -4.26 ± 0.05 kcal/mol.